Cumhuriyet Medical Journal, 44(1): 62-66, 2022
DOI: http://dx.doi.org/10.7197/cmj.1088573

Cumhuriyet Medical Journal

| cmj.cumhuriyet.edu.tr | Founded: 2004 Available online, ISSN:1305-0028 Publisher: Sivas Cumhuriyet Üniversitesi

Association between systemic inflamatuary index and epicardial adipose tissue in patients with Type 2 Diabetes Mellitus

Levent Özdemir[1*], Vural Polat[2]

[1]*King Fahad Specialist Hospital, Department of Cardiology, Tabouk, Saudia Arabistan*
[2]*Sivas University, Faculty of Medicine, Department of Cardiovascular Surgery, Sivas, Turkey*
**Corresponding author*

Research Article

History

Received: 16/03/2022
Accepted: 29/03/2022

ABSTRACT

Objective: Epicardial adipose tissue is the visceral fat located between the myocardium and the pericardium. Increases in epicardial adipose tissue are closely associated with the occurrence of cardiovascular diseases. The systemic immune inflammation index is a new parameter developed to determine the inflammatory status of patients. In our study, we aimed to evaluate the relationship between systemic immun inflammation index and epicardial adipose tissue in patients with diabetes mellitus.
Method: 119 patients with T2DM and 50 volunteers were included to study. SII was obtained with formulatıon of neutrophil/lymphocyte x platelet. Epicardial fat tissue was obtained by transthoracic echocardiography. The relationship between systemic immune inflammation index and epicardial adipose tissue was evaluated in patients with Diabetes Mellitus
Results: In our study, ıt was shown that epicardial adipose tissue was higher in diabetic patients. There was a significant correlation between Body surface area , duration of diabetes mellitus, HbA1c, systemic immune inflammation index, mean platelet volume , neutrophil lymphocyte ratio and epicardial adipose tissue. In linear regression analysis, it was observed that duration of diabetes mellitus (β =0.049 (0.011-0.087); P=0.011) and SII (β=0.013 (0.001-0.018) P=0.008) were independent predictors of EAT.
Conclusions: In our study, it was shown that there is a significant relationship between epicardial adipose tissue and systemic immune inflammation index in diabetic patients. In patients with diabetes mellitus, systemic immune inflammation index may provide a useful estimate of epicardial adipose tissue, which has been shown to be associated with cardiovascular events.

Keywords*:* Systemic inflamatuary index, epicardial adipose tissue, diabetes mellitus

Tip 2 Diabetes Mellitus hastalarında sistemik inflamatuar indeks ve epikardiyal yağ dokusu arasındaki ilişki

ÖZ

Amaç: Epikardiyal yağ dokusu (EAT), miyokard ile perikard arasında yer alan viseral yağdır. EAT'daki artışlar, kardiyovasküler hastalıkların ortaya çıkması ile yakından ilişkilidir. 'Sistemik immün inflamasyon indeksi' (SII), hastaların inflamatuar durumunu belirlemek için geliştirilmiş yeni bir parametredir. Çalışmamızda diyabetes mellituslu hastalarda sistemik inflamatuar indeks ile EAT arasındaki ilişkiyi değerlendirmeyi amaçladık.
Yöntem: Çalışmaya T2DM'li 119 hasta ve 50 gönüllü dahil edildi. "Nötrofil/lenfosit x trombosit" formülü ile SII elde edildi. Transtorasik ekokardiyografi ile epikardiyal yağ dokusu değerlendirildi. Diabetes Mellitus'lu hastalarda SII ve EAT arasındaki ilişkiye bakıldı.
Bulgular: Çalışmamızda diyabetik hastalarda EAT'nin daha yüksek olduğu gösterilmiştir. BSA, diabetes mellitus süresi, HbA1c, SII, MPV, NLR ve EAT arasında anlamlı bir ilişki vardı. Lineer regresyon analizinde diabetes mellitus süresinin (β =0.049 (0.011-0.087); P=0.011) ve SII'nın (β=0.013 (0.001-0.018) P=0.008) EAT'nin bağımsız belirteçleri olduğu görüldü.
Sonuç: Çalışmamızda diyabetik hastalarda EAT ve SII arasında anlamlı bir ilişki olduğu gösterilmiştir. Diabetes mellituslu hastalarda SII, kardiyovasküler olaylarla ilişkili olduğu gösterilmiş olan EAT'nin yararlı bir tahminini sağlayabilir.

