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The Relationship Between Increased Epicardial Fat Thickness and Left Ventricular Hypertrophy and Carotid Intima-Media Thickness in Patients With Nonfunctional Adrenal Incidentaloma

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Abstract

Background: Emerging evidences indicate that patients diagnosed with Adrenal Incidentaloma (AI) may present cardiovascular complications. Epicardial fat thickness (EFT) has recently been described as a new risk factor and an active player in metabolic syndrome and cardiovascular disease.
Objectives: We aimed to evaluate the relationship between EFT and left ventricular hypertrophy and carotid intima-media thickness, which are both strong predictors of cardiovascular morbity and mortality, in patients with nonfunctioning AI.
Patients and Methods: We evaluated 51 patients (36 females and 15 males) diagnosed with AI and 35 (29 females, 6 males) age, gender and body mass index (BMI) matched healthy controls in terms of cardiovascular risk parameters. Epicardial fat was identified as the echo-free space between the outer wall of the myocardium and the visceral layer of the pericardium.
Results: Epicardial fat thickness was significantly higher in patients with AI when compared to the control group (0.89 $\pm$ 0.32 cm vs. 0.74 $\pm$ 0.26 cm; P = 0.023). left ventricular (LV) mass index and median carotid intima-media thickness (CIMT) were also higher in subjects with AI than in controls (99.8 g/m^2 vs. 86.9 g/m^2; P = 0.024 and 7.5 mm (5.5 - 11.5) vs. 6.5 mm (4.5 - 9.5); P = 0.017). There was a positive correlation between EFT, LV mass index, EFT and CIMT (r = 0.315, P = 0.004; r = 0.363, P < 0.001; respectively).
Conclusions: In this study we showed that EFT, measured by echocardiography is higher in subjects with AI when compared to healthy controls. epicardial fat thickness had the best independent correlation with AI in multiple logistic regression analysis. Incidentaloma is also associated with increased left ventricular mass index and CIMT. Adrenal incidentaloma patients may show early cardiac changes, such as increased left ventricular mass and increased CIMT.

Keywords: Adrenal Incidentaloma, Epicardial Fat, Atherosclerosis

1. Background

Adrenal incidentaloma (AI) is an adrenal mass that is discovered incidentally during a radiologic examination performed for indications other than to investigate for primary adrenal disease. The association of AI with morbidity is not well known and its management is still controversial. Emerging evidence indicates that patients diagnosed with adrenal incidentaloma may present cardiovascular complications. Although AI are considered hormonally inactive, previous studies have shown that adrenal incidentalomas may be related to increased incidence of cardiovascular conditions (1). Patients with AI can have metabolic disturbances with high prevalence of dyslipidemia, hypertension, impaired glucose tolerance and metabolic syndrome (2, 3). These cardiovascular conditions tend to be more frequent in patients with subclinical cushing's syndrome (SCS); though, they can also be found in patients with nonfunctioning adrenal masses (1). epicardial fat thickness (EFT) has been alleged as a new risk factor and an active player in metabolic syndrome and cardiovascular disease (4). Epicardial fat tissue can be considered as a metabolically active endocrine organ and it expresses and secretes cytokines, vasoactive substances, adipokines and growth factors that can influence the myocardium and coronary arteries. Increased EFT is related to various clinical conditions, such as obesity, diabetes, metabolic syndrome, adrenal incidentaloma, growth hormone defi-

ciency and polycystic ovary syndrome (5). In one study, epicardial fat was shown to be related with increased left ventricular mass in healthy subjects with a wide range of adiposity (6). Whether this relationship also exists in patients with AI requires further investigations. Previous data demonstrated an increased rate of atherosclerosis indicators, such as higher levels of adipocytokines, insulin resistance and increased carotid intima-media thickness (CIMT) in patients with AI (3, 5).

2. Objectives

In this study, we aimed to evaluate the relationship between EFT, left ventricular hypertrophy and CIMT in patients with AI, which are both strong predictors of cardiovascular morbity and mortality.

