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INVESTIGATION OF THE RELATIONSHIP BETWEEN EPICARDIAL FAT TISSUE THICKNESS AND HEMOGLOBIN A1c LEVELS

EPİKARDİYAL YAĞ DOKUSU KALINLIĞI İLE HEMOGLOBİN A1c DEĞERLERİ ARASINDAKİ İLİŞKİNİN İNCELENMESİ

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Abstract

Introduction: There is a linear relationship between Epicardial adipose tissue (EAT) thickness and cardiovascular diseases and diabetes mellitus (DM). However, the relationship between HbA1c, which is a direct measure of blood sugar regulation in DM and EAT has not been questioned. In this study, the relationship between EAT and HbA1c was investigated.

Materials and Methods: A total of 90 patients who were admitted to our cardiology clinic were included in the study consecutively. The EATs of the patients were measured by echocardiography and compared with their HbA1c values.

Results: Body mass index, fasting blood glucose, HbA1c and body weight are positively correlated with EAT ($p<0.05$)

Conclusion: In this study, it was shown that there is a direct relationship between HbA1c and EAT, and it was emphasized that EAT can guide the follow-up of preclinical diabetes and glucose control.

Keywords: Epicardial adipose tissue, diabetes mellitus, hemoglobin A1c

Öz

Amaç: Epikardiyal yağ dokusu (EYD) kalınlığı ile kardiyovasküler hastalılar ve diabetes mellitus (DM) arasında doğrusal bir ilişki vardır. Fakat DM'de kan şekeri regülâsyonun doğrudan bir ölçüsü olan HbA1c ile EYD arasındaki ilişki sorgulanmamıştır. Bu çalışmada EYD ile HbA1c arasındaki ilişki sorgulandı.

Materyal ve Metot: Kardiyoloji kliniğimize başvuran toplam 90 hasta ardışık olarak çalışmaya dâhil edildi. Hastaların EYD'leri ekokardiyografi ile ölçüldü ve onların HbA1c değerleri ile karşılaştırıldı.

Bulgular: Vücut kitle indeksi, açlık kan şekeri, HbA1c, vücut ağırlığı ile EYD arasında doğrusal bir ilişki bulundu ($p<0.05$).

Sonuç: Bu çalışmada, HbA1c ve EYD arasında doğrudan bir ilişki olduğu gösterildi ve EYD'nin preklinik diyabetin takibinde ve glikoz kontrolünde rehberlik edebileceği vurgulandı.

Anahtar kelimeler: Epikardiyal yağ dokusu, diabetes mellitus, hemoglobin A1c

Introduction

The adipose tissue ingrained between the myocardium and visceral pericardium is defined as epicardial adipose tissue (EAT) and it has similar biologically features to visceral adipose tissue[1,2]. Increased thickness of EAT has associated with the presence of diabetes mellitus (DM), coronary artery disease (CAD) and metabolic syndrome[3].

Diabetes mellitus (DM) is a chronic multisystem disease that is common all over the world and its prevalence is increasing markedly[4]. The DM leads to many complications like cardiovascular disease, diabetic neuropathy and retinopathy, chronic kidney disease[5-7]. In order to control the DM complications and determine its prognosis, there is a need for diagnostic methods that will monitor whether diabetes is under long-term control and determine the treatment protocol accordingly.

Hemoglobin A1c has been relevant as an indicator of mean blood glucose concentrations and has a significant role in evaluating DM control. The close relationship between cardiovascular risk and HbA1c levels has also been broadly presented[8,9]. The relationship of EAT on DM and cardiovascular diseases has been previously examined in many studies[10,11]. However, we could not find any study examining the relationship between EAT and HbA1c in our literature research. If a direct relationship can be found between these two parameters, which are indicators of cardiovascular diseases, it will be possible to predict both how well long-term sugar regulation of DM is achieved and a cardiovascular complication that may occur due to DM in the future. In this study, it was aimed to investigate whether there is a relationship between HbA1c and EAT, which are two independent parameters known to be directly related to cardiovascular diseases and DM.