Anahtar sözcükler*:* Sistemikİnflamatuar indeks, epikardiyal yağ dokusu, Diabetes Mellitus

Süreç

Geliş: 16/03/2022
Kabul: 29/03/2022

[a] *drolevent@gmail.com* *https://orcid.org/0000-0002-1253-5673* [b] *vrlpolat@gmail.com* *https://orcid.org/0000-0001-9553-3990*

How to Cite: Özdemir L, Polat V (2022) Association between systemic inflamatuary index and epicardial adipose tissue in patients with Type 2 Diabetes Mellitus, Cumhuriyet Medical Journal, March 2022, 44 (1): 62-66

Introduction

Diabetes mellitus (DM) is associated with an increased incidence of cardiovascular disease and is a strong predictor of heart disease[1,2]. In addition to traditional risk factors, such as obesity and dyslipidemia, novel risk factors for instance chronic low-grade inflammation is also very common and play an important role for the initiation and progression of heart disease in patients with DM[3,4]. Systemic immune inflammation index (SII) (platelet x neutrophil/lymphocyte) was developed to determine the inflammatory and immunothrombotic status of patients. It has been suggested that SII is more valuable than neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in predicting inflammatory status and prognosis in a variety of cardiovascular disease[5].

Epicardial adipose tissue (EAT) is the visceral fat depot of the heart and has been shown to be associated with cardiovascular diseases [6]. Increased visceral adiposity, proinflammatory activity, impaired insulin sensitivity, are associated with risk of atherosclerosis, and increased of mortality rate. EAT is also considered a novel cardiovascular risk factor in the population. EAT is associated with inflammation and acts as an endocrine organ that produces many bioactive adipokines[7]. In our study, we aimed to evaluate the relationship between SII, which is known to be strongly associated with inflammation, and EAT in patients with type 2 DM (T2DM).

Material and Methods

Our study included 119 consecutive patients with T2DM who applied to our clinic and 50 healthy people as a control group between October 1, 2022 and October 31, 2022. Written or verbal informed consent was received from all patients, and the study protocol was approved by the hospital's local ethics committee in accordance with the Helsinki Declaration and Good Clinical Practice Guidelines (No:2022-01/33). The patients with T2DM were included in the study according to American Diabetes association guidelines criteria[8]. The control group was consisted of healthy volunteers who had no history of disease and wıthout any abnormality in the physical examination. Patients with a history of coronary artery disease, angina pectoris and acute coronary syndrome, patient with suspected coronary artery disease and positive noninvasive test results (wall motion abnormality in echocardiography, evidence of ischemia in treadmill exercise or myocardial single-photon emission computed tomography), heart failure, moderate to severe heart valve disease, rheumatic and collagen tissue diseases, inflammatory diseases, active infection, hematological disease, chronıc kidney disease, malignancy, pulmonary hypertension, and chronic obstructive pulmonary disease were excluded from the study.

