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Evaluation of epicardial adipose tissue thickness and inflammatory parameters in smokers and non-smokers

Yasin Emrah Soylu[1], Resit Coskun[2], Adalet Ozcicek[3], Cuma Mertoglu[4], Yusuf Kemal Arslan[5], Fatih Ozcicek[3]

[1]Gumushane State Hospital, Department of Internal Medicine, Gumushane, Turkey
[2]Erzincan Binali Yildirim University, Faculty of Medicine, Department of Cardiology, Erzincan, Turkey
[3]Erzincan Binali Yildirim University, Faculty of Medicine, Department of Internal Medicine, Erzincan, Turkey
[4]Inonu University, Faculty of Medicine, Department of Medical Biochemistry, Malatya, Turkey
[5]Erzincan Binali Yildirim University, Faculty of Medicine, Department of Biostatistics, Erzincan, Turkey

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Abstract

Smoking is the leading cause of preventable death. Epicardial adipose tissue (EAT) surrounds the heart surface and creates local and systemic effects secreting the hormones, cytokines, inflammatory mediators. Previous studies demonstrated that both smoking and EAT have a strong association with inflammation and atherosclerosis. Our study aimed to determine the relationship of smoking with EAT thickness and inflammation by evaluating smokers and non-smokers. A total of 259 healthy male and female participants between the ages of 18-65, without a history of chronic disease and with a body mass index within normal limits, were included in a study. EAT thickness measurements were made by transthoracic echocardiography and EAT thicknesses of smokers and non-smokers were compared. In addition, the effects of smoking and EAT thickness on different inflammatory parameters were evaluated. When the EAT thicknesses were compared between smokers and non-smokers (2.60±1.2), a statistically significant difference was found in favor of smokers (3.84±1.84) ($p<0.001$). A moderate positive correlation was found among age, body mass index, smoking duration in years, pack/year and EAT thickness. The difference among waist circumference, the number of cigarettes smoked daily, diastolic blood pressure, fasting blood glucose, ALT, AST, total cholesterol, triglyceride, LDL-cholesterol, CRP, uric acid, platelet count, MPV values, platelet/lymphocyte ratio and EAT thickness were found meaningful, but the weak correlation in different ratios were determined. Smoking was found to be the most important determinant of EAT thickness. Other determinants of EAT thickness were age, body mass index, CRP and female gender. The significant statistical relationship between smoking and EAT thickness suggests that smoking increases EAT thickness and inflammatory parameters. Co-assessment of the EAT and blood inflammatory parameters in smokers may guide the initiation of medical treatment in primary prevention or other therapies.

Keywords: Smoking, epicardial adipose tissue, inflammation

Introduction

Although the relationship between smoking and the pathophysiology of many diseases has been known for many years, it continues to cause deaths at an alarming rate worldwide despite the measures taken to quit smoking. Since many harmful chemical compounds released by tobacco smoke, cigarette exposure causes endothelial and platelet dysfunction, lipid metabolism disorder, oxidative stress, inflammation and atherosclerosis [1,2]. Worldwide, approximately 7.2 million people die each year due to smoking-related diseases and this number is expected to increase gradually [3].

Epicardial adipose tissue (EAT) covers up to 80% of the heart surface. It is an active tissue secreting hormones, cytokines, and inflammatory mediators. EAT also provides the mechanical protection of the heart and slightly meets the heart's energy demand [4]. The harmful and protective effects of EAT are in a delicate balance. For instance, EAT cells increase leptin production while impairing adiponectin secretion in hypertensive, metabolic syndrome, coronary artery disease (CAD) patients and obese individuals. Decreased adiponectin leads to endothelial dysfunction, systemic inflammation and increased oxidative stress. Besides, an increase in leptin causes atherogenic changes in the endothelium by releasing inflammatory cytokines that negatively affect blood lipid levels [5-7]. Regarding favorable effects, EAT releases the cardioprotective adrenomedullin [8]. Since there is no separating fascia layer between the EAT and myocardium, it can be deemed a source of inflammatory mediators that directly affect the tissue,