3. Patients and Methods

The present study was a case-control study. We sequentially selected 51 patients (36 females and 15 males) diagnosed with AI and 35 (29 females and 6 males) age, gender and body mass index (BMI) matched healthy controls between February 2012 and May 2014 in ankara Numune education and research hospital at the department of endocrinology and metabolism. The study size was determined according to inclusion and exclusion criteria. The control group was selected from the general population. An informed consent was obtained from all participants. The study protocol was approved by the local ethics committee.

Patients, who had a history of pheochromocytoma, Cushing's syndrome, aldosteronoma, arterial hypertension, morbid obesity, diabetes mellitus, cardiovascular disease, cerebrovascular disease, chronic inflammatory disease, chronic hepatitis, malignancy and those who were smokers, were excluded from the study. All patients and controls underwent physical examination including measurement of blood pressure, weight (kg) and height (m). body mass index (BMI) was calculated as follows: BMI = weight (kg)/height (m^2) . Pheochromocytoma was excluded by normal limits of urinary fractionated metanephrines using liquid chromatography with the mass spectrometric method. For the primary aldosteronism (PA), we collected blood samples in the morning, after the patient had been standing up for at least two hours and seated for 5 - 15 minutes (7, 8). primary aldosteronism was excluded when the upright plasma aldosterone to plasma renin activity ratio was lower than 20. After a 12 - hour overnight fasting, venous blood samples were collected from patients and controls in the morning for laboratory test parameters. Serum cortisol, plasma adenocorticotropic hormone (ACTH), upright plasma aldosterone and plasma renin activity, urinary catecholamines, metanephrine, normetanephrine and urinary free cortisol excretion were determined in basal conditions. In the study patients, these tests were within normal limits. All patients performed overnight 1-mg dexamethasone test for screening Cushing's syndrome. Suppression was adequate when morning cortisol was below 1.8 μg/dL. When the plasma cortisol supression was inadequate, two-day 2-mg classic dexamethasone suppression test was performed. The CIMT was measured by the same physician from a non-invasive ultrasound of the bilateral common carotid arteries as well as internal and external carotid arteries, using a high-resolution B-mode ultrasound machine (Hitachi® EUB 7000 HV) with a 6 to 13 MHz linear array transducer imager. All of the scans were recorded. The intima-media thickness was defined as the distance between the leading edge of the vessel lumen-intima interface and the leading edge of the media-adventitia interface. Mean CIMT wall measurements from left and right side were averaged.

Each patient had a transthoracic 2D-echocardiography using commercially available equipment (GE Vingmed Ultrasound, Vivid 7Pro, Horten, Norway) using a 2.5-MHz transducer. All examinations were recorded and evaluated by a second sonographer blinded to patient and control groups. Standard parasternal and apical views were obtained in the left lateral decubitis position. Left ventricular mass was derived from M-mode measurements obtained from parasternal long-axis. The following variables were systematically derived: End-diastolic interventricular septum (IVS) thickness, end-diastolic posterior wall (PW) thickness, Left Ventricular end-diastolic Diameter (LVD). The M-mode left ventricular mass was calculated using the Penn equation: LV mass = 1.04 [(LVD + IVS + PW)^3 - LVD^3] - 13.6 g; LV mass index was derived by dividing LV mass value to body surface area.

Epicardial fat was identified as the echo-free space between the outer wall of the myocardium and the visceral layer of the pericardium. epicardial fat thickness was measured perpendicularly on the free wall of the right ventricle at end-systole in three cardiac cycles. Maximum EFT was measured at the point on the free wall of the right ventricle along the midline of the ultrasound beam, parallel to aortic valve. Three sets of measurements were averaged.

3.1. Definitions

Adrenal incidentaloma lesions were incidentally discovered by computed tomography (CT) or magnetic resonance imaging (MRI) scan in patients who were evaluated for unrelated diseases such as abdominal pain, urolithiasis

or cholelithiasis. The radiologic characteristic of masses was consistent with benign lesions (size < 4 cm, precontrast HU less than 10; 10 minute washout > 50%; 15 minute washout > 60%). In labaratory analysis the range of normal levels were for serum fasting blood glucose: 70 - 109 mg/dL, uric acid: 2.4 - 5.7 mg/dL, insulin: 2.6 - 24.9 μIU/mL, homocysteine: 5 - 12 μmol/L, high-sensitivity C-reactive protein (hsCRP): 0 - 5 mg/L, fibrinogen: 200 - 400 mg/dL, thyroid stimulating hormone (TSH): 0.27 - 4.2 μIU/mL, free T3: 2.0 - 4.4 pg/mL, free T4: 0.93 - 1.7 ng/dL.