The following demographic characteristics were obtained for all patients; age, gender, duration of diabetes, smoking status and body surface area. Moreover, body surface area (BSA) was calculated wıth medcalc software (free version). Blood pressure (BP) was measured with a mercury sphygmomanometer while sitting just after 5 minutes of waiting period in the supine position. Furthermore, glycosylated hemoglobin (HbA1c), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) were calculated using the automated analyzer. after more than 8 hours fasting period. The blood leukocyte, neutrophil and platelet counts, hemoglobin levels, and other whole blood count parameters were measured in a blood cell counter using an Abbott Cell-Dyn® 3700 System (Abbott Diagnostics, Santa Clara, CA, USA). SII was calculated as platelet count multiplied by the NLR . All patients were evaluated by Vivid 7 system (GE Medical Systems, Milwaukee, WI, USA; a 3.5 MHz transducer) at the left lateral position for echocardiographic evaluation. All patients were monitored during the echocardiographic examination. Echocardiographic standard techniques such as M-Mode, two-dimensional, color doppler, pulsed and continuous wave were performed. End-diastolic inter ventricular septal diameter (IVSD), posterior wall diameter (PWD), left ventricle end-diastolic (LVEDD) and end-systolic dimensions (LVESD) were measured with the M-Mode method. Trans mitral left ventricle inflow waves (E and A waves) were measured with a pulsed doppler and then the E/A ratio was calculated in the apical four chamber view. Left ventricle ejection fraction (LVEF) was calculated by Simpson's method by using apical two and four chamber views. EAT thickness was measured beside the free wall of the right ventricle in diastole while using parasternal long and short axis views. EAT thickness was calculated the average of the two measurements made from the parasternal long and short axes[9].

Statistical Analysis

All parameters were inserted into the IBM SPSS Statistics 22.0 package program and analysed. Continuous parameters were represented mean ± standard deviations and categorical parameters were expressed numbers and percentage. Kolmogorov-Smirnov test was performed to determine whether the homogeneous distribution in the both groups. Student's t test or Mann Whitney U test was used to examine whether there was a significant difference between the groups in terms of the characteristics and measurements. Categorical comparisons were made using the Chi-square test. Pearson or Spearman correlation tests were used to examine the significance of the linear relationship between the variables. EAT. SII, NLR, MPV, HBA1C, and duration of T2DM which p values less than 0.05 were included in the multiple linear regression analysis to determine the independent variables in predicting EAT. For $p<0.05$, the results were considered statistically significant.

Results

Demographic, clinical and laboratory parameters of the patients are shown in Table 1. There was no significant difference between age, gender, systolic and diastolic blood pressure, LDL-C, HDL-C, triglyceride, creatinine, BSA. Otherwise neutrophil, lymphocyte, platelets, NLR, MPV, SII, and Hba1c were different between the groups.

LVEDD, LVESD, LVEF, LA diameter, IVS, PW and mitral A wave were not different between groups. Mitral E wave (p<0.001), Em wave (p<0.001), E/A ratio (p<0.001), E/Em ratio (p=0.014), EAT (p<0.001) were significantly different between the groups (Table 2)

BSA, duration of T2DM, HbA1c, SII, MPV, NLR which were observed a significant correlation with EAT which were included to linear regression analysis. The analysis showed that the duration of T2DM (β =0.049 (0.011-0.087); P=0.011) and SII (β=0.013 (0.001-0.018) P=0.008) were independent predictors of EAT.

Discussion

In our study, we evaluated the relationship between SII which is a new inflammatory parameter and EAT in patients with T2DM. SII and EAT values were higher in diabetic patients than the control group. There was a significant correlation between SII, duration of T2DM, HbA1c, MPV, NLR and EAT in diabetic group. In the regression analysis, it was observed that duration of T2DM, SII were independent predictors of EAT.

Table 1. Clinical and demographic characteristics of groups.

	Diabetes Mellitus (n=119)	Control Group (n=50)	p
Age (years)	55.6 ± 6.6	56.1 ± 5.3	0.748
Female sex, n (%)	73(61.3)	27(54.0)	0.375
Hypertension, n (%)	70 (58.8)	30 (60)	0.765
Body Surface Area	1.91 ±0.2	1.98 ±0.3	0.156
Disease Duration (years)	9.6 ±2.4	-	-
Systolic BP (mmHg)	126.1 ± 14.2	121.7 ± 110.1	0.654
Diastolic BP (mmHg)	83.5 ± 9.6	82.3± 10	0.701
hsCRP (mg/dl)	0.79 ± 0.3	0.73 ± 0.2	0.223
Serum creatinine (mg/dl)	0.96 ± 0.2	0.89 ± 0.2	0.541
Hemoglobin, g/dl	13.2±1.0	13.8±2.0	0.456
White blood cell 10^3/mL	6.7±1.6	6.5±1.6	0.123
Neutrophil, 10^3/mL	4,8±1.4	4,2±1.3	**0.003**
Lymphocyte, 10^3/mL	2.0±0.5	2.1±0.5	**0.046**
Platelets, 10^3/mL	220 ± 52	204 ± 54	**0.001**
NLR	2.4 ±1.2	2.0± 0.6	**0.005**
MPV	6.7 ±3.9	4.6 ±3.6	**0.001**
SII (median) [IQR] (x10^3)	640 (323-1767)	328(234-1514)	**<0.001**
Hba1c	7.3±1.2	5.2±0.1	**<0.001**
Total cholesterol (mg/dl)	211 ± 55	213± 37	0.456
Low density lipoprotein cholesterol (mg/dl)	118 ± 32	116 ± 34	0.746
High density lipoprotein cholesterol (mg/dl)	38.6 ± 11	40.1 ± 18	0.575
Triglyceride (mg/dl)	197 ± 62	188± 47	0.276

