

Reversal of metabolic syndrome with weight loss decreases epicardial fat more than weight loss alone in women with obesity

Obez kadınlarda kilo vererek metabolik sendromun düzelmesi yalnızca kilo vermeye kıyasla epikardiyal yağ kalınlığını daha fazla azaltır

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ABSTRACT

Objective: In this study, we aimed to investigate the impact of weight loss with diet and exercise on echocardiographically measured epicardial fat thickness (EFT) in women with obesity and whether the change in EFT can be different between the groups whose metabolic syndrome (MetS) status has changed or remained the same with weight loss.

Methods: Seventy four women with obesity who were scheduled for a one-year weight reduction (WR) program were prospectively enrolled in the study. Anthropometric, laboratory, clinical, and echocardiographic parameters were assessed at baseline and after one year for twenty eight women who completed the program and had weight reduction. At the end of one year, all the participants were divided into two groups on the basis of whether their MetS status had changed or remained the same.

Results: Body mass index was significantly reduced from 37.17±5.94 to 31.61±5.55 kg/m² (p<0.001) after the one-year WR program. A significant reduction in EFT was noted after weight loss compared with baseline measurements (0.51±0.15 cm to 0.39±0.14 cm, p=0.001). The decrease in EFT was significantly higher in the patient group with reversal of MetS than in the group whose MetS status did not change with weight loss (0.16±0.68 cm vs. 0.09±0.07 cm, p=0.018, respectively). Reversal of MetS was found to be an independent predictor of the change in EFT.

Conclusion: Long-term, sustained weight loss can significantly reduce echocardiographic EFT, and EFT can be used as an indicator of metabolic profile for WR interventions in women with obesity.

ÖZET

Amaç: Çalışmanın amacı obez kadınlarda diyet ve egzersiz ile kilo vermenin ekokardiyografik olarak ölçülen epikardiyal yağ kalınlığı (EYK) üzerine olan etkisini ve EYK'daki değişimin metabolik sendrom (MetS) durumunda değişiklik olan ve olmayan hasta grupları arasında fark gösterip göstermediğini incelemek idi.

Yöntemler: Bir yıllık kilo verme programına dahil edilmesi planlanan yetmiş dört obez kadın hasta prospektif olarak çalışmaya dahil edildi. Antropometrik, laboratuvar, klinik ve ekokardiyografik parametreler başlangıçta ve programı tamamlayarak kilo vermeyi başaran yirmi sekiz olgu için 1 yıl sonunda tekrar değerlendirildi. 1 yılın sonunda hastalar MetS durumu değişen ve değişmeyenler olarak iki gruba ayrıldı.

Bulgular: Vücut kitle indeksi, 1 yıllık kilo verme programından sonra 37.17±5.94'ten 31.61±5.55 kg/m²'ye (p<0.001) önemli ölçüde azaldı. Kilo verme sonrası bazal ölçümlere kıyasla EYK değerinde anlamlı düzeyde azalma kaydedildi (0.51±0.15 cm'den 0.39±0.14 cm, p=0.001). EYK'daki azalma, MetS durumu kilo verme ile düzelen hasta grubunda, MetS durumu değişmeyen gruba göre anlamlı olarak daha yüksekti (sırasıyla, 0.16±0.68 cm ve 0.09±0.07 cm, p=0.018). MetS durumunun değişmesi EYK değişikliği için bağımsız belirleyici olarak bulundu.

Sonuç: Obez kadınlarda uzun süreli, sürekli kilo kaybı ekokardiyografik olarak ölçülen EYK'nı önemli ölçüde azaltabilir ve EYK kilo verme müdahaleleri için metabolik profilin bir göstergesi olarak kullanılabilir.