*Corresponding Author: Resit Coskun, Erzincan Binali Yildirim University, Faculty of Medicine, Department of Cardiology, Erzincan, Turkey
E-mail: r_coskun79@hotmail.com

myocardium and coronary arteries [9, 10]. EAT measurement with transthoracic echocardiography is an inexpensive procedure that can be performed in a short time. When EAT thickness is evaluated with biochemical and metabolic parameters, it can predict many diseases [11]. High levels of proinflammatory and prothrombotic substances in patients with thick EAT may trigger the coagulation system and inflammatory processes, leading to plaque rupture and thrombus formation, ultimately resulting in diseases such as acute myocardial infarction [12]. As known, EAT, an indicator of visceral adiposity, is well correlated with metabolic syndrome components. The basis of metabolic syndrome is considered to be obesity and insulin resistance. Previously, a significant correlation was found among EAT thickness and metabolic syndrome components such as blood pressure, triglyceride and high-density lipoprotein (HDL) levels and fasting blood sugar. Worsening of any of these components increases EAT thickness [13].

Many studies have shown that neutrophil, lymphocyte, platelet count and mean platelet volume (MPV) values or the ratios of these values are used as inflammatory markers in the ready-to-use complete blood count test [14,15]. Recently conducted studies have been demonstrated the important role of monocytes, HDL cholesterol and monocyte/HDL ratio in the process of inflammation and atherosclerosis [16,17]. Uric acid and C-reactive protein (CRP) are also markers associated with inflammation [18,19]. Although various studies on inflammation and atherosclerosis were conducted, limited publications evaluated EAT thickness and inflammation in smokers. The present study aimed to reveal the relationship among smoking, EAT thickness and inflammation using easily applicable and non-invasive methods such as transthoracic echocardiography and laboratory parameters.

Materials and Methods

This study was carried out between July 2018 and July 2019. Participants were divided into two groups as smokers and non-smokers, who applied to the Erzincan Binali Yildirim University, Mengucek Gazi Training and Research Hospital, Internal Medicine outpatient clinic. Participants consisted of men and women aged 18-65 years. The study was approved by the Erzincan Binali Yıldırım University Faculty of Medicine Clinical Research Ethics Committee (Date: 26.06.2018 Issue No: 25/16). For an individual to be considered a smoker, it was required to be an active smoker and have a smoking history of at least five packs/year [Pack/year = (Number of cigarettes smoked per day /20)×(Year smoked)]. For an individual to be considered a smoker, it was required to be an active smoker and have a smoking history of at least five packs/year [Pack/year=(Number of cigarettes smoked per day / 20)×(Year smoked)]. EAT thickness measurements of the participants were made by transthoracic echocardiography. Body mass index [Body mass index (BMI)=Body weight (kg) / Height (m^2)], those below 18.5 kg/m^2 and over 24.99 kg/m^2, those with active infection, diabetes mellitus, chronic liver disease, chronic renal failure, hypothyroidism-hyperthyroidism and hypertension (HT), patients with left ventricular dysfunction, CAD, revascularization anamnesis and patient with poor echogenicity were excluded. A total of 259 people were retrieved, including 119 smokers (24 women, 95 men) and 140 non-smokers (37 women and 103 men), after those who did not meet the criteria were excluded from the study. Informed consent forms were obtained from all individuals participating in the study.