BP, blood pressure; CRP, C-reactive protein;; NLR, neutrophil/lymphocyte ratio; MPV, mean platelet volume; SII, systemic immune-inflammatory index, HbA1c, glycated hemoglobin

Table 2. Echocardiographic findings

Ejection fraction	59.0 ±2.0	59.4 ±2.1	0.467
IVS, cm	1.06 ±0.09	1.04 ±0.07	0.801
PW,cm	1.03 ±0.07	1.01 ±0.07	0.802
LVDD,cm	4.4 ±1.4	4.4 ±1.1	0.765
LVSD,cm	3.2 ±0.2	3.1 ±0.3	0.789
Pulmonary artery pressure, mmHg	27.5 ±2.6	26.7 ±1.9	0.345
E wave, cm/s	60.8 ±9.3	74.3 ±17.0	<0.001
A wave, cm/s	70.1 ±11.0	72.2 ±13	0.256
E/A ratio	0.82 ±0.18	1.01 ±0.32	<0.001
E/Em ratio	10.1 ±3.5	8.8 ±1.6	<0.001
Epicardial Fat Tissue, mm	5.7 ± 0.7	4.9±0.7	<0.001

Table 3. Univariate and multivariate analysis for prediction of EAT.

	Univariate analysis		Multivariate analysis	
	r	p	OR (95% CI)	p
Body surface area	0.233	**0.002**		
Disease duration	0.498	**<0.001**	0.049(0.011-0.087)	**0.011**
HbA1c	0.471	**<0.001**		
SII	0.503	**<0.001**	0.013(0.001-0.018)	**0.008**
MPV	0.212	**0.003**		
NLR	0.302	**0.001**		

NLR, neutrophil/lymphocyte ratio; MPV, mean platelet volume; SII, systemic immune-inflammatory index, HbA1c, glycated hemoglobin,

Diabetes mellitus is one of the most common metabolic diseases through worldwide and is characterized as a metabolic disorder of carbohydrates, proteins and lipids[10]. The incidence of DM has increased in recent years and has become a serious public health threat[11]. Abnormally accumulating visceral fat is a risk factor for insulin resistance, which can reduce insulin sensitivity, increase the expression and secretion of proinflammatory cytokines in adipose tissue, and promote the development of DM and cardiovascular diseases[12-14]. In order to better understand the relationship between EAT and DM, various studies have been conducted to investigate the amount of EAT in patients with and without DM. Many studies have shown that EAT volume is significantly higher in DM patients[15-17]. In our study, we found higher EAT in diabetic patients compared to the control group as similar results of previous studies.

Epicardial adipose tissue covers a significant portion of the heart surface and constitutes 20% of the total heart weight. EAT is located in the atrioventricular and interventricular grooves, along the large branches of the coronary arteries, around the atrium, beside the free wall of the right ventricle and nearby the apex of the left ventricle[18-20]. As a metabolically active endocrine organ, EAT produces hormones, cytokines and other vasoactive substances that affect coronary atherogenesis and myocardial functions[21,22]. The direct effect of EAT on the heart is thought to be due to the diffusion of free fatty acids and adipokines between EAT and the vessel wall and underlying myocardium[23]. The adipokines may have effects on myocytes that are an important condition for cardiovascular outcome[23]. The relationship between myocardial involvement and cardiac diseases is important.