3.2. Statistical Analysis

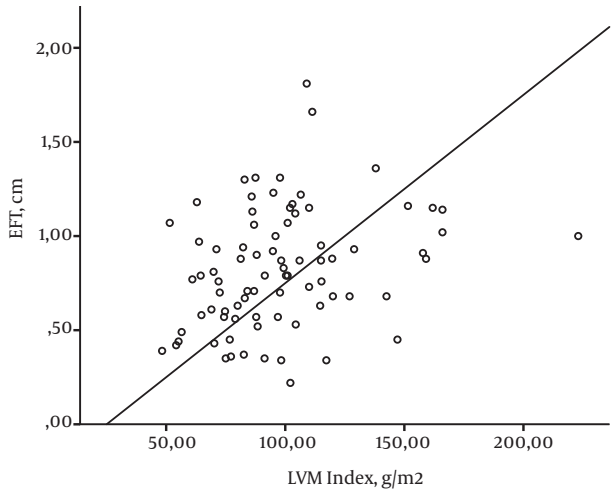
Statistical package for social sciences for windows 18.0 (SPSS Inc., Chicago, IL) was used for statistical analysis of the data in this study. The Shapiro-Wilk test was used to test the normality of the continuous data. Normally distributed continuous data were presented as mean $\pm$ standard deviation; non-normally distributed continuous data were presented as median (minimum-maximum); and categorical variables were presented as number of cases (percentages). Group comparisons were performed using Student's t test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Nominal data were analyzed by Pearson's Chi-square or Fisher's exact test, where applicable. Degrees of association between continuous variables were evaluated by Spearman's rank correlation analyses. Correlation between two parameters were evaluated by Pearson's correlation analysis. The optimal cut-off point of EFT to determine incidentaloma was evaluated by receiver operator characteristic (ROC) analysis, giving the maximum sum of sensitivity and specificity for the significant test. Determining the best predictors, which discriminate cases and controls from each other, was evaluated by multiple logistic regression analysis. Any variable whose univariable test had a p value of < 0.25 was accepted as a candidate for the multivariable model along with all variables of known clinical importance. Adjusted odds ratios, 95% confidence intervals and Wald statistics also were calculated. A p value of < 0.05 was considered statistically significant.

4. Results

A total of 51 AI patients and 35 controls were included in the study. Gender, height, weight, BMI, systolic and diastolic blood pressure were similar between incidentaloma and control groups. The mean age of the patient group was 52.57 $\pm$ 10.24 and the mean age of the control group was 52.09 $\pm$ 7.75 (P = 0.804). Adrenal incidentalomas were found unilateral in 41 cases (80%). Fourteen (27%) were localized in the right adrenal gland and the 27 (53%) were in the left gland. Bilateral adrenal incidentaloma masses were seen in 20% of all cases. The mean diameter of the adrenal adenomas was 23.9 $\pm$ 10.52 mm. Plasma fasting glucose, HbA1c, serum lipid levels, uric acid, homocysteine, high sensitivity C-reactive protein, fibrinogen, TSH, free T3 and free T4 levels were not found significantly different between the two groups (Table 1). The EFT was found significantly higher in patients with adrenal incidentaloma when compared to the control group (0.89 $\pm$ 0.32 cm vs. 0.74 $\pm$ 0.26 cm; P = 0.023). The LV mass index was also higher in subjects with adrenal incidentaloma than in controls [99.8 g/m^2 (55.2 - 166) vs. 86.9 g/m^2 (48.3 - 223); P = 0.024].

When CIMT was compared between the two groups, median CIMT was significantly higher in patients with AI [7.5 mm (5.5 - 11.5) vs. 6.5 mm (4.5 - 9.5); P = 0.017] (Table 1). There was a positive correlation between EFT, LV mass index, EFT and CIMT (r = 0.315, P = 0.004; r = 0.363, P < 0.001; respectively) (Figure 1 and 2).