Obesity, defined as excessive adipose tissue, is an important public health problem and has a rapidly increasing prevalence worldwide. Obesity is a risk factor for numerous diseases, such as hypertension, diabetes, stroke, obstructive sleep apnea, and coronary heart disease. It is also well known that obesity is associated with increased cardiovascular morbidity and mortality.^[1-3]

Besides the amount of fat, body fat distribution is an important issue. Evidence shows that increased visceral adipose tissue (VAT) may cause metabolic syndrome (MetS) and insulin resistance.^[4] Epicardial adipose tissue (EAT) is a kind of VAT, which secretes hormones, inflammatory cytokines and chemokines as an endocrine organ.^[5] Measurement of epicardial fat thickness (EFT) by echocardiography is a reliable,

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easy, inexpensive, and non-invasive method.^[6] Echocardiographic assessment of EAT has been suggested as a new index of visceral and cardiac adiposity.^[7]

Few studies have investigated the impact of weight loss with bariatric surgery, diet, or exercise programs on EFT as a reliable marker of cardiovascular risk. However, there is not enough data comparing the change in EFT between individuals with obesity who reversed a MetS diagnosis and those whose MetS status did not change with weight loss. In this prospective study, we aimed to elucidate the impact of significant weight loss with diet and exercise program on echocardiographically measured EFT as well as to compare the change in EFT between the groups whose MetS status changed or remained the same with weight loss, in women with obesity.

METHODS

Subjects

This prospective and interventional study was conducted on women with obesity who presented to the Obesity Management Center of Antalya Training and Research Hospital. Seventy four women aged between 18 and 65 years with body mass indices ≥ 30 kg/m² were recruited consecutively. Atherosclerotic vascular diseases (such as cardiovascular disease, cerebrovascular disease, and peripheral arterial disease), reduced ejection fraction (<50%), permanent pacemaker, heart valve disease greater than mild in severity, arrhythmia, uncontrolled diabetes mellitus, hypo and hyperthyroidism, renal failure, hepatic failure, the presence of active infection, chronic systemic inflammatory disease, pulmonary disease, malignancy, pregnancy, severe coagulopathy, drug or alcohol addiction, major depression, and psychosis were the exclusion criteria of the study. Patients who were already receiving medications that modulate EFT, such as statins, glucagon-like peptide 1 (GLP-1) receptor antagonists, sodium-glucose co-transporter inhibitors (SGLT2i) and individuals who had low image quality were excluded. The principles of the Declaration of Helsinki were followed throughout the study, its protocol was approved by the Ethics Committee of Antalya Training and Research Hospital (Approval Date: December 26, 2019; Approval Number: 2019-397), and informed consent was obtained from each participant.

The patients underwent a weight loss program that included medical, behavior, nutrition, and exercise components, which lasted one year. Among the selected participants, twenty eight individuals completed the program and achieved a weight loss of mean 13.79 kg.

Anthropometric and echocardiographic examinations were conducted

at baseline and at the end of the program (after one year) for twenty eight individuals who completed the one-year weight loss program. The program, which is entirely based on lifestyle modification and carried out by healthcare staff consisting of doctors, dietitians, psychologists, physiotherapists, and nurses lasted for a year. The dietitian suggested general healthy eating principles as well as personalized diet programs, diets of 1200-1400 or 1600-1800 calorie sample menus according to their current and target weights. Diet planning was done so that approximately 12%-15% of daily energy was provided from proteins, 25%-30% from fats, and 55%-60% from carbohydrates. The patients were taught calorie calculation using a booklet with sample menus and calorie lists that could be used in calorie calculation. The patients recorded all the foods they consumed daily on the homework forms given, and these forms were evaluated by the dietitian at each visit. In the physiotherapist interview, the type, duration, frequency, and intensity of exercise were decided on an individual basis, taking into account the age, sex, conditioning, preferences, living conditions, and needs of the person. However, in general, aerobic physical activities and muscle-strengthening resistance exercises that an individual could do at home were recommended. In the psychologist evaluation; the existence of conditions such as binge eating, night eating, and emotional eating disorders were evaluated. Emotions that caused eating behavior other than hunger were de-

Abbreviations:

<i>BMI</i>	<i>Body mass index</i>
<i>BP</i>	<i>Blood pressure</i>
<i>CRP</i>	<i>C-reactive protein</i>
<i>EAT</i>	<i>Epicardial adipose tissue</i>
<i>EFT</i>	<i>Epicardial fat thickness</i>
<i>GLP-1</i>	<i>Glucagon-like peptide 1</i>
<i>HC</i>	<i>Hip circumference</i>
<i>HDL-C</i>	<i>High-density lipoprotein cholesterol</i>
<i>HOMA-IR</i>	<i>Homeostasis model assessment of insulin resistance</i>
<i>HT</i>	<i>Hypertension</i>
<i>LAV</i>	<i>Left atrial volume</i>
<i>LAVI</i>	<i>Left atrial volume index</i>
<i>LDL-C</i>	<i>Low-density lipoprotein cholesterol</i>
<i>LVM</i>	<i>Left ventricular mass</i>
<i>LVMi</i>	<i>LVM index</i>
<i>MetS</i>	<i>Metabolic syndrome</i>
<i>MRI</i>	<i>Magnetic resonance imaging</i>
<i>SGLT2i</i>	<i>Sodium-glucose co-transporter inhibitors</i>
<i>TDI</i>	<i>Tissue Doppler imaging</i>
<i>VAT</i>	<i>Visceral adipose tissue</i>
<i>WC</i>	<i>Waist circumference</i>

terminated. Cognitive behavioral therapy was administered to eligible patients. In the next step, groups of 12-20 people were formed, and group meetings were held first once a week and then every 15 days until they reached their target weight. The aim of the meetings was to initiate a modification of consciousness in patients with the purpose of instilling a habit of healthy living and nourishment as a vital behavior. Group meetings were held once a month for the last four months, aiming to maintain the target weight.

Clinical information and current cardiovascular medication use were obtained from each patient. Height, weight, waist circumference (WC), and hip circumference (HC) were measured when fasting and standing with standard measuring tools. WC was measured to the nearest 0.5 cm on bare skin during mid-respiration, at the natural indentation between the tenth rib and the iliac crest. Body mass index (BMI) was calculated as body weight divided by height squared (kg/m^2). Waist to hip ratio was calculated as WC divided by HC. The blood pressure (BP) was measured after at least 10 minutes of rest in a sitting position. The mean of three measurements from each patient was recorded. Patients were defined as having hypertension (HT) if their systolic BP was >140 mm Hg, their diastolic BP was >90 mm Hg, or they were using an antihypertensive medication.^[8] Blood samples were obtained after overnight fasting. Fasting blood glucose, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides, C-reactive protein (CRP), fasting glucose, fasting insulin, c-peptide, and homeostasis model assessment of insulin resistance (HOMA-IR) were all recorded.

C-peptide levels and complete blood counts were measured using standard methods. HOMA-IR was calculated using the method described by Matthews et al.^[9] NLR was defined as the log e neutrophil count/ log e lymphocyte count within the peripheral blood. Diagnosis of diabetes mellitus was based on current criteria established by American Diabetes Association.^[10] MetS was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III criteria,^[11] but WC >80 cm was accepted as MetS criterion for Turkish women.^[12] Delta (d) values were obtained by subtracting one-year values from the baseline values.

At the beginning and after the weight loss, the

patients' MetS status was determined according to whether they had MetS or not. The patients who had three or more of the MetS criteria were accepted as having MetS. After weight loss, these criteria were re-evaluated and individuals who had two or less of the criteria were accepted as having a reversal of MetS. At the end of one year, the patients were divided into two groups as those whose MetS status had changed (patients who had reversal of MetS) or not (patients who had MetS both at the beginning and after weight loss and patients who did not have MetS).