Various studies have shown that there is a significant correlation between EAT and inflammatory markers such as NLR and PLR[24,25]. SII was created by combining NLR and PLR, has been accepted as a new inflammatory marker and prognostic indicator in recent studies[2,26,27]. Several studies have suggested that SII may comprehensively represent the inflammatory state compared with NLR, as well as neutrophil and lymphocyte counts[28,29]. In our study, we observed a significant correlation between SII, NLR and EAT. However, in the regression analysis, it was observed that SII was an independent predictor of EAT and the relationship between SII and EAT was stronger than NLR and EAT. Some studies shown that there is a significant relationship between the duration of the T2DM and cardiac disease in diabetic patients[30]. In our study, we found that there was a significant relationship between duration T2DM and EAT.

Study limitation

Our study is a single-center and included a small number of patients. The lack of clinical outcome can be considered as a deficiency. Cardiac magnetic resonance imaging, which can better show EAT volume, was not used. Our findings should be supported by larger multicenter studies.

Conclusion

In our opinion SII which is easily available and has been shown to be superior to NLR in predicting EAT. According to our findings, we think that in patients with DM, SII may be clinically beneficial to predict EAT.

Conflict of interest

There is not a conflict of interest

References

1. Clarke P, Gray A, Legood R, J Leal, R R Holman. The impact of diabetes-related complications on health-care costs: results from the UK prospective diabetes study (UKPDS Study no. 65). Diabet Med. 2003; 20:442–50.
2. A joint editorial statement by the American diabetes association, the national heart, lung and blood institute, the juvenile diabetes foundation international, the national institute of diabetes and digestive and kidney diseases, the American heart association. Diabetes mellitus: a major risk factor for cardiovascular disease. Circulation. 1999; 100:1132–43.
3. Xiaoyou Su, Jing Xu, Chao Zheng. The relationship between non-alcoholic fatty liver and skeletal muscle mass to visceral fat area ratio in women with type 2 diabetes. BMC Endocrine Disorders. 2019; 19:76.
4. Montecucco F, Liberale L, Bonaventura A, Vecchiè A, Dallegri F, F Carbone F et al. The Role of Inflammation in Cardiovascular Outcome. Curr Atheroscler Rep. 2017; 19:11.
5. Yang YL, Wu CH, Hsu PF, Chen SC, Huang SS, Chan WL,et al. Systemic immune inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. Eur J Clin Invest. 2020;50: e13230.