Measurements Made in the Outpatient Clinic

Stethoscope and air sphygmomanometer (Er-Ka, Germany) were used in the outpatient setting for blood pressure measurements of individuals. The pulse rate was recorded by palpation from the radial artery, and those whose heart rate was not rhythmic were excluded. Weight and height meters were performed using the length and weight data (SECA, SecaGmbH&Co. KG. Germany). The patients' body mass indexes were calculated by dividing the weight by the square of the height in meters and recorded. The World Health Organization stated that those with a body mass index between 18.5 kg/m^2 and 24.99 kg/m^2 were considered average weight. We included people with a body mass index regarded as average weight. Waist circumference measurement using a non-elastic length gauge was measured from the region that coincides with the midpoint of the last rib that can be palpated with the superior iliac crista. A cardiologist performed transthoracic echocardiography procedures. It was obtained from parasternal and apical windows with HD11XE (Philips-Netherlands) brand echocardiography device and S4-2 transducer (frequency range, 2-4 MHz echocardiography probe, Philips-Netherlands) in the cardiology outpatient clinic. Patients with an ejection fraction of at least 60% were included. EAT measurements were taken from the parasternal long-axis window by the cardiologist using two-dimensional echocardiography. EAT thickness measurements were made at the end of systole from the widest part of the echolucent area between the right ventricular free wall and the parietal pericardium, where the line drawn as perpendicular as possible to the aortic annulus determined as the anatomical landmark.

Biochemical Measurements

Serum glucose, alanin aminotransferaz (ALT), aspartat transaminaz (AST), creatinine, uric acid (Spectrophotometric analysis, BeckmanCoulter AU2700, Olympus Corporation, Japan); total cholesterol, HDL cholesterol, and plasma triglyceride concentrations (Oxidation-based technique, BeckmanCoulter AU 2700, Japan); troid stymulane hormone (TSH) (Chemiluminescence study, immunoassay system, Centaur XP, Siemens Healthcare, Germany); complete blood count (Laser optic reading, XN-1000, Sysmex Corporation, Japan); CRP (Nephelometric method, BN II, Siemens Healthcare, Germany) were studied in the morning hours after at least 10 hours of fasting in the central laboratory of our hospital.

Statistical analysis

The data were analyzed using the program "Statistical Package for the Social Sciences (SPSS) 22.0" (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). The conformity of the variables to the normal distribution was examined using the Kolmogorov-Smirnov test. While the variables were summarized, mean±standard deviation and median (minimum-maximum) values were presented as descriptive statistics. While making comparisons between groups, Student's t-test was used for normally distributed data, while the Mann-Whitney U test was used for undistributed data. The Chi-square test was used in the evaluation of categorical data. Correlation analysis was performed with the Spearman correlation test for non-parametric data. Variables associated with EAT thickness were determined in the correlation analysis and the variables found significant in the correlation analysis were included in the

linear regression analysis. While performing the linear regression analysis, age and gender were kept constant in the model as biological factors. Statistical significance level was accepted as $p<0.05$.

Results

The average age of 259 individuals was found to be 32.5±11.9 years. When all individuals were evaluated, the mean body mass index was found to be 22.3±1.9 kg/m². The mean EAT thickness was calculated as 3.17±1.65 mm and the median value of the EAT thickness was 3 mm (minimum 1 mm-maximum 8 mm).

It was determined that 119 of the 259 individuals (45.9% of all patients) were smokers and 140 were non-smokers (54.1% of all individuals). The mean number of cigarettes per day was calculated as 21.1±8.5 and the mean duration of smoking was calculated as 14.5±11 years. The mean cigarettes number in packs/year were calculated as 15.9±16.5 packs/year, and the median value of smoking in packs/year was ten packs/year (minimum five packs/year and maximum 90 packs/year). Sixty-one women (23.6%) and 198 men (76.4%) were included in to present study. It was determined that 24 (39.3%) of the female participants and 95 (48%) of the male participants were smokers. When smoking rates were evaluated based on gender, there was no statistically significant difference (p=0.237). When smoking and non-smoking groups were compared, a statistically significant difference was found between EAT thickness ($p<0.001$) and pulse rate (p=0.044) (Table 1, Figure 1). Additionally, HDL-cholesterol ($p<0.001$), triglyceride ($p<0.001$), uric acid ($p<0.001$), monocytes count ($p<0.001$), monocyte/HDL ratio ($p<0.001$), CRP (p=0.001) 0.001), white blood count (WBC) (p=0.002), platelet/lymphocyte ratio (p=0.002), platelet count (p=0.003), neutrophil count (p=0.015) and ALT (p=0.049) levels were statistically significant in favor of smokers (Table 2, Figure 2,3). When smoking and non-smoking groups were compared, although a statistically significant difference was observed for height and weight values, it was determined that there was no statistically significant difference between body mass indexes. It was determined that there were no statistically significant differences between age, waist circumference, systolic blood pressure and diastolic blood pressure values (Table 1). Additionally, no statistically significant difference was found among fasting blood glucose, lymphocyte count, AST, creatinine, total cholesterol, low density lipoprotein (LDL) cholesterol, TSH, MPV levels, MPV/Platelet and neutrophil/lymphocyte ratios (Table 2).