Two-dimensional echocardiography and EFT

Each subject underwent transthoracic 2D and Doppler echocardiography according to the recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging.^[13] Standard parasternal and apical views were obtained in the left lateral decubitus position using a Phillips iE33 ultrasound machine (Philips Medical Systems, Andover, USA) with a 3.5 MHz transducer. EFT was identified as the echo-free space in the pericardial layers on 2D echocardiography. It was measured on the free wall of the right ventricle at end-diastole, from both parasternal long axis and parasternal short axis views, using the mean of three consecutive beats as previously described (Figure 1).^[14] Left ventricular mass (LVM) was estimated using the anatomically validated formula of Devereux et al.^[15] Left atrial volume (LAV) was calculated using the biplane Simpson method. LVM and LAV were adjusted to body surface area and height as LVM in-

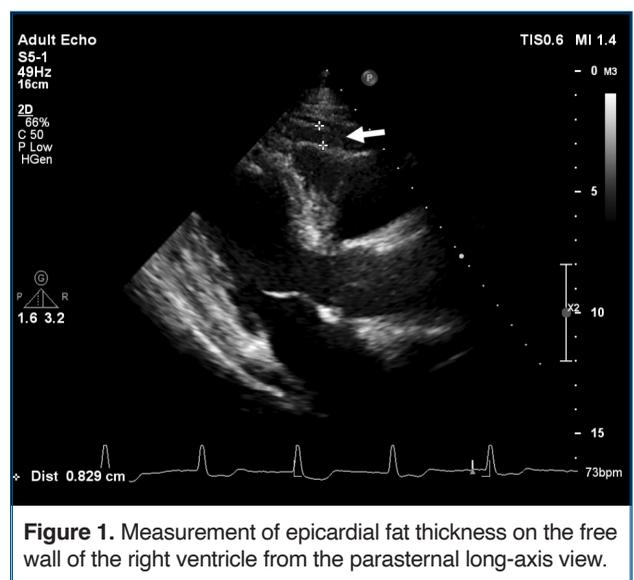


Figure 1. Measurement of epicardial fat thickness on the free wall of the right ventricle from the parasternal long-axis view.

Table 1. Baseline characteristics of the study population, including the patient groups of MetS status changed and unchanged after one-year weight loss program

	All patients (n=28)	MetS status unchanged (n=18)	MetS status changed (n=10)	<i>p</i>
Age (years)	54±9	53.6±7.6	55.4±11.9	0.620
Diabetes mellitus (n)	12 (42.9)	5 (41.8)	7 (70.0)	0.050
Hypertension (n)	13 (46.4)	7 (38.9)	6 (60.0)	0.433
Metabolic syndrome (n)	16 (57.1)	6 (33.3)	10 (100)	<0.001
Body mass index (kg/m ²)	37.2±5.9	38.1±6.7	35.5±4.2	0.278
Waist circumference (cm)	107.9±15.1	112.4±16.6	105.5±11.3	0.254
Waist to hip ratio	0.92±0.11	0.94±0.10	0.87±0.11	0.131

Data are presented as mean±standard deviation for continuous variables and as frequency (%) for categorical variables.
MetS: Metabolic syndrome.

dex (LVMI), LVM/height, LAV index (LAVI), and LAV/height. Early mitral inflow velocity (E wave), late mitral inflow velocity (A wave), and E/A ratio were also recorded. Early diastolic velocity of the medial mitral annulus (e) was recorded using tissue Doppler imaging (TDI), and E/e ratio was also evaluated. All measurements were performed by a single investigator who was blinded to the clinical data of the patients. For the reliability of the EFT average measurement, the interclass correlation coefficient for the intra-observer variability was 0.912 (95% confidence interval [CI] 0.903-0.958; $p < 0.001$).

Statistical analysis

Discrete and continuous variables were presented as mean ± standard deviation. The comparison of the change in the variables from baseline to one-year weight loss was performed with a paired t-test. The Shapiro-Wilk test was used to determine the assumption of normality. Comparisons of normally distributed continuous variables were performed with the Student's t-test and with the Mann-Whitney U test for non-parametric continuous variables. The relationships between two categorical variables were determined by the chi-squared test. Changes (Δ) in study parameters were calculated as subtracting one-year values from the baseline values. The relationships between Δ EFT and Δ selected anthropometric and echocardiographic measures were calculated using Pearson's correlation coefficients analysis. The linear regression analysis was performed to define the independent predictors of Δ EFT. Intraclass correlation coefficient was calculated with a 95% confidence interval to evaluate the reliability of the EFT mea-

surements. p value of < 0.05 was considered statistically significant. Statistical analyses were performed using the SPSS statistical software (version 25) (IBM Corp., Armonk, NY, USA).