Materials and Methods

This prospective cohort study was conducted at a tertiary hospital in Turkey. A total of 90 (52 diabetics and 38 nondiabetics-the control group) patients who were admitted to our cardiology clinic included between February 2021 and May 2021 were included in the study consecutively. Patients with echogenic anomalies, left ventricular dysfunction, any effusion, abnormal thyroid function were excluded from the study. Participants were divided into two groups; group 1 had 52 patients with DM (the patient group), and group 2 consisted of 38 non-diabetic patients (the control group). All participants were informed and obtained consent before study. This study was approved by the local ethics committee.

Echocardiography examination was performed on all participants. After at least eight hours of fasting, blood samples were taken from the antecubital vein and sent to the laboratory. All participants' blood pressures were measured on the physical examination. Systolic blood pressure ≥140 mmHg, diastolic ≥90 mmHg, or a need for antihypertensive medication was defined as hypertension. Total cholesterol ≥220 mg/dl and/or triglyceride ≥150 mg/ dl was defined as hyperlipidemia. Diagnosis of DM was based on the criteria of American Diabetes Association[12].

The transthoracic echocardiography was performed using an echocardiographic device (Hitachi Arietta 750) with the patient in the left lateral decubitus position, with a 3.0-MHz transducer. Echocardiographs were performed by two cardiologists. We measured the EFT from the parasternal long-axis view as the echo-free space on the free wall of the right ventricle to the epicardium at end-systole[13]. We chose the thickest area of epicardial fat to measure the EFT. We noted the mean point of the three cardiac cycles.

- *Statistical analysis*

The data is shown as mean ± standard deviation or median (interquartile range) for continuous variables and as proportions for categorical variables. Homogeneity of group variances are tested by the Levene test and distribution of the data for normality is tested by the Shapiro–Wilk test. Normally distributed continuous variables are tested with t-test and Mann Whitney U test is used for the variables which are not normally distributed. Categorical variables are examined using Chi-square test. Linear regression analysis was used to evaluate the explanatory power of the variables on epicardial adipose tissue thickness. p-values <0.05 were considered statistically significant.

Results

The mean age of the study population was 54.26 ± 14.17 and 52.2% (n=47) was female. The diabetic patients constituted 57.8% (n=52) of the patients and 42.2% (n=38) of the patients were non-diabetic. The study groups were statistically similar in term of gender, hypertension, cardiovascular diseases, and atrial fibrillation ($p > 0.05$). Dyslipidemia was more common (p=0.001), and body mass index were significantly higher in diabetic patients (p=0.002). The comparison of the study groups can be found in Table 1.

Epicardial adipose tissue was thicker in diabetic patients compared to normal population (4.7 ± 2.2 mm vs. 2.5 ± 1.8 mm, respectively, $p<0.001$). Body mass index, fasting blood glucose, HbA1c and body weight are positively correlated with EAT ($p<0.05$) (Table 2). Scatter-dot graphs of EAT between HbA1c and BMI cab be found in Figure 1 and 2.

Linear regression analysis was performed to detect the explanatory power of age, HbA1c, FBG, creatinine, BMI on epicardial adipose tissue. Regression analysis revealed that age, HbA1c and BMI are independently associated with EAT thickness (Table 3).

Table 1. Baseline characteristics and laboratory results of the study groups.

	Diabetic patients (n=52)	Non-diabetic patients (n=38)	p
Age, mean±SD, y	57.0 (52.0-65.0)	48.5 (41.0-62.2)	0.030
Female	31 (59.6%)	16 (42.1%)	0.100
Hypertension	27 (51.9%)	12 (31.6%)	0.054
Cardiovascular diseases	11 (21.1%)	6 (15.8%)	0.521
Dislipidemia	24 (46.1%)	5 (13.1%)	0.001
Atrial fibrillation	5 (9.6%)	2 (5.3%)	0.446
Height, m	1.65 ± 0.01	1.69 ± 0.08	0.030
Weight, kg	79.7±12.8	74.7±14.8	0.094
Body mass index	29.5±5.03	26.0±4.9	0.002
Glucose, mg/dL	114.0 (97.0-133.5)	92.5 (88.0-97.2)	<0.001
Hemoglobin A1c	6.6 (6.0-7.97)	5.0 (4.8-5.1)	<0.001
Creatinine, mg/dL	0.88 (0.77-1.02)	0.78 (0.70-0.88)	0.004
Epicardial adipose tissue	4.7 ± 2.2	2.5 ± 1.8	<0.001

Table 2. Pearson correlation analysis of epicardial adipose tissue and other variables

	p	r
Body mass index (kg/m^2)	0.001	0.345
Fasting blood glucose	0.004	0.298
HbA1c	<0.001	0.470
Creatinine	0.166	0.147
Height	0.816	0.025
Weight	<0.001	0.398

Table 3. Linear regression analysis of the variables associated with epicardial adipose tissue.

Variable	Odds Ratio	95% Confidence Interval	p-value
Age	0.215	0.002 – 0.068	0.037
HbA1c	0.330	0.152 – 0.786	0.004
Fasting blood glucose	0.021	-0.010 – 0.012	0.844
Creatinine	0.009	-1.908 – 2.101	0.924
Body mass index	0.094	0.009 – 0.178	0.031
Constant		-6.824 – -1.003	0.009

Discussion

The present study finds that body mass index, fasting blood glucose, HbA1c and body weight are positively correlated with EAT.

Many studies have shown the relationship of EAT with glucose intolerance, metabolic syndrome, high blood pressure, and atherosclerosis[10,14-16]. Epicardial fat is also associated with diabetes mellitus[11]. Similar to previous studies, we found thicker EAT in patients with DM and those with high BMI. In this study, we found a positive correlation between fasting blood glucose and HbA1c. To our knowledge, this has not been questioned in previous studies.

Before discussing the possible mechanisms on the pathophysiology of this relationship, we would like to say that this relationship may provide a practical benefit to clinicians. Because examining EAT is both a simple and practical method. And even if the fasting blood glucose is normal and diabetes is not diagnosed in individuals with high EAT thickness, it should be kept in mind that HbA1c may be high, and the patients can be diagnosed and treated in the prediabetes period.

HbA1c is described as the stable bring closer of glucose to the N-terminal valine of the β-chain of hemoglobin. The process of HbA1c formation consists of an irreversible structural rearrangement step and a reversible hemoglobin glycation step and happens continuously in vivo along the entire lifetime of erythrocytes (120 days), depending on plasma glucose levels[17].

There are studies showing that HbA1c is associated with the development of cardiovascular disease even in people who do not have DM or cardiac disease yet[18]. Both EAT and HbA1c are associated with cardiovascular disease independent of diabetes. Also, EAT is increased in individuals with T2 DM independently of total body fat or BMI[19]. Similarly, another

study found that type 1 DM was associated with an increase in EAT independent of BMI and hyperlipidemia[20]. Both EAT and HbA1c are associated with cardiovascular disease independent of diabetes. Therefore, it was not surprising that the two were positively correlated with each other.

There are many reasons for the linear relationship between HbA1c and epicardial adipose tissue. We think that the first of these is an indirect mechanism due to the increased cardiovascular risk factors like obesity, HT. However, in a study it was shown that EAT was correlated with insulin resistance and impaired glucose tolerance[21]. Adipose tissue secrete pro-inflammatory substances like TNF-α and PAI-1. Systemic micro-inflammation increases insulin resistance and causes the onset and exacerbation of atherosclerosis[22]. As this inflammation leads to atherosclerosis, thick EAT may have a direct effect on HbA1c by increasing the level of glycated hemoglobin independent of obesity and DM.

EAT's free fatty acids uptake and release capacity is bigger than the other visceral adipose tissue and it has a higher rate of insulin-induced lipogenesis than the other visceral adipose depots[23,24].

This study has some limitations. First of all, it was done with a small group. Since other factors such as BMI, hyperlipidemia, and CAD that may affect EAT have not been ruled out, it have not been determined how much the relationship between EAT and HbA1 is affected by other factors.

In conclusion, this study is the first to show a direct relationship between HbA1c and EAT. It has been shown that EAT can guide the follow-up of preclinical diabetes and glucose control. In addition, EAT was thicker in the DM group compared to the Control group.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Ethical approval

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