As a result of the correlation test performed to determine the parameters related to the EAT thickness, a moderate positive correlation was found among age, body mass index, year and pack/year smoking values and EAT thickness. Differences among waist circumference, the number of cigarettes smoked daily, diastolic blood pressure, fasting blood glucose, ALT, AST, total cholesterol, triglyceride, LDL-cholesterol, CRP, uric acid, platelet count, MPV values, platelet/lymphocyte ratio and EAT thickness were found meaningful, but the weak correlation in different ratios were determined (Table 3). To determine the factors predicting EAT thickness, the statistically meaningful parameters found in the correlation analysis were included in the linear regression analysis. Only one of the highly correlated variables was added to the model. Age and gender were kept constant in the model as biological factors (Table 4).

Table 1. Demographic, clinical data and epicardial adipose tissue thicknesses of smokers and non-smokers

Parameter	Grup-1 (Smokers), n=119	Grup-2 (Non-smokers), n=140	p value
Age (years)**	34.1±13.1 29 (19-65)	31.2±10.8 28 (18-63)	0.141
Height(cm)**	172.9±8.5 173 (151-198)	166.2±8.3 165 (146-195)	<0.001
Weight(kg)**	67.1±8.9 68 (45-95)	61.7±8.8 60 (45-92)	<0.001
Body Mass Index (kg/m²)**	22.4±1.9 22.9 (18.5-24.9)	22.3±2 22.7 (18.5-24.9)	0.657
Waist circumference(cm)*	82.4±8.5 82 (65-105)	80.5±7.9 80.5 (64-100)	0.130
Systolic Blood Pressure (mmHg)**	114.1±9.6 110 (90-140)	113.2±8.8 110 (100-140)	0.355
Diastolic Blood Pressure (mmHg)**	75.8±6.2 80 (60-90)	75.1±5.6 80 (60-90)	0.215
Pulse Rate (beats/minute)**	81.4±7.3 82 (64-96)	79.6±8 78 (64-118)	0.044
EAT Thickness (mm)**	3.84±1.84 3 (1-8)	2.60±1.2 2 (1-6)	<0.001

* Student's t test was applied.
** Mann-Whitney U test was applied.
(Results in the table are presented as mean±standard deviation and median (minimum-maximum) values).
EAT: Epicardial Adipose Tissue

As a result of linear regression analysis, age, body mass index, smoking and CRP were significant determinants for EAT thickness. In terms of EAT thickness, it was concluded that 1 unit increase in age increased 0.075 mm, 1 unit increase in body mass index increased 0.172 mm and 1 unit increase in CRP increased 0.139 mm of tissue. The effect of smoking on EAT thickness was determined to be 0.815 mm. It was determined that the male gender had reduced the EAT thickness by 0.221 mm than females. With the mentioned variables, 62.3% of the change in EAT thickness can be explained (R2=0.623, adjusted R2=0.615) (Table 4).

