ORIGINAL RESEARCH

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# Plasma Fibrinogen to Albumin Ratio as an Indicator of Endothelial Dysfunction in Smoking

## Sigara Kullanımında Endotel Fonksiyon Bozukluğu Göstergesi Olarak Plazma Fibrinojen Albumin Oranı

Şeyda Arslan[1], Hilmi Furkan Arslan[2], Zuhal Aydan Sağlam[3]

[1]Bulancak State Hospital, Department of Family Medicine, Giresun, Turkey
[2]Giresun University Maternity and Children Training and Research Hospital, Department of Medical Biochemistry, Giresun, Turkey
[3]University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of Family Medicine, İstanbul, Turkey

## Abstract

**Objective:** Smoking causes endothelial dysfunction by causing systemic inflammation. Our aim is to investigate the predictive role of fibrinogen albumin ratio (FAR), neutrophil lymphocyte ratio, platelet lymphocyte ratio (PLR), monocyte lymphocyte ratio (MLR), monocyte high-density lipoprotein ratio (MHR), mean platelet volume (MPV), systemic immune inflammatory index (SII) and systemic inflammatory response index (SIRI) which are the newest markers of systemic inflammation, in smoking.

**Method:** The study was planned as a single-center, prospective case-control study. People aged between 20-45 years [n=76; female/male (n)=37/39] who met the inclusion criteria were included. Two groups consisting of smokers (n=38) and non-smokers (n=38) were compared according to demographic data and biochemical values. p-value was accepted as <0.05 in terms of statistical significance.

**Results:** The proportion of men in the study group was 51.3% [total n=76; mean age 30.18±5.75 years; female/male (n):37/39]. There was no significant difference between the two groups of smokers (n=38) and non-smokers (n=38) in terms of gender and age (p=0.386, p=0.296, respectively). The average amount of smoking was 22.84±11.48 packs/year and 29.73±9.94 packs/day. FAR, MPV, MHR, MLR and SIRI were significantly higher and PLR was significantly lower in the smokers than the other group (p<0.05). According to the ROC analysis, the areas under the curve of FAR, MHR, MLR, SIRI, MPV and PLR were determined as 0.70, 0.90, 0.83, 0.80, 0.69 and 0.66, respectively (p<0.001). The variants with the highest sensitivity were monocytes and MPV, and the variant with the highest specificity was monocytes. FAR was positively correlated with MHR, MLR, SIRI (p=0.00, r=0.34; p=0.05, r=0.2; p=0.03, r=0.24, respectively).

## Öz

**Amaç:** Endotel disfonksiyonu, nitrik oksit (NO) sentezinde azalmayla beraber endotelin gevşeme ve kasılma fonksiyonlarının bozulmasıdır. Sigaranın sistemik enflamasyona yol açarak endotel disfonksiyonu yaptığı bilinmektedir. Yeni enflamasyon belirteçleri olan fibrinojen albumin oranını (FAR) sigara kullanımında oluşan sistemik enflamasyonun göstergesi olarak araştırdık. Beraberinde nötrofil lenfosit oranını (NLR), trombosit lenfosit oranını (PLR), monosit lenfosit oranını (MLR), monosit yüksek dansiteli lipoprotein oranını (MHR), ortalama trombosit hacmini (MPV), sistemik immün enflamatuvar indeksini (SII) ve sistemik enflamatuvar yanıt indeksini (SIRI) araştırdık.

**Yöntem:** Bu çalışma tek merkezli, prospektif vaka-kontrol çalışması olarak planlanmış olup, çalışmaya başvuranlardan dahil edilme kriterlerine uygun olup, 20-45 yaş aralığında bilinen hiçbir hastalığı ve ilaç 3 kullanımı olmayan 76 kişi dahil edildi. Sigara kullanan (n=38) ve kullanmayan (n=38) bireylerden oluşturulan iki grup; yaş, boy, kilo, paket/yıl ve adet/gün olarak içilen sigara miktarı ve laboratuvar değerleri açısından karşılaştırıldı. p-değerinin 0,05'in altında olduğu durumlar istatistiksel olarak anlamlı sonuçlar şeklinde değerlendirildi.