Figure 1. Correlation Analysis of Left Ventricular Mass and Epicardial Fat Thickness



There was a positive and significant correlation between LVM index and EFT (r = 0.315; P = 0.004).

Receiver operating characteristic (ROC) curve analysis showed an EFT thickness of 0.874 cm to be the optimal cut-off to discriminate the patient and control groups. The associated sensitivity and specificity were 61.2% and 77.1%, respectively. The positive and negative predictive values were 78.9% and 58.7%. The corresponding area under the ROC curve was 0.650 (95%CI: 0.529 - 0.771) (Figure 3).

The area under the curve (AUC) was statistically significant [AUC = 0.650 (95%CI: 0.529 - 0.771), P = 0.019]. The best cut-off value of EFT was 0.874 and at this value sensitivity was 61.2%, specifity was 77.1%, positive and negative predic-

Table 1. Comparison of General Characteristics and Labaratory Parameters of Patients with Adrenal Incidentalomas and Controls[a,b]

	Adrenal Incidentalomas (n = 51)	Controls (n = 35)	P Value
Age[a], years	52.57 ± 10.24	52.09 ± 7.75	0.804
Gender, F/M	36/15	29/6	0.193
Height[a], cm	164.06 ± 7.89	160.51 ± 7.29	0.038
Weight[a], kg	81.69 ± 13.25	77.80 ± 12.30	0.173
BMI[a], kg/m^2	30.32 ± 4.54	30.24 ± 4.70	0.931
SBP[a], mm/Hg	125.61 ± 21.48	125.49 ± 16.92	0.989
DBP[a], mm/Hg	79.11 ± 13.75	78.24 ± 9.60	0.893
HbA1c[b], %	5.80 (4.8 - 6.3)	5.80(5.2 - 6.6)	0.975
Glucose[a], mg/dL	93.29 ± 7.74	91.20 ± 11.44	0.349
Triglyceride[b], mg/dL	118 (45 - 405)	136 (66 - 272)	0.358
Total Cholesterol[a], mg/dL	207.73 ± 50.94	206.71 ± 32.63	0.918
HDL-C[b], mg/dL	51 (30 - 100)	52 (30 - 89)	0.377
LDL-C[a], mg/dL	128.20 ± 34.48	122.49 ± 29.45	0.426
Uric acid[a], mg/dL	5.36 ± 1.26	4.94 ± 1.09	0.120
Insulin[b], μIU/mL	11.7 (4.3 - 48.7)	8.9 (3.6 - 29)	0.034
HOMA-IR[b]	2.9 (0.9 - 11.1)	2.0 (0.7 - 7.3)	0.025
Homocysteine[b], μmol/L	9.4 (2.5 - 29.5)	8.6 (2.7 - 22.0)	0.986
hsCRP[b], mg/L	2.5 (0.4 - 22.8)	2.2 (0.5 - 17)	0.623
Fibrinogen[a], mg/dL	410.57 ± 98.66	390.60 ± 63.99	0.258
TSH[b], mIU/L	1.7 (0.01 - 4.9)	2.1 (0.02 - 7)	0.550
Free T3[b], pg/mL	3.0 (1.2 - 5.1)	2.9 (1.0 - 3.5)	0.681
Free T4[b], ng/dL	1.2 (0.9 - 1.7)	1.1 (0.9 - 1.07)	0.631
CIMT[b], mm	7.5 (5.5 - 11.5)	6.5 (4.5 - 9.5)	0.017
EFT[a], cm	0.89 ± 0.32	0.74 ± 0.26	0.023
Median LVM index[b], g/m^2	99.8 (55.2 - 166)	86.9 (48.3 - 223)	0.024

Abbreviations: BMI, body mass index pressure; CIMT, carotid intima-media thickness; DBP, diastolic blood pressure; EFT, epicardial fat thickness; HDL-C, high-density lipoprotein cholesterol; hsCRP, high sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; LVM, left ventricular mass; SBP, systolic blood; TSH, thyroidstimulating hormone.
[a]Values are presented as mean ± SD.
[b]Values are presented as median (min-max).

tive values were 78.9% and 58.7%; respectively.