Table 2. Laboratory data of smokers and non-smokers

Parameter	Grup-1 (Smokers), n=119	Grup-2 (Non-smokers), n=140	p value
Fasting Blood Glucose (mg/dL)**	89.8±10.4 89 (64-124)	91±8.9 91 (72-123)	0.278
ALT (U/L)**	17.8±7.7 16 (6-41)	16.3±7.2 14 (7-46)	0.049
AST (U/L)**	19.2±4.7 20 (10-40)	19.3±5.3 18 (12-36)	0.072
Creatinine (mg/dL)**	0.83±0.17 0.86 (0.40-1.16)	0.83±0.13 0.8 (0.52-1.25)	0.117
Total Cholesterol (mg/dL)**	167.4±44 163 (77-383)	169.6±34.6 170.5 (100-306)	0.264
HDL- Cholesterol (mg/dL)* *	43.3±10.3 43 (22-81)	50.7±11.3 49.5 (23-77)	<0.001
Triglyceride (mg/dL)**	119.2±69.1 100 (19-394)	99.2±66.6 77 (36-399)	<0.001
LDL- Cholesterol (mg/dL)**	100.3±38.8 96.2 (28.2-301.2)	99.1±29.1 99 (14.2-200.6)	0.555
TSH (mIU/L)**	1.85±0.94 1.65 (0.62-4.40)	1.85±0.87 1.63 (0.58-4.49)	0.699
CRP (mg/L)**	4.76±3.21 3.63 (0.15-18)	3.30±1.83 3.13 (0.12-12.9)	0.001
Uric Acid (mg/dL)**	4.85±1.16 4.90 (2-9.1)	4.26±1.02 4.10 (2.2-7.1)	0.001
WBC (103/mm³)**	7.8±2.1 7.4 (4-13.5)	7±1.8 6.8 (3-12.2)	0.002
MPV (fL)*	10.2±0.99 10.3(6.7-12.5)	10.5±0.90 10.4 (8.2-13.4)	0.104
Platelet Count (103/mm³)**	262.1±59.6 260 (125-473)	288.5±68.7 279.5(151-491)	0.003
Neutrophil Count (103/mm³)**	4.68±1.77 4.21 (2.21-9.87)	4.12±1.53 3.81 (0.59-9.41)	0.015
Lymphocyte Count (103/mm³)*	2.29±0.57 2.28 (1.24-3.99)	2.21±0.58 2.13 (0.80-4.42)	0.256
Monocyte Count (103/mm³)**	0.61±0.22 0.56 (0.23-1.51)	0.48±0.16 0.46 (0.16-1.04)	<0.001
MPV/Platelet Ratio**	0.04±0.01 0.04 (0.2-0.9)	0.04±0.01 0.04 (0.2-0.8)	0.051
Neutrophil/Lymphocyte Ratio**	2.16±0.97 1.85 (0.69-6.16)	1.97±0.92 1.85 (0.72-6.48)	0.091
Platelet/Lymphocyte Ratio**	121±39.1 114.9 (49.2-246.4)	138.8±47.8 129.2 (47.8-310.5)	0.002
Monocyte/HDL Ratio**	15.1±7.6 13.2 (4.8-47.1)	10.1±4.1 9.4 (3.47-24)	<0.001

* Student's t test was applied.
** Mann-Whitney U test was applied.
(Results in the table are presented as mean±standard deviation and median (minimum-maximum) values.
HDL; High-Density Lipoprotein, LDL; Low-Density Lipoprotein, TSH; Thyroid Stimulating Hormone, CRP; C-Reactive Protein, WBC; White Blood Count, MPV; Mean Platelet Volume. ALT; Alanine Aminotransaminase, AST; Aspartate Aminotransferase

Table 3. Correlation analysis of the parameters showing a significant relationship with the epicardial adipose tissue thickness

Parameter	Correlation coefficient (rs)	p value
Age (years)	0.577	<0.001
Body Mass Index (kg/m²)	0.410	<0.001
Waist circumference(cm)	0.329	<0.001
Number of Daily Smoked Cigarettes (piece)	0.339	<0.001
Smoking Period (years)	0.467	<0.001
Smoking Per Pack/Year	0.443	<0.001
Diastolic Blood Pressure (mmHg)	0.154	0.013
Fasting Blood Glucose (mg/dL)	0.152	0.015
ALT (U/L)	0.169	0.006
AST (U/L)	0.143	0.021
Total Cholesterol (mg/dL)	0.282	<0.001
Triglyceride (mg/dL)	0.263	<0.001
LDL- Cholesterol (mg/dL)	0.294	<0.001
CRP (mg/L)	0.398	<0.001
Uric Acid (mg/dL)	0.163	0.009
MPV (fL)	- 0.153	0.014
Platelet Count (103/mm³)	- 0.141	0.023
Platelet/Lymphocyte Ratio	- 0.151	0.015