**Bulgular:** Çalışma grubunun %51,3'ü erkekti [total n=76; yaş ort: 30,18±5,75 yıl; kadın/erkek (n): 37/39]. Sigara kullanan (n=38) ve kullanmayan (n=38) iki grup arasında cinsiyet ve yaş açısından anlamlı fark yoktu (sırasıyla p=0,386, p=0,296). Sigara kullanma miktarları ortalama 22,84±11,48 paket/yıl ve 29,73±9,94 adet/gün idi. İki grup karşılaştırıldığında, sigara içen grupta FAR, MPV, MHR, MLR ve SIRI anlamlı olarak yüksek, PLR ise anlamlı olarak düşük saptandı (p<0,05). ROC analizine göre FAR, MHR, MLR, SIRI, MPV ve PLR eğrisi altında kalan alanlar sırasıyla 0,70, 0,90, 0,83, 0,80, 0,69 ve 0,66 olarak belirlendi (p<0,001). ROC analizi sonucunda, duyarlılığı en yüksek olan değişkenler monosit ve MPV iken, özgüllüğü en yüksek olan değişken monosit olarak

**Address for Correspondence:** Şeyda Arslan, Bulancak State Hospital, Department of Family Medicine, Giresun, Turkey
**E-mail:** seydatokalaktp@gmail.com **ORCID:** orcid.org/0000-0003-0731-0231 **Received:** 22.08.2023 **Accepted:** 08.12.2023

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## Abstract

**Conclusion:** Our study suggests that new inflammatory markers can be used to predict the inflammatory process in endothelial dysfunction caused by smoking. It may be beneficial to conduct new studies with larger number of participants to see whether these markers can also be predictors of other silent inflammatory processes in non-smokers.

**Keywords:** Endothelial dysfunction, fibrinogen albumin ratio, inflammation, monocyte, smoking

## Öz

bulundu. FAR ile PLR negatif yönde korele iken MHR, MLR ve SIRI pozitif yönde korele bulundu (p=0.00, r=0.34; p=0.05, r=0.2; p=0.03, r=0.24, sırasıyla).

**Sonuç:** Çalışmamız sigaranın neden olduğu endotel disfonksiyonunda inflamatuar süreci öngörmek için yeni inflamatuvar belirteçlerin kullanılabileceğini düşündürmektedir. Bu belirteçlerin sigara içmeyenlerdeki diğer sessiz inflamatuvar süreçlerin habercisi olup olamayacağını görmek için daha fazla katılımcıyla yeni çalışmalar yapılması faydalı olabilir.

**Anahtar kelimeler:** Endotel disfonksiyonu, enflamasyon, fibrinojen albumin oranı, monosit, sigara

## Introduction

Endothelial dysfunction is defined as decreased nitric oxide synthesis and impairment of relaxation-contraction functions (1). Cardiovascular risk factors such as smoking, diabetes, atherogenic dyslipidemia, abdominal obesity, hypertension and age initiate the inflammatory process by disrupting the endothelial structure (2,3). Atherosclerosis is a chronic and progressive disease characterized by endothelial dysfunction and inflammation. Deterioration of vascular tone, increased cytokine production, accumulation of inflammatory cells in the endothelium, and migration of smooth muscle cells to the damaged area cause atherosclerotic plaque formation (4).

Smoking causes disorders in the hemostatic system and lipid profile and endothelial dysfunction (5). It also predisposes the body to thrombosis and disrupts the procoagulant fibrinolytic activity of the endothelium (6). While smoking suppresses anti-inflammatory cytokines, it causes systemic inflammation in the body by using pro-inflammatory cytokines and acute phase proteins such as C-reactive protein (CRP) and fibrinogen (7).

The increase in plasma viscosity is associated with cardiovascular diseases because it leads to a procoagulant state. The main substances that increase viscosity are fibrinogen and lipoproteins. Fibrinogen may play a triggering role in cardiovascular diseases by increasing viscosity or by affecting the platelets and fibrin formation mechanism. Increased fibrinogen in chronic smokers contributes to the inflammatory and atherosclerotic basis (8). In a prospective study, it was shown that increased fibrinogen and CRP have an effect on the pathogenesis of cardiovascular diseases (9,10).