RESULTS

From a total of seventy four participants with obesity, twenty eight women completed the one-year weight loss program. The mean age of our study group was 54±9 years. Baseline demographic and clinical characteristics of the study group are summarized in Table 1. Changes in anthropometric and echocardiographic measurements and biochemical values are shown in Table 2. Patients lost an average of 13.79±4.65 kg with an average decrease of 14.8% within the one-year weight loss program. Mean BMI reduced from 37.17±5.94 kg/m² to 31.61±5.55 kg/m² ($p < 0.001$). Mean WC decreased from 109.93±15.06 cm to 97.46±15.58 cm ($p < 0.001$).

EFT significantly decreased from 0.51±0.15 cm to 0.39±0.14 cm ($p = 0.001$) after this weight loss program. There were no significant differences between baseline and after weight-loss echocardiographic measurements including LVM, LAV, E/A and E/e ratios. In the laboratory tests, there was a significant decrease in fasting glucose, fasting insulin, HOMA-IR, CRP, and a significant increase in HDL-C levels.

At the onset of the study, 16 patients had MetS. After weight loss, 10 of the 16 patients experienced a reversal of MetS. 6 patients whose MetS diagnosis did not reverse and 12 patients who did not have MetS both at the beginning and after the one-year weight loss program comprised the pa-

Table 2. Changes of anthropometric, biochemical, and echocardiographic measurements in women with obesity after one-year weight loss program

	Baseline (n=28)	After one year (n=28)	p
Body weight (kg)	92.81±12.49	79.02±12.38	<0.001
Body mass index (kg/m ²)	37.17±5.94	31.61±5.55	<0.001
Body surface area (m ²)	1.93±0.12	1.80±0.14	<0.001
Waist circumference (cm)	109.93±15.06	97.46±15.58	<0.001
Hip circumference (cm)	120.60±11.34	112.10±13.29	<0.001
Waist/hip	0.97±0.22	0.83±0.02	0.075
Epicardial fat thickness (cm)	0.51±0.13	0.39±0.10	<0.001
Systolic blood pressure (mm Hg)	123.75±17.03	116.78±9.92	0.017
Diastolic blood pressure (mm Hg)	77.14±10.49	76.42±6.78	0.726
Total cholesterol (mg/dL)	212.85±46.23	218.57±38.51	0.167
LDL-cholesterol (mg/dL)	127.53±36.87	132.07±27.16	0.217
HDL-cholesterol (mg/dL)	59.53±13.76	65.28±15.16	<0.001
Triglyceride (mg/dL)	126.25±62.15	110.87±45.47	0.056
Fasting glucose (mg/dL)	105.14±20.22	99.32±15.57	0.029
Fasting insulin (uIU/mL)	8.22±3.12	5.06±1.73	<0.001
HOMA-IR	2.00±0.82	1.26±0.47	0.001
C-peptide (µg/L)	2.49±0.52	2.85±1.28	0.674
C-reactive Protein (mg/dL)	6.03±5.86	3.34±2.66	0.018
Neutrophil lymphocyte ratio	1.85±1.08	1.80±0.49	0.846
Mitral E velocity (E) (cm/sn)	0.76±0.19	0.75±0.17	0.911
Mitral A velocity (A) (cm/sn)	0.91±0.19	0.88±0.17	0.172
Medial mitral annular velocity (e) (cm/sn)	7.9±0.24	7.3±1.5	0.174
E/A	0.84±0.21	0.87±0.24	0.344
E/e	0.98±0.02	0.11±0.30	0.174
Left ventricular mass (g)	165.12±34.34	164.7±71	0.933
Left ventricular mass index	85.34±16.89	91.45±17.61	0.034
Left ventricular mass/height	1.05±0.24	1.04±0.22	0.917
Left atrial volume (mL)	36.20±8.59	37.03±12.06	0.692
Left atrial volume index	18.75±4.03	20.66±6.66	0.111
Left atrial volume/height	0.22±0.05	0.23±0.07	0.677