In cases with a p value < 0.05, rs is interpreted as follows to comment on the correlation
rs: 0.00-0.19: No or negligibly low relationship
0.20-0.39: Poor relationship
0.40-0.69: Moderate relationship
0.70-0.89: Strong relationship
0.90-1.00: Very strong relationship
The plus or minus sign at the beginning of the values indicates the direction of the relationship (positive correlation or negative correlation).
ALT; Alanine Transaminase, AST; Aspartate Aminotransferase, MPV; Mean Platelet Volume, LDL; Low-Density Lipoprotein, CRP; C-Reactive Protein

Table 4. Parameters associated with the increase in epicardial adipose tissue thickness according to the results of linear regression analysis

Parameter	Regression coefficient	Standard error	p value
Fixed Term	-3.875	0.737	<0.001
Age (years)	0.075	0.006	<0.001
Gender	-0.221	0.152	0.148
Body mass index (kg/m²)	0.172	0.035	<0.001
Smoker	0.815	0.133	<0.001
CRP (mg/L)	0.139	0.026	<0.001

R2 (Explanatory coefficient) = 0.623, adjusted R2 = 0.615.
CRP; C-Reactive Protein

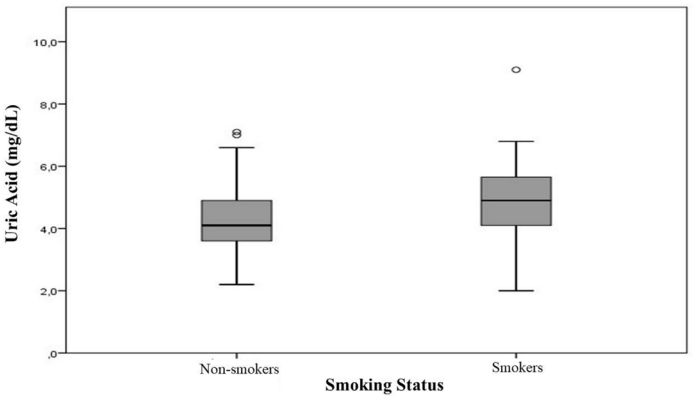

Figure 1. Distribution of epicardial adipose tissue thickness values of smokers and non-smokers