Normal albumin levels have antiatherogenic and anti-inflammatory effects in the body. Therefore, the decrease in albumin causes an increase in pro-inflammatory markers along with an increase in systemic inflammation in the body and is linked to oxidative stress (11). In a study, it was shown that serum albumin value varies in smokers and has an important role in the development of coronary artery disease in those people (12). In subsequent studies, serum albumin was shown to be a strong risk factor for MI when other risk factors were adjusted (13).

Studies have reported that high fibrinogen/albumin ratio (FAR) is an important marker for inflammation and atherosclerosis (9). Neutrophil/lymphocyte ratio (NLR) levels have been found to be quite high in diseases that cause endothelial damage, such as diabetes, myocardial infarction, atherosclerosis and hypertension, and are considered a poor prognostic factor (14). The diagnostic role of monocyte/lymphocyte ratio (MLR) in showing the level of inflammation in cardiovascular and autoimmune diseases has been proven (15). Monocyte/high-density lipoprotein (HDL) ratio (MHR) is emerging as a new prognostic indicator in predicting oxidative stress and systemic inflammation levels in the atherosclerosis process (16). Platelet/lymphocyte ratio (PLR), which is an important indicator of inflammation and thrombosis, is used in many diseases (17). Mean platelet volume (MPV) indicates platelet activation in vascular diseases (18). The role of inflammation in all stages of cancer has been proven, and the increase in systemic inflammatory response index (SIRI) levels, an important inflammatory marker, has been shown to be valuable in predicting survival in cancer patients (19). Systemic immune inflammatory index (SII), a new marker, shows the immune response and inflammation in the body more strongly than other markers (20).

In this study, we aimed to investigate FAR, a new inflammatory marker, as an indicator of endothelial dysfunction due to smoking. In addition, it is planned

to study MLR, NLR, PLR, MPV, MHR, SII and SIRI as inflammatory markers in smokers.

## Materials and Methods

### Study group

This study was planned as a single-center, prospective case-control study. Seventy-six participants aged 20-45 years, who applied to the outpatient clinics between November 2021 and April 2022, were included according to inclusion criteria. Individuals who had chronic lung, liver and kidney diseases, connective tissue diseases, acute or chronic infection, malignancy, metabolic syndrome, obesity, pregnancy status, menopause, chronic diseases such as hypertension and diabetes mellitus, severe trauma or surgery in the last 6 months, cardiac disease, any chronic medication, Coronavirus disease-2019 in the last 6 months and active alcohol users were excluded. Demographic data and biochemical values of the groups were compared among two groups as smokers (n=38) and non-smokers (n=38).

### Ethics Committee Approval

This study was approved (dated: 06/03/2020 and numbered: 2213) by Clinical Research Ethics Committee of University of Health Sciences Turkey, İstanbul Training and Research Hospital. The expenses of the study were covered by University of Health Sciences Turkey, İstanbul Training and Research Hospital. All participants were informed about the study and their consent was obtained.

### Sample Size

Cohen's d effect size was 0.80; α value 0.05; the power (1-β) value was taken as 0.80, and the minimum number of samples required for statistical comparison of two independent groups was calculated as n=30 participants for each group through the G*Power version 3.1.9.4 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany).

### Statistical Analysis

Statistical analyzes were performed with the help of SPSS version 28.0 program. To assess the normality of the data, Kolmogorov-Smirnov test was used. Mean, standard deviation and median values were used when presenting descriptive analyzes. Two-sample independent test was used for parametric variables and Mann-Whitney U test was used for non-parametric variables. Receiver operating characteristic (ROC) analysis was applied to evaluate the performance of the tests with diagnostic accuracy, sensitivity, specificity and area under the curve (AUC) values. Pearson Correlation test was used to evaluate the relationships between quantitative variables by accepting the variables that had a significant relationship with the FAR as independent variables. p-value was accepted as <0.05 in terms of statistical significance.