LDL: low-density lipoprotein; HDL: high-density lipoprotein; HOMA-IR: homeostasis model assessment of insulin resistance.

tient group whose MetS status did not change. The comparison of MetS criteria in patients at baseline and after one-year weight loss program is shown in Table 3. There was no significant difference in the medical treatment of the patient groups in terms of antihypertensives, metformin, and fenofibrates (Table 4). The change in EFT (Δ EFT) was significantly higher in the patient group with reversal of MetS compared with that of the group whose MetS status

did not change with weight loss (0.16 ± 0.07 cm vs. 0.09 ± 0.08 cm, $p=0.018$, respectively) (Table 5, Figure 2). Correlation analysis showed a statistically significant correlation between Δ EFT and the use of antidiabetic medication ($r=0.456$, $p=0.022$), LVMI ($r=-0.444$, $p=0.018$), and reversal of metabolic status ($r=0.513$, $p=0.005$) (Table 6). In linear regression analysis to define the independent predictors of Δ EFT, among antidiabetic medication, Δ LVMI

Table 3. Metabolic syndrome criteria at baseline and after one-year weight loss program

	Baseline (n=28) n (%)	After one-year (n=28) n (%)	<i>p</i>
Fasting glucose \geq 100 mg/dL or Rx	16 (57.1)	12 (42.9)	0.289
Blood Pressure \geq 130/85 mm Hg or Rx	12 (42.9)	2(7.1)	0.002
HDL-cholesterol $<$ 50 mg/dL	2 (7.1)	2 (7.1)	1.000
Waist circumference $>$ 80 cm	28 (100)	27 (96.4)	1.000
Triglyceride \geq 150 mg/dL	10 (35.7)	3 (10.7)	0.016
MetS Criteria \geq 3	16 (57.1)	6 (21.4)	0.002

HDL: high-density lipoprotein; MetS: metabolic syndrome.

Table 4. Comparison of medical treatment between the patient groups of metabolic syndrome status changed and unchanged after 1-year weight loss program

	MetS status unchanged n (%)	MetS status changed n (%)	<i>p</i>
Metformin	2 (12.5)	5 (55.6)	0.058
Antihypertensives	5 (28)	4 (40)	0.677
Fenofibrate	2 (12.5)	2 (22.2)	0.602

MetS: metabolic syndrome.

Table 5. Comparison of delta (Δ) values of various clinical variables between the patient groups of MetS status changed and unchanged after one-year weight loss program

	MetS status unchanged	MetS status changed	<i>p</i>
Δ EFT	-0.86 \pm 0.69	-1.78 \pm 0.66	0.002
% Δ EFT	17.20 \pm 11.96	32.92 \pm 9.85	0.002
Δ BMI	-5.85 \pm 2.17	-5.01 \pm 1.48	0.286
Δ BW	-14.71 \pm 5.19	-12.15 \pm 3.04	0.167
Δ WC	-11.56 \pm 4.8	-14.10 \pm 5.34	0.208
Δ FG	-4.56 \pm 13.51	-10.75 \pm 15.06	0.319
Δ FI	-3.58 \pm 4.51	-2.42 \pm 2.21	0.496
Δ HOMA-IR	-0.73 \pm 0.92	-0.75 \pm 0.62	0.963
Δ CRP	-2.76 \pm 3.8	-2.9 \pm 5.73	0.951

Delta (Δ) values were obtained by subtracting one-year values from the baseline values.

EFT: epicardial fat thickness; BMI: body mass index; BW: body weight; WC: waist circumference; FG: fasting glucose; FI: fasting insulin; HOMA-IR: Homeostasis model assessment of insulin resistance; CRP: C-reactive protein.