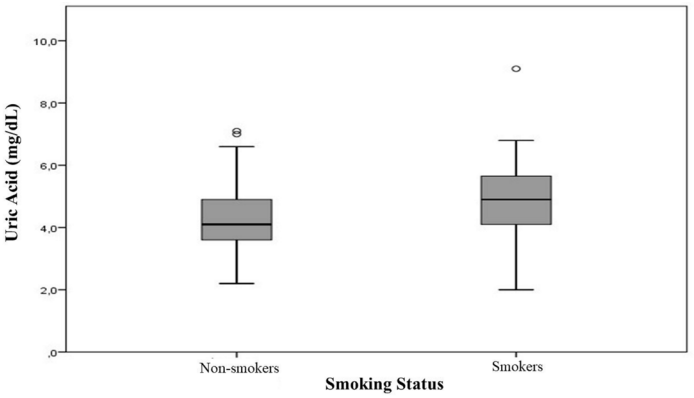

Figure 2. Distribution of uric acid values of smokers and non-smokers

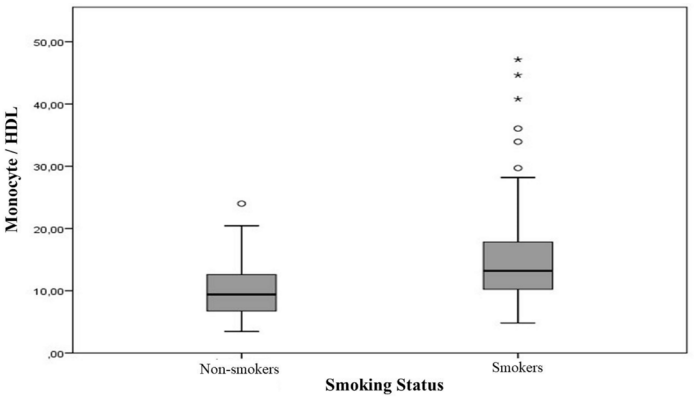

Figure 3. Distribution of monocyte/HDL ratio values of smokers and non-smokers

Discussion

The present study reached two important results. Firstly, we obtained the effects of smoking on EAT thickness and various inflammatory parameters. Additionally, the variables associated with EAT thickness were determined and the main factors that could affect the increased EAT thickness were revealed. The current study results determined that smokers had a significantly greater EAT thickness than non-smokers. We found that heart rate, HDL-cholesterol, triglyceride, uric acid, monocyte count, monocyte/HDL ratio, CRP, total WBC, platelet/lymphocyte ratio, platelet count, neutrophil count and ALT levels significantly increased in favor of smokers. In addition, the main determinants

of EAT thickness were age, female gender, body mass index, CRP and smoking, with a strong significance. In a current study, age and body mass index were moderately correlated with EAT thickness. Iacobellis et al. determined that the increase in EAT thickness is directly related to the risk of developing metabolic syndrome [20]. In another study, EAT thickness increase was associated with at least two components of the metabolic syndrome, such as HT, hyperglycemia, and dyslipidemia [21]. Similarly, significant positive correlations were found in the present study among EAT thickness increase and waist circumference, diastolic blood pressure, fasting blood glucose, total cholesterol, triglyceride and LDL-cholesterol values. EAT thickness increases by 22% over the age of 65 due to enlarged fat mass, particularly in women [22]. Our linear regression analysis concluded that one year increase in age increased EAT thickness by 0.075 mm and a 1 unit increase in body mass index increased 0.172 mm of tissue. Additionally, having a male gender was associated with reduced EAT thickness by 0.221 mm than females. With the mentioned variables, 62.3% of the change in EAT thickness can be explained. However, there are other parameters (37,7%) affecting EAT thickness that we have not taken into consideration. It has been determined that the EAT thickness of individuals with a body mass index above 27 kg/m^2 is twice as much as those with a body mass index of less than 27 kg / m2 [23,24]. In line with the previous study, the present study results show that female gender and older age are associated with a thicker EAT.

Previous studies postulated that the high blood CRP levels may predict inflammation and possible atherosclerosis [25,26]. The current study showed that smoking and high blood CRP levels are significant determinants for increased EAT thickness. Additionally, while a moderate positive correlation was found among smoking in years, packs/year and EAT thickness, a weak correlation was found between the number of cigarettes smoked per day and EAT thickness. Consistently with our results, in a study by Rom et al. a positive correlation was found between the duration of smoking in packs/year and CRP levels [27]. Again, in a study by Alyan et al. a positive correlation was found among the number of cigarettes smoked daily, smoking duration and hs-CRP [28]. In the present study, in accordance with the literature, CRP levels in smokers were markedly above the cut-off value. In addition, the CRP levels were statistically much higher in smokers than in non-smokers.

The relationship between inflammatory parameters and atherosclerosis is well described before [29]. Considering the close relationship between EAT thickness and inflammation [30], it can be suggested that EAT will be thicker in smokers. In the present study, the mean EAT thickness was 2.6 mm in non-smokers and 3.8 mm in smokers. A previous study showed that an EAT thickness of approximately 2.5 mm is the cutoff for predicting the presence of significant atherosclerosis [31]. During routine screening, the evaluation of epicardial adipose tissue thickness may be considered in smokers with high inflammatory markers.