6. Gottdiener JS, Arnold AM, Aurigemma GP, J F Polak, R P Tracy, D W Kitzman, et al. Predictors of congestive heart failure in the elderly: the cardiovascular health study. J Am Coll Cardiol.2000; 35:1628–37.
7. Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. JAMA. 1979; 241:2035–58.
8. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2014; 37: 81-90.
9. Dereli S, Bayramoğlu A, Yontar OC, Cerşit S, Gürsoy MO. Epicardial fat thickness: A new predictor of successful electrical cardioversion and atrial fibrillation recurrence. Echocardiography. 2018; 35:1926-31.
10. Levesque C. Medical management of type 2 diabetes. J Nurse Pract. 2011; 7:492–01.
11. Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type2 diabetes mellitus-present and future perspectives. Nat Rev Endocrinol. 2011; 8:228–36.
12. Mahabadi Amir A, Massaro Joseph M, Rosito Guido A, Levy D, Murabito JM, Wolf PA, O'Donnell CJ et al. Association of pericardial fat, intrathoracic fat, and visceral abdominal at with cardiovascular disease burden: The Framingham Heart Study. Eur Heart J. 2009; 30:850–6.
13. Yun CH, Lin TY, Wu YJ, Liu CC, Kuo JY, Yeh H et al. Pericardial and thoracicperi-aortic adipose tissues contribute to systemic inflammation and calcified coronary atherosclerosis independent of body fat composition, anthropometric measures and traditional cardiovascular risks. Eur J Radiol. 2012; 81:749–56.
14. Nolan CJ, Damm P, Prentki M. Type 2 diabetes across generations: from pathophysiology to prevention and management. Lancet. 2011; 378:169–81.
15. Iacobellis G, Diaz S, Mendez A, Goldberg R. Increased epicardial fat and plasma leptin in type 1 diabetes independently of obesity. Nutr Metab Cardiovasc Dis NMCD. 2014; 24:725–29.
16. Cetin M, Cakici M, Polat M, Suner A, Zencir C, Ardic I et al. Relation of epicardial fat thickness with carotid intima-media thickness in patients with type 2 diabetes mellitus. Int J Endocrinol. 2013; 2013:1-6.
17. Iacobellis G, Barbaro G, Gerstein HC. Relationship of epicardial fat thickness and fasting glucose. Int J Cardiol. 2008; 128:424–26.
18. Al Chekakie MO, Welles CC, Metoyer R, Ibrahim A, Shapira AR, Cytron J et al. Pericardial fat is independently associated with human atrial fibrillation. J Am Coll Cardiol. 2010; 56:784–22.
19. Nakanishi K, Fukuda S, Tanaka A, Otsuka K, Sakamoto M, Taguchi H ,et al. Peri-atrial epicardial adipose tissue is associated with new-onset non valvular atrial fibrillation. Circ J. 2012; 76:2748–54.
20. Wong CX, Abed HS, Molaee P, Nelson AJ, Brooks AG, Sharma G et al. Pericardial fat is associated with atrial fibrillation severity and ablation outcome. J Am Coll Cardiol. 2011; 57:1745- 51.
21. Yudkin JS, Stehouwer CD, Emeis JJ, S W Coppack. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol. 1999; 19:972–78.
22. Nakanishi K, Fukuda S, Tanaka A, Otsuka K, Sakamoto M, Taguchi H et al. Peri-atrial epicardial adipose tissue is associated with new-onset non valvular atrial fibrillation. Circ J. 2012; 76:2748–54.
23. Baloglu I, Turkmen K, Selcuk NY, Tonbul HZ, Ozcicek A, Hamur H et al. The Relationship Between Visceral Adiposity Index and Epicardial Adipose Tissue in Patients with Type 2 Diabetes Mellitus. Exp Clin Endocrinol Diabetes. 2021; 129:390-5
24. Derya MA, Demir V, Ede H. Relationship between neutrophil/lymphocyte ratio and epicardial fat tissue thickness in patients with newly diagnosed hypertension J Int Med Res. 2018; 46: 940–50.
25. Emin MA, Hamur H, Demirtas I, Bakirci EM, Ozcicek A, Ozcicek A et al. Predictors of epicardial adipose tissue in patients with type 2 diabetes mellitus *Diabetol Metab Syndr 2014;* 6: 55-59
26. Nie D, Gong H, Mao X, Li Z. Systemic immune-inflammation index predicts prognosis in patients with epithelial ovarian cancer: a retrospective study. Gynecol Oncol. 2019; 152:259–64.
27. Seo M, Yamada T, Morita T, Y Furukawa, S Tamaki, Y Iwasaki et al. Prognostic value of systemic immune-inflammation index in patients with chronic heart failure. Eur Heart J. 2018;39:564-69.
28. Huang Y, Gao Y, Wu Y, Lin H. Prognostic value of systemic immune-inflammation index in patients with urologic cancers: a meta-analysis. Cancer Cell Int. 2020; 20:1-8.
29. Bağcı A, Aksoy F, Baş HA. Systemic Immune-Inflammation Index May Predict the Development of Contrast-Induced Nephropathy in Patients with ST-Segment Elevation Myocardial Infarction. Angiology. 2021 Jul 12;33197211030053.
30. Bjerg L, Gudbjörnsdottir S, Franzén S, Carstensen B, Witte DR, Jørgensen ME, et al. Duration of diabetes-related complications and mortality in type 1 diabetes: a national cohort study International Journal of Epidemiology, 2021 30;50:1250-59