## Results

Participants consisted of 37 women and 39 men. Two groups were formed as smokers (n=38) and non-smokers (n=38). The mean age was 29.78±5.75 years. The average height was 170.22±8.51 cm, the average weight was 69.44±12.62 kg and body mass index (BMI) were 23.86 kg/m$^2$. No statistically significant difference was found between the demographic data of the two groups (p>0.05) (Table 1). The smoking rates of the individuals were 22.84±11.48 pack/year and 29.73±9.94 pcs/day. No statistically significant difference was observed when smoking amounts of smokers were compared according to gender (p>0.05) (Table 2).

The levels of white blood cell (WBC), neutrophil, monocytes, lymphocyte, MPV, fibrinogen, MHR, MLR, SIRI and FAR were significantly higher in smokers compared to non-smokers (p<0.05). Albumin and PLR levels were found to be significantly lower in the smokers (p<0.05). HDL values were found to be significantly higher in non-smokers, while triglyceride (TG) and low-density lipoprotein (LDL) values were significantly higher in smokers (p<0.05) (Table 3).

**Table 1. Comparison of demographic data of the participants**

| Mean ± SD | All participants | Non-smokers (n=38) | Smokers (n=38) | p-value |
|---|---|---|---|---|
| Age (years) | 29.78±5.75 | 29.42±4.63 | 30.90±5.73 | 0.296 |
| Gender, n (%) | | | | |
| Female | 37 (48.7%) | 19 (50.00%) | 18 (42.50%) | 0.386 |
| Male | 39 (51.3%) | 19 (50.00%) | 20 (57.50%) | |
| Height (cm) | 169.61±8.51 | 168.34±7.95 | 170.89±8.94 | 0.174 |
| Weight (kg) | 68.92±12.62 | 67.34±10.20 | 70.50±14.52 | 0.261[a] |
| Body mass index (kg/m$^2$) | 23.86±2.54 | 23.87±2.16 | 23.85±2.91 | 0.175[a] |

[a]Student's t-test, Mann-Whitney U test, SD: Standard deviation

**Table 2. Comparison of participants' cigarette use by gender**

| Mean + SD | Female (n=18) | Male (n=20) | p-value |
|---|---|---|---|
| Pack/year | 20.38±12.28 | 25.05±10.86 | 0.264 |
| Pcs/day | 27.94±9.02 | 31.40±10.46 | 0.573 |

Mann-Whitney U test, SD: Standard deviation

According to the ROC analysis, the AUC of FAR, MHR, MLR, SIRI, MPV and PLR were determined as 0.70, 0.90, 0.83, 0.80, 0.69 and 0.66, respectively (p<0.001) (Table 4). Monocyte had the highest sensitivity (90.48%) and specificity (92.30%) among all of the inflammatory markers when cut-off point was calculated as 0.50 $10^9$/L. The AUC for monocytes was 93.7% (95% confidence interval: 0.60-0.83) (p<0.001) (Table 4, Figure 1).

A significant positive correlation was found between FAR and the new inflammatory markers MHR, MLR and SIRI (p=0.00, r=0.34; p=0.05, r=0.22; p=0.03, r=0.24) (Table 5).

