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Carotid intima-media thickness in postmenopausal women is associated with an endometrial thickness greater than 5 mm

Grubość błony środkowej i wewnętrznej tętnicy szyjnej u kobiet po menopauzie jest związana z grubością endometrium większą niż 5mm

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Abstract

Aim: *The aim of this study was to investigate the relationship between ultrasonographic carotid intima-media thickness (C-IMT) and visceral fat thickness (VFT) and an endometrial thickness (ET) of more than 5 mm in postmenopausal women.*

Methods: *C-IMT, VFT, and ET measurements were performed in 63 postmenopausal women using ultrasonography. The relationships between ultrasonographic data and demographic data, anthropometric measurements, such as waist circumference, metabolic syndrome parameters, and insulin resistance were examined. Moreover, the role of VFT and C-IMT in predicting an ET of more than 5 mm was investigated.*

Results: *Only the C-IMT was higher in the ultrasonographic measurements of women with an ET >5 mm (p = 0.03). Insulin resistance was also significantly higher in these women (p = 0.03). ET showed a positive correlation with VFT and body mass index (BMI) (r = 0.286, p = 0.02 and r = 0.249, p = 0.04), and C-IMT showed a positive correlation with age, pregnancy, parity, and time since menopause (p<0.05). Multivariate analysis showed that high-C-IMT levels were associated with an ET >5 mm (p = 0.04).*

Conclusions: *There was a positive correlation between the ultrasonographic measures of VFT and ET, and high-C-IMT levels were independently associated with an ET>5 mm. Thus, C-IMT may be a predictor of pathologic ET in the postmenopausal period.*

Key words: **menopause** / **carotid intima-media thickness** / **body fat distribution** / / **endometrial thickness** /

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Streszczenie

Cel pracy: *Celem pracy była zbadanie związku między grubością błony środkowej i wewnętrznej tętnicy szyjnej (C-IMT) a grubością tkanki tłuszczowej trzewnej (VFT) oraz grubością endometrium (ET) większą niż 5 mm u kobiet po menopauzie.*

Metody: *Pomiary C-IMT, VFT, i ET wykonano u 63 kobiet po menopauzie przy pomocy ultrasonografii. Zbadano związek między wynikami ultrasonograficznymi a danymi demograficznymi, pomiarami antropometrycznymi, takimi jak obwód w talii, parametry zespołu metabolicznego i oporności na insulinę. Co więcej, oceniono role VFT i C-IMT w przewidywaniu ET większego niż 5 mm.*

Wyniki: *Tylko C-IMT było wyższe w pomiarach ultrasonograficznych u kobiet z ET >5 mm (p = 0.03). Insulinooporność była również istotnie wyższa u tych kobiet (p = 0.03). ET wykazało pozytywną korelację z VFT i BMI (r = 0.286, p = 0.02 i r = 0.249, p = 0.04), a C-IMT wykazało pozytywną korelację z wiekiem, ciążą, rodnością i czasem od menopauzy (p<0.05). Analiza wieloczynnikowa pokazała że wyższe poziomy C-IMT wiązały się z ET >5 mm (p = 0.04).*

Wnioski: *Wykazano pozytywną korelację między ultrasonograficznymi pomiarami VFT i ET, a wysokie poziomy C-IMT niezależnie wiązały się z ET>5 mm. Dlatego C-IMT może być predyktorem patologicznego ET u kobiet pomenopauzie.*

Słowa kluczowe: **menopauza** / **grubość błony środkowej i wewnętrznej tętnicy szyjnej** / / **dystrybucja tkanki tłuszczowej** / **grubość endometrium** /

Introduction

The postmenopausal period has been characterized by an increased risk of cardiovascular disease (CVD) and metabolic syndrome (MS) [1]. Furthermore, obesity has often been associated with MS and increased insulin resistance [1,2]. Increased adiposity is defined as the storage of unconsumed energy and is known to contribute to endocrine dysregulation [2]. Several reports have suggested that increased adipose tissue serves as a primary source of circulating estrogens, which are synthesized from androgen precursors and, if not regulated properly, can increase CVD and endometrial thickness (ET) [3-5].

Recently, body fat distribution has been shown to more strongly correlate with increased ET than the amount of adipose tissue [5]. Indeed, visceral fat mass, one component of the increased abdominal adiposity found in the postmenopausal period, has been associated with MS and ET [5, 6]. Although waist circumference (WC) has been utilized as an easy-to-measure marker of visceral adipose tissue, its specificity has been poor [7]. WC measures not only visceral adipose tissue but also subcutaneous adipose tissue, which is another component of abdominal fat mass [5]. In other words, visceral fat tissue measurements may be significantly different among women with the same WC value [7]. In a few studies investigating the relationship between ET and body fat distribution during the postmenopausal period, methods such as dual x-ray absorptiometry and body composition analysis have been used to obtain measurements of visceral fat tissue; however, these methods are expensive, not as accessible and practical as ultrasonography, and result in exposure to radiation [5, 7]. In recent years, advancements in adipose tissue measurements using ultrasonography have made these analyses cheap, practical, repeatable, and simple to perform. In addition, ultrasonography has produced results that are consistent with other reliable methods such as computed tomography [8].

Previous studies have shown that ultrasonography measurements of the carotid intima-media thickness (C-IMT) are reproducible, simple, and consistent and correlate very well with pathohistological measurements [9]. C-IMT is a marker of systemic inflammation and has been positively correlated with atherosclerosis resulting from endothelial dysfunction [10]. C-IMT has also been shown to be a useful marker for CVD and MS [11, 12]. High body mass index (BMI), diabetes mellitus, and hypertension, all of which are MS components, have also been shown to contribute to increased ET [13-15]. However, an examination of C-IMT and its effect on ET has not been investigated.

An ET value exceeding 5 mm has been shown to increase the risk of endometrial cancer in the postmenopausal period [16]. Currently, several studies have demonstrated the connection between body fat distribution and ET, although the association with an ET greater than5 mm in clinical practice has not been determined [5, 7, 17]. Thus, we aimed to investigate the relationship between ultrasonographic measurements of C-IMT, visceral fat thickness (VFT) and ET, with the ultimate goal of establishing a reliable and simple method to determine ET.

Materials and Methods

This prospective study was carried out in Merkezefendi State Hospital with approval from the Ethical Committee of Celal Bayar University. The study was conducted on 64 postmenopausal women who were admitted to the outpatient clinic of gynecology for an annual gynecological examination between October and December 2014. Postmenopausal subjects provided informed consent before inclusion in the study; all subjects had started natural menopause at least one year previously. Diabetes mellitus, hypertension, uterine bleeding, endometrial polyps, smoking, hormone replacement therapy, and any medication known to influence ET, such as hypolipidemic or hypoglycemic medications, were used as exclusion criteria. Blood pressure above 140/90 mmHg or antihypertensive use was accepted as the criteria of hypertension. The use of oral antidiabetics and insulin or a fasting blood glucose (FBG) >115 mg/dL (normal range: 70-115 mg/dL) was accepted as the criteria of diabetes mellitus.

Age, age at menopause, time since menopause (age – age at menopause), pregnancy and term parity were evaluated as demographic data.

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Anthropometric and metabolic measurements

The participants' weights and heights were measured without shoes and with light clothing. BMI was calculated with the formula: weight (kg) / height (m)^2. WC was measured from the middle point of the border of the iliac crest and the last costa after normal expiration in an upright position. Hip circumference (HC) was measured from where the hip protruded the most. Blood pressure was measured using an automated sphingomanometric procedure after resting in a seated position for at least 5 minutes. The mean (n=2