DISCUSSION

The main findings of this study were the significant decrease in EFT with weight loss, and the decrease in EFT was significantly higher in patients who reversed their MetS diagnosis with weight loss than in those whose MetS status was unchanged. In addition, reversal of MetS status is an independent predictor of the change in EFT, and the parameters associated with insulin resistance improve with weight loss in women with obesity.

Commonly used measurements for generalized adiposity are BMI and WC; however, they are not strong indicators of visceral adiposity. Evidence shows that increased visceral adiposity is associated with cardiovascular risk more strongly than generalized adiposity and is considered one of the key components of MetS.^[16] Visceral fat reduction provides a significant improvement in cardiometabolic profile.^[17]

EFT, a kind of VAT, has been suggested to be a reliable method for assessing visceral adiposity.^[7] The relationship between EFT and cardio-metabolic risk factors has been shown in several clinical studies.^[18] EFT can be measured by 2D echocardiography as an objective, readily available, and noninvasive method. It has been previously shown that echocardiographic epicardial fat reflects magnetic resonance imaging (MRI) measured intra-abdominal visceral fat.^[7] In this study, echocardiographic epicardial fat was used as a marker of visceral adiposity.

Substantial weight loss is the primary target for reducing cardiometabolic risk in people with obesity. EFT, as a modifiable factor for cardiovascular diseases, may serve as a therapeutic target for weight loss interventions.^[19] There is data suggesting that EAT

and reversal of metabolic status, we found that only reversal of MetS is the independent predictor of Δ EFT (Table 7).

Table 6. Correlation analysis between Δ EFT and various clinical variables

Variables	r	p
Age	0.148	0.452
Δ BMI	0.175	0.374
Δ WC	0.218	0.434
Δ HOMA-IR	0.080	0.732
Δ FI	-0.005	0.981
Δ Triglyceride	0.356	0.088
Δ CRP	0.152	0.546
Δ FG	0.172	0.421
Δ HDL-C	-0.284	0.178
Δ LAVI	-0.072	0.720
Δ LVMI	-0.444*	0.018
Reversal of MetS status	0.561**	0.002
Antidiabetic medication	0.523**	0.007
Antihypertensive medication	0.293	0.130
Antihyperlipidemic medication	0.313	0.128

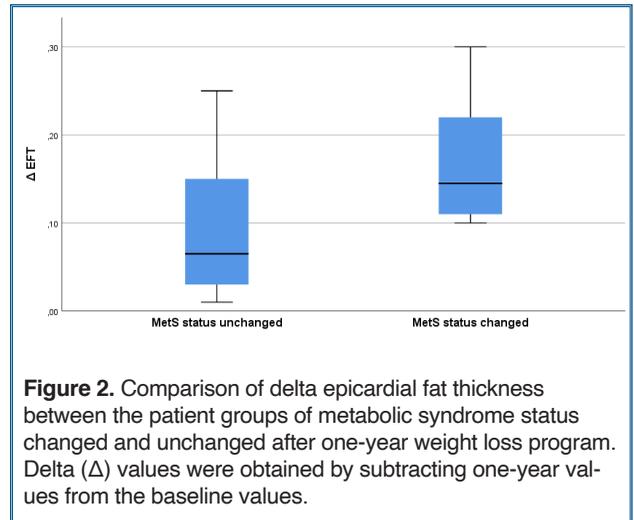
*Correlation is significant at the 0.05 level.
**Correlation is significant at the 0.01 level.
Delta (Δ) values were obtained by subtracting one-year values from the baseline values.
EFT: epicardial fat thickness; BMI: body mass index; BW: body weight; WC: waist circumference; FG: fasting glucose; FI: fasting insulin; HOMA-IR: homeostasis model assessment of insulin resistance; CRP: C-reactive protein; HDL-C: high-density lipoprotein cholesterol; LAVI: left atrial volume index; LVMI: left ventricular mass index; HDL: high-density lipoprotein; HOMA-IR: homeostasis model assessment of insulin resistance.