**Table 3. Comparison of laboratory data of the groups**

| Mean ± SD | Non-smokers (n=38) | Smokers (n=38) | p-value |
|---|---|---|---|
| White blood cell ($10^9$/L) | 6.73±1.51 | 8.47±2.22 | **<0.001[a]** |
| Hemoglobin (g/dL) | 13.85±1.34 | 14.05±2.18 | 0.150 |
| Platelet ($10^9$/L) | 256.67±57.69 | 258.92±50.17 | 0.912[a] |
| Neutrophil ($10^9$/L) | 3.98±1.08 | 5.07±1.86 | **<0.001** |
| Monocyte ($10^9$/L) | 0.38±0.12 | 0.66±0.18 | **<0.001[a]** |
| Lymphocyte ($10^9$/L) | 2.19±0.60 | 2.47±0.76 | **0.027** |
| MPV (fL) | 9.86±1.02 | 10.48±0.78 | **0.005[a]** |
| Fibrinogen (mg/dL) | 262.02±47.05 | 601.62±57.18 | **0.002[a]** |
| Albumin (g/L) | 48.52±2.15 | 46.85±4.30 | **0.004[a]** |
| NLR | 1.97±0.59 | 2.18±1.06 | 0.150 |
| PLR | 124.48±30.00 | 111.24±33.89 | **0.013** |
| MHR | 0.01±0.00 | 0.01±0.01 | **<0.001[a]** |
| MLR | 0.18±0.06 | 0.28±0.10 | **<0.001** |
| SII | 499.81±163.43 | 565.49±284.65 | 0.231 |
| SIRI | 0.77±0.33 | 1.52±0.95 | **<0.001** |
| FAR | 5.41±1.01 | 6.47±1.27 | **<0.001[a]** |
| Cholesterol (mg/dL) | 174.87±32.28 | 186.1±43.37 | 0.112[a] |
| LDL (mg/dL) | 96.90±32.10 | 111.92±40.07 | **0.042[a]** |
| TG (mg/dL) | 92.66±46.61 | 124.44±70.33 | **0.007[a]** |
| HDL (mg/dL) | 59.20±18.46 | 49.89±11.52 | **0.004** |

[a]Student's t-test, Mann-Whitney U test, MPV: Mean platelet volume, NLR: Neutrophil/lymphocyte ratio, MHR: Monocyte/high-density lipoprotein ratio, MLR: Monocyte/lymphocyte ratio, SII: Systemic immune inflammatory index, SIRI: Systemic inflammatory response index, FAR: Fibrinogen/albumin ratio, LDL: Low-density lipoprotein, TG: Triglyceride, HDL: Monocyte/high-density lipoprotein

**Table 4. Receiver-operator curve analysis of novel inflammatory markers**

| | Area under the curve | Cut-off | Sensitivity | Specificity |
|---|---|---|---|---|
| Monocyte ($10^9$/L) | 0.93 | >0.50 | 90.48% | 92.30% |
| MPV (fL) | 0.69 | >9.55 | 90.48% | 41.10% |
| PLR | 0.66 | ≤100.56 | 54.76% | 82.50% |
| MHR | 0.90 | >0.09 | 85.71% | 84.60% |
| MLR | 0.83 | >0.20 | 80.95% | 79.50% |
| SIRI | 0.80 | >0.86 | 80.95% | 84.60% |
| FAR | 0.70 | >5.35 | 83.33% | 53.80% |

FAR: Fibrinogen/albumin ratio, MPV: Mean platelet volume, SIRI: Systemic inflammatory response index, MLR: Monocyte/lymphocyte ratio, MHR: Monocyte/high-density ratio, PLR: Platelet/lymphocyte ratio

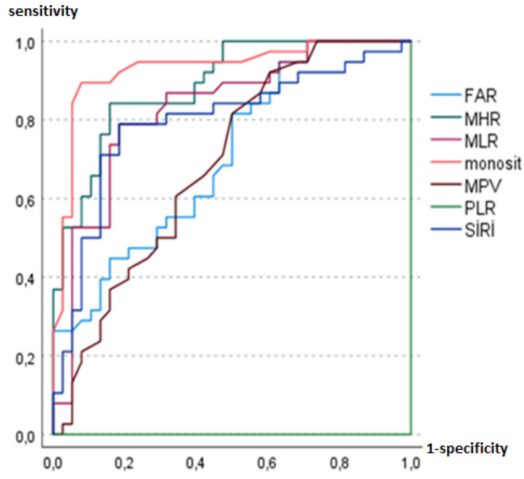


**Figure 1.** Receiver operator curve analysis graphic

*FAR: Fibrinogen/albumin ratio, SIRI: Systemic inflammatory response index, PLR: Platelet/lymphocyte ratio, MHR: Monocyte/high-density ratio, MLR: Monocyte/lymphocyte ratio, MPV: Mean platelet volume*