Multivariate logistic regression analysis was performed to evaluate the independent associates of AI. The model included gender, body weight, CIMT, uric acid, homeostasis model assessment-estimated Insulin resistance (HOMA-IR), LV mass index and EFT (Table 2). Among other variables, EFT was found to be the only independent associate [OR: 3.505 (95% CI: 1.158 - 10.611; P = 0.026)]. Furhtermore, CIMT, uric acid, HOMA-IR and LV mass index, which were statistically significant in univariate analysis, lost significance in multivariate logistic regression analysis (P > 0.05).

We compared the values of steroidogenesis hormones in EFT $\geq$ 0.874 and EFT < 0.874 groups. Plasma ACTH, plasma cortisol, urinary cortisol, dexamethasone suppression test, DHEA-S, plasma aldosterone and plasma renin activity were similar between the groups (Table 3). No significant single correlation was found between steroidogenesis hormone levels and EFT thickness (Table 4). By using the "weighted average method" patients were divided to quartiles according to EFT measurements (EFT< 0.59 cm = quartile 1, 0.59 - 0.82 cm = quartile 2, 0.83 -1.04 cm = quartile 3, >1.04 cm = quartile 4). No statistically significant difference was observed between EFT quartiles and mean plasma cortisol levels (P = 0.089).

Table 2. Multiple Logistic Regression Analysis Model for Gender, Weight, Carotid Intima-Media Thickness, Uric Acid, Homeostasis Model Assessment-Estimated Insulin Resistance, Left Ventricular Mass Index and Epicardial Fat Thickness

Variables	Odds Ratio (OR)	95%CI for OR		Wald	P Value
		Lower Limit	Upper Limit		
Male factor	1.183	0.323	4.337	0.064	0.800
Weight	0.994	0.952	1.038	0.071	0.790
CIMT mean	1.363	0.850	2.185	1.652	0.199
Uric acid	1.201	0.764	1.889	0.632	0.427
HOMA-IR	1.236	0.884	1.729	1.538	0.215
LVM index	1.006	0.987	1.025	0.326	0.568
EFT $\geq$ 0.874	3.505	1.158	10.611	4.926	0.026

Abbreviations: CIMT, Carotid intima-media thickness; EFT, Epicardial fat thickness; LVM, Left ventricular mass.

Table 3. Comparison of the Values of Steroidogenesis Hormones With Epicardial Fat Thickness (EFT) $\geq$ 0.874 and EFT < 0.874 Groups[a,b]

Variables	Epicardial Fat Thickness $\geq$ 0.874	Epicardial Fat Thickness < 0.874	P Value
Plasma ACTH[a], pg/mL	22 (4.3 - 168)	16.2 (4.3 - 42.6)	0.4433
Plasma cortisol[b], μg/dL	16.1 $\pm$ 4.4	13.9 $\pm$ 3.9	0.0960
Urinary cortisol[b], μg/24 h	40.5 $\pm$ 16.8	41.4 $\pm$ 25.5	0.9267
DST[b], μg/dL	1.2 $\pm$ 0.56	1.1 $\pm$ 0.33	0.7556
DHEA-S[b], μg/dL	97.1 $\pm$ 50.3	89.9 $\pm$ 90.7	0.7680
Plasma aldosterone[b], ng/dL	131.7 $\pm$ 117.6	165.1 $\pm$ 123.6	0.4079
Plasma renin activity[a], ng/ml/h	2.5 (0.26 - 19.6)	3.3 (0.58 - 28.5)	0.4041

Abbreviation: DST, Dexamethasone suppression test.
[a]Values are presented as median (min - max).
[b]Values are presented as mean $\pm$ SD.

Table 4. Single Correlation Between Hormone Levels and Epicardial Fat Thickness

Variables	Epicardial Fat Thickness	
	r	P
Plasma ACTH	0.0435	0.7690
Plasma cortisol	0.2037	0.1649
Urinary cortisol	0.2312	0.3409
DST	0.0806	0.5820
DHEA-S	0.1802	0.3078
Plasma aldosterone	0.0362	0.8271
Plasma renin activity	-0.0038	0.9817