Table 7. Linear regression analysis of Δ EFT

	95% CI			p
	OR	Lower	Upper	
Reversal of MetS status	0.558	0.344	0.575	0.004
Antidiabetic medication	0.227	-0.410	1.223	0.312
Δ LVMI	-0.134	-0.031	0.016	0.522

Delta (Δ) values were obtained by subtracting one-year values from the baseline values.
CI: confidence interval; EFT: epicardial fat thickness; LVMI: left ventricular mass index; MetS: metabolic syndrome; OR: odds ratio.

volume can be modified by pharmaceutical interventions, including GLP-1 receptor antagonists, SGLT2 inhibitors, and statins.^[20-22] There are several studies, with a limited number of subjects, that investigated the impact of weight loss on EFT. In a systematic review and meta-analysis, Rabkin and Campbell^[23] compared 11 studies that evaluated the reduction in epicardial fat by diet, exercise, and bariatric surgery weight loss interventions. With the exception

**Figure 2.** Comparison of delta epicardial fat thickness between the patient groups of metabolic syndrome status changed and unchanged after one-year weight loss program. Delta (Δ) values were obtained by subtracting one-year values from the baseline values.

of two studies that found insufficient evidence of a reduction, a significant reduction in EAT was shown in the remainder of these studies. In a recent review and meta-analysis by Launbo et al.,^[24] 10 studies that investigated the change in EAT by weight loss interventions including diet, exercise, bariatric surgery, and pharmaceutical interventions were evaluated. It was reported that exercise, diet, bariatric surgery, and pharmaceutical interventions can reduce EAT volume. Therefore, consistent with previous studies, we found a significant reduction in echocardiographically assessed EFT after the one-year weight loss program, comprising diet and exercise. No correlation between the reduction in EFT and change in any anthropometric measures was shown; however, a statistically significant correlation was found between Δ EFT and the use of antidiabetic medication as well as the reversal of MetS.

The difference of our study from similar studies is that we compared the change in EFT between the groups whose MetS status changed or was unchanged with weight loss. To the best of our knowledge, our study was the first to investigate this issue, and we found that the reduction in EFT was significantly higher in the patients with reversal of MetS with weight loss than that in those whose MetS status did not change. Reversal of MetS was shown as an independent predictor of change in EFT. Our findings, therefore, emphasize the association of EAT with metabolic profile.

There are conflicting results on the impact of weight reduction on left ventricular structure and

diastolic function.^[25-27] We did not show significant improvement in LAV, LVM, or left ventricular diastolic function assessed by E/A and E/e; this may have been related to the degree or duration of weight loss. There was a statistically significant increase in LVMI after weight loss. We evaluated the increase in LVMI without any change in the LVM as associated with the weight loss of the patients. We also showed an improvement in parameters associated with insulin resistance and a significant reduction in CRP as a marker of inflammation, with weight loss.

Limitations

Our study had certain limitations, including the relatively small sample size, which was mainly owing to the difficulty in achieving significant WR in the absence of surgical methods. Similar studies investigating the impact of weight loss with diet and/or exercise also had a limited number of patients. Second, our findings could only be applied to women with obesity and not men with obesity. Third, echocardiography may not be the optimal technique for quantification of epicardial fat; it is a linear measurement and, therefore, may not correlate with the total volume. However, because of the limitations of MRI and computerized tomography, such as high costs, experienced operator requirements and radiation exposure, echocardiography remains a reliable, easy, and accurate method. Further large-scale studies are needed to confirm our findings.

Conclusion

Echocardiographically measured EFT can be reduced by sustained weight loss with diet and exercise in asymptomatic women with obesity. Echocardiographic EFT can be a follow-up criterion for weight loss interventions as well as an indicator for metabolic profile.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Antalya Training and Research Hospital (Approval Date: December 26, 2019; Approval Number: 2019-397).

Informed Consent: Informed consent was obtained from the participants of this study.

Peer-review: Externally peer-reviewed.

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Keywords: Echocardiography, epicardial fat thickness, metabolic syndrome, obesity, weight loss

Anahtar Kelimeler: Ekokardiyografi, epikardiyal yağ kalınlığı, metabolik sendrom, obezite, kilo verme