**Table 5. Correlation assessment between of fibrinogen to albumin ratio and other measurements**

| (n=76) | Correlation coefficient (r) | p-value |
|---|---|---|
| Age (year) | 0.22 | **0.05** |
| Height (cm) | -0.17 | 0.13 |
| Weight (kg) | -0.05 | 0.69 |
| Pack/year | 0.37 | **0.02** |
| Pcs/day | 0.08 | 0.62 |
| White blood cell ($10^9$/L) | 0.35 | **0.00** |
| Hemoglobin (g/dL) | -0.09 | 0.40 |
| Platelet ($10^9$/L) | 0.21 | 0.06 |
| Neutrophil ($10^9$/L) | 0.27 | 0.01 |
| Monocyte ($10^9$/L) | 0.40 | **0.00** |
| Lymphocyte ($10^9$/L) | 0.27 | **0.01** |
| MPV (fL) | -0.02 | 0.90 |
| NLR | 0.04 | 0.75 |
| PLR | -0.13 | 0.26 |
| MHR | 0.34 | **0.00** |
| MLR | 0.22 | **0.05** |
| SII | 0.13 | 0.23 |
| SIRI | 0.24 | **0.03** |
| Cholesterol (mg/dL) | 0.39 | **0.00** |
| LDL (mg/dL) | 0.45 | **0.00** |
| TG (mg/dL) | 0.11 | 0.34 |
| HDL (mg/dL) | -0.09 | 0.44 |

Pearson Correlation. MPV: Mean platelet volume, NLR: Neutrophil/lymphocyte ratio, PLR: Platelet/lymphocyte ratio, MHR: Monocyte/high-density ratio, MLR: Monocyte/lymphocyte ratio, SII: Systemic immune inflammatory index, SIRI: Systemic inflammatory response index, LDL: Low-density lipoprotein, TG: Triglyceride, HDL: Monocyte/high-density lipoprotein

## Discussion

It is known that fibrinogen is one of the most important factors determining plasma viscosity. As fibrinogen levels increases, flow of blood cells slows down, they tend to stick together and viscosity increases. These events cause atherosclerotic changes in vessels. As a result, it has been shown that the increase in plasma fibrinogen levels is effective in the process starting with endothelial dysfunction and progressing to atherosclerosis (21-23). Albumin is decreased in inflammation and is associated with high mortality in cardiovascular diseases (24). In the British Regional Heart Study, it was found that low albumin levels were associated with smoking (25). Karahan et al. (26) found FAR levels more sensitive compared to fibrinogen or albumin values alone in predicting venous insufficiency. In another study, FAR was found to be high in patients with stable angina pectoris, which was associated with lower mortality (27).

In our study, in accordance with the literature, fibrinogen levels were found to be high and albumin levels were low in smokers (25). FAR, one of the markers we used to predict endothelial dysfunction in smoking, was found to be high in the smoking group. The early stage of atherosclerosis is endothelial dysfunction, and previous studies have shown that FAR is high in atherosclerosis. In conclusion, our study suggests that high FAR may indicate endothelial dysfunction.

In a study, WBC, neutrophil and lymphocyte counts were found to be high in smokers (28). Similar effects of smoking were revealed in the study of Gumus et al. (29). In the study of Kutlu and Demirbas (30) MPV was found to be significantly higher in smoking individuals while no significant difference was found in platelet count. In our study, WBC, neutrophil, lymphocyte, monocytes and MPV levels were found to be significantly higher in the smokers group. It is well known that platelets are involved in the atherosclerotic process and MPV shows the platelet activation. In our study, platelet count not statistically significant difference between groups. But MPV levels were found to be significantly higher in smokers, similar to the studies that examining the hemogram parameters of smokers (18). When we evaluated the parameters that increase with smoking, MPV was found to be one of the parameters with the highest sensitivity. Our study suggests that high MPV levels predict endothelial dysfunction in smokers.

NLR is a biomarker that has gained importance in showing morbidity and mortality in the atherosclerotic process (14). In the study by Çekici et al. (31), when two groups consisting of smokers and non-smokers were compared, the NLR value was found to be higher in the smokers group. In our study, NLR levels were found to be higher in smokers compared to the other group, but this elevation was not statistically significant. As reported above, our study group consisted of people without any comorbidities and lower mean age unlike other studies. Besides, few number of participants of our study may have caused this difference.