As a result of the inhibition of the cyclooxygenase enzyme and increased thromboxane synthesis, platelets' adhesion and aggregation properties increase [32]. Although an increase in platelet activity is observed in chronic smokers, their life span is shortened [33]. In our study, similar to previous studies, it was determined that the platelet count was significantly lower in smokers than in non-smokers. However, in the context of MPV and MPV/platelet values, no statistically significant difference was found between the two groups, although they are used as inflammatory markers. In a recent study, when smokers and non-smokers were compared, it was determined that WBC, neutrophil, monocyte counts and neutrophil-to-lymphocyte ratio (NLR) increased in smokers. A positive correlation was found between smoking in packs/year and neutrophil count, monocytes count and NLR values. No statistically significant difference was found in terms of the lymphocyte count levels between smokers and non-smokers [34]. In accordance with the literature, the present study determined that WBC, neutrophil count and monocyte count significantly increased and platelet-to-lymphocyte ratio values decreased in favor of smokers.

Considering the close relationship between atherosclerosis, inflammation and smoking, it can be concluded that HDL levels will decrease, triglyceride levels and monocyte/HDL ratio will increase in smokers. A previous study determined that HDL levels decreased and triglyceride and LDL levels increased in smokers. A positive correlation was found among smoking in packs/year and triglyceride, LDL and total cholesterol levels. A negative correlation was found between smoking in packs/year and HDL [35]. In line with the literature, we determined that HDL levels are decreased, triglyceride levels and monocyte/HDL ratio increase in smokers. In addition, a statistically significant difference was found between HDL, triglyceride and monocyte/HDL ratio when smokers and non-smokers were compared. No statistically significant difference was found between total cholesterol and LDL levels.

Blood uric acid levels have been found to be strongly associated with systemic inflammatory markers such as CRP and interleucin-6 [36]. In a study evaluating the occurrence of subclinical coronary atherosclerosis in smokers, uric acid levels were significantly higher in smokers than in non-smokers [37]. According to Pekmez et al., exposure to cigarette smoke for more than sixty days increased uric acid levels in rats [38]. The present study's positive correlation and statistically significant relationship between smoking and uric acid levels suggest that smoking has an inflammatory effect.

Since cigarettes possess a high nicotine ratio, smoking increases circulating catecholamines, thus stimulating the sympathetic nervous system resulting in increased heart oxygen demand, myocardial contraction, heart rate and blood pressure [39]. A comprehensive meta-analysis study determined that smoking is also associated with high resting heart rate levels. The resting heart rate of a person who smokes an average of 20 cigarettes a day increases by seven beats/minute. However, there was no significant difference in blood pressure values and HT risks of smokers [40]. In our study, it was determined that the heart rate of smokers increased significantly compared to non-smokers. However, no statistically significant difference was found between them in systolic and diastolic blood pressure values. We thought that the absence of a significant change in blood pressure values in long-term smokers might be due to the decrease in the body's neurochemical responses to the chemical content of cigarettes.

Conclusion

The present study determined the positive correlation between

smoking and EAT thickness. Smoking was also well-correlated with inflammatory and metabolic markers. EAT measured by echocardiography, a non-invasive and easily accessible method, may help predict the risk of atherosclerotic events in smokers. Co-assessment of the EAT and blood inflammatory parameters in smokers, in addition to traditional risk assessment, may guide the initiation of medical treatment in primary prevention or other therapies. In the light of large-scale studies, EAT thickness can be accepted as one of the risk factors for atherosclerosis and used routinely over time in smokers.

Study Limitations: The effects of passive cigarette smoke could not be evaluated. Although the same cardiologist made all EAT thickness measurements, the echocardiography procedure is clinician-dependent. Considering millimetric measures were made, it can be thought that errors may have occurred. Due to the single-center and cross-sectional nature of the study, the inability to establish a cause-effect relationship to interpret the findings and the number of patients not reflecting the entire population are also limitations.

Conflict of interests

The authors declare that they have no competing interests. Financial Disclosure All authors declare no financial support

Financial Disclosure

The authors declare that they have received no financial support for the study.

Ethical approval

The study was approved by the Erzincan Binali Yıldırım University Faculty of Medicine Clinical Research Ethics Committee (Date: 26.06.2018 Issue No: 25/16).

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