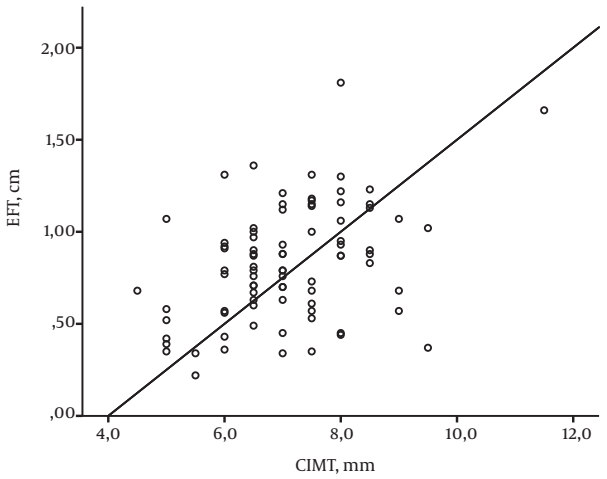
Abbreviation: DST, Dexamethasone suppression test.

5. Discussion

In this study we showed that EFT, measured by transthoracic echocardiography is higher in subjects with AI when compared to healthy controls. The EFT was the best independent associate of AI in multiple logistic regression analysis. Incidentaloma was also associated with increased left ventricular mass index and CIMT.

Based on the findings of recent studies, patients with

Figure 2. Correlation Analysis of Epicardial Fat Thickness and Carotid Intima-Media Thickness



There was a positive and significant correlation between EFT and CIMT (r = 0.363; P < 0.001).

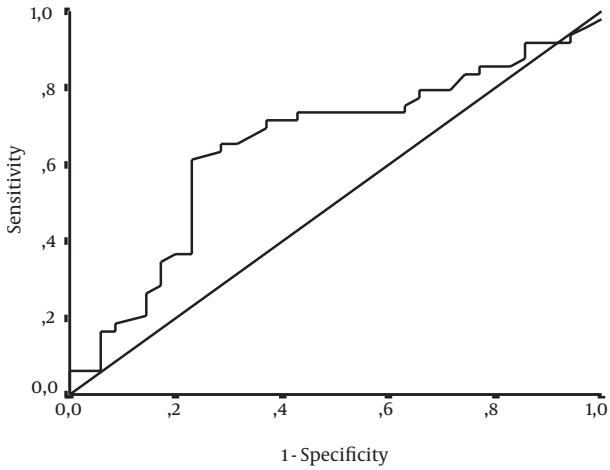


Figure 3. Receiver Operating Characteristic (ROC) Curve Analysis of Epicardial Fat Thickness in Discriminating the Adrenal Incidentaloma and Control Groups

AI have increased cardiovascular risk (3, 7). Patients with AI have increased prevalence of metabolic syndrome and impaired endothelial function (9, 10). Patients with incidentalomas have higher hypertension prevalence and higher risk of atherosclerosis measured as increased CIMT (3). Iacobellis et al. showed early LV structural changes in asymptomatic non-functioning AI, such as increased left ventricular mass (6). Although the exact mechanism underlying increased cardiovascular risk remains unknown, different mechanisms have been suggested by previous studies. Ermetici et al. showed increased adipokine levels in patients with AI (11). We measured high sensitivity C-reactive protein and fibrinogen levels as inflammatory risk markers, but we could not find any difference between nonfunctioning AI and control groups. Others suggested that increased morning cortisol or insulin resistance were associated with increased cardiovascular complications (12, 13). Some authors hypothesed that subclinical cortisol hypersecretion in nonfunctioning AI patients may affect carbohydrate and insulin metabolism. High rates of hypertension, diabetes and obesity can be seen in nonfunctioning AI (14). In our study, HOMA-IR was significantly higher in AI patients in univariate analysis, yet lost significance in multiple logistic regression analysis model.

Echocardiographically-determined LV hypertrophy was shown to predict cardiovascular morbidity and mortality independent of clinical risk factors including age, gender, smoking, and diabetes (15). Furhermore, CIMT is another predictor of anatomic extent of atherosclerosis and cardiovascular risk (16). We found significantly increased LV mass index and CIMT values in patients with AI, which may indicate increased risk of cardiovascular disease.

The main finding in our study was that increased EFT was observed in patients with nonfunctioning AI. Moreover, in multiple logistic regression analysis, EFT had the best independent correlation with AI. In AI patients, EFT $\geq$ 0.874 cm was found to be 3.505 folds higher compared to controls. Epicardial fat tissue has recently been described as a new risk factor and an active player in cardiovascular disease (17). The biomolecular characteristic of the epicardial fat and its clinical significance have been broadly described by Iacobellis (18, 19). Furthermore, EFT can be considered as a metabolically active endocrine organ and it expresses and secretes cytokines, vasoactive substances, adipokines and growth factors that can influence myocardium and coronary arteries. Epicardial fat had the most significant independent correlationg with myocardial fat (20). Iacobellis et al. reported that EFT and LVM, as measured with echocardiography, are higher in subjects with adrenal incidentaloma and mild Cushing' s syndrome when compared to healthy controls (21). Our findings are consistent with these results.

In a recent study, a high incidence of impaired glucose tolerance (36%) and undiagnosed type 2 diabetes mellitus (5%) were seen in patients with AI when compared to healthy controls. They hypothesized that the subtle autonomous cortisol secretion of the AI may cause an acquired condition of insulin resistance in otherwise normoglycemic and nonobese subjects (1). Barutcu et al. established that HOMA-IR was 5.53 $\pm$ 4.4 in patients with AI while 2.63 $\pm$ 1.46 (P = 0.005) in the control group (22). Peppa et al. found increased frequency of insulin resis-

tance in AI patients when compared with the healthy control group 10. Ermetici et al. showed increased levels of interleukin (6), adiponectin, resistin, tumor necrosis factor α, and monocyte chemoattractant protein-1, which may be the cause of subclinical inflammation in patients with AI. They stated that this insulin resistance may be associated with metabolic syndrome (11). In our study, we did not assess cytokine levels in AI patients, therefore the reason for insulin resistance could not be accurately determined. We hypothesize that increased EFT may be due to insulin resistance, which was observed as higher degrees in patients with nonfunctioning AIs. Nevertheless, increased EFT may be due to other risk factors such as subclinical inflammation, increased resistin or some cytokines. Further studies are needed in this regard. In our study, only nonfunctional adrenal incidentalomas and healthy controls were recruited. In addition, we measured CIMT as a non-invasive indicator of subclinical atherosclerosis and found significantly higher values in the AI group. A positive correlation was found between EFT, LV mass index, EFT and CIMT. The EFT was an independent associate in multiple logistic regression analysis. In addition, CIMT was also shown to correlate with EFT in previous studies (23, 24). As the subjects in the AI group were hormonally inactive and traditional cardiovascular risk factors were similar between groups, we can speculate that increased epicardial fat tissue may be responsible for these early cardiac and vascular changes. However, this hypothesis should be investigated in larger patient groups.

The limitation of our study was the limited number of patients and controls. The evaluation of EFT was made by two-dimentional echocardiography instead of three-dimentional volumetric measurements made by computerized tomography (CT) or cardiac magnetic resonance imaging (MRI).

5.1. Conclusions

In conclusion, adrenal incidentaloma patients may reveal early cardiac changes, such as increased left ventricular mass and increased CIMT. Therefore they should be closely followed for increased cardiovascular complications. Epicardial fat thickness is increased in these patients and is positively correlated with LVM index and CIMT. Epicardial fat may be related to earlier cardiac abnormalities in patients with adrenal incidentaloma. Therefore, echocardiographic measurement of epicardial fat thickness may be a routine part of evaluation of these patients. Prospective studies are needed to investigate the contribution of increased epicardial fat in the development of adverse cardiovascular events in patients with adrenal incidentalomas.

Footnote

Authors' Contribution: Study concept and design: Narin Nasiroglu Imga, Ozgul Ucar Elalmis; acquisition of data: Deniz Sahin; analysis and interpretation of data, Bercem Aycıcek Dogan, Dilek Berker, drafting of the manuscript: Serdar Guler; critical revision of the manuscript for important intellectual content: Mazhar Muslum Tuna; Statistical analysis: Ozgul Ucar Elalmis, Narin Nasiroglu Imga; Administrative, technical, and material support: Narin Nasiroglu Imga; Study supervision: Narin Nasiroglu Imga, Serdar Guler.

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