PLR is an indicator of inflammation in endothelial dysfunction and is also used as a marker for atherosclerosis and cardiovascular disease (17). In our study, PLR values of the two groups were compared and it was found to be significantly lower in the smoking group consistent with the study of Gumus et al. (29).

Demirbaş et al. (32), analyzed MHR, MLR and PLR as new inflammatory markers showing inflammation and oxidative stress in vitiligo and found them significantly higher in vitiligo patients than controls. Therefore these parameters were suggested as new indicators of inflammation in vitiligo patients (32). Many studies have investigated MHR in various diseases. MHR has gained importance in demonstrating systemic inflammation. High MHR is an increased risk for cardiovascular diseases (33). It has been shown that, in atherosclerosis the number of monocytes increase whereas HDL level remains low. We showed that the number of monocytes was significantly higher in the smoking group ($p<0.05$). According to ROC analysis, the sensitivity and specificity of monocyte was found to be the highest variable among the parameters increasing due to smoking. It is known that monocytes play a role in the first step of the atherosclerotic process and the number of monocytes increase in cardiovascular diseases (15,16). As the levels of MHR and MLR which are suggested as new inflammatory markers are evaluated, both were found to be significantly higher in the smokers group ($p<0.05$). The cut-off value we obtained in the ROC analysis was calculated as 0.09 for MHR and 0.20 for MLR. According to the results, we think that these two markers may be stimulatory and/or predictive in endothelial dysfunction due to smoking.

In a study, it was found that SIRI values of 285 patients with nasopharyngeal cancer were more significant in predicting the survival of patients compared to cancer staging (34). In another study, SIRI values were found to be an important predictor of survival in patients with pancreatic cancer (35). When other inflammation markers were examined, it was observed that they were not as strong as SIRI (36). This marker has been mostly investigated to determine the prognosis of cancer patients. The relationship between smoking and SIRI has not been investigated before, and our study shows the relationship between SIRI and smoking-induced inflammation.

Studies have shown that systemic inflammation has a very important role in the formation of cancer cells (37). SII has been found to be a strong predictor of survival for patients diagnosed with colorectal cancer. It was even found important in distinguishing high-risk among patients with the same cancer stage. In this study, SII was found to be more valuable when compared to other inflammation markers (38). In another study, many parameters were examined and NLR, PLR and SII were found to be significantly higher in patients with kerataconus. Here, the reason for the high SII was thought to be the role of endothelial dysfunction rather than chronic inflammation (39). In our study, SII was found to be high in smokers, but high SII was not statistically significant in demonstrating smoking-related endothelial dysfunction.

We think that this issue should be examined with more number of participants and comprehensive studies.

## Conclusion

We showed that biomarkers such as FAR, MPV, PLR, MHR, MLR and SIRI may predict endothelial damage caused by smoking. Our study may inspire new and exhaustive ones investigating new inflammatory markers to predict silent inflammatory processes in healthy individuals.

### Ethics

**Ethics Committee Approval:** This study was approved (dated: 06/03/2020 and numbered: 2213) by Clinical Research Ethics Committee of University of Health Sciences Turkey, İstanbul Training and Research Hospital.

**Informed Consent:** All participants were informed about the study and their consent was obtained.

**Peer-review:** Externally and internally peer-reviewed.

### Authorship Contributions

Concept: Ş.A., H.F.A., Z.A.S., Design: Ş.A., H.F.A., Z.A.S., Data Collection or Processing: Ş.A., H.F.A., Analysis or Interpretation: Ş.A., H.F.A., Z.A.S., Drafting Manuscript: Ş.A., H.F.A., Critical Revision of Manuscript: Ş.A., H.F.A., Z.A.S., Final Approval and Accountability: Ş.A., H.F.A., Z.A.S., Supervision: Ş.A., H.F.A., Z.A.S., Writing: Ş.A., H.F.A., Z.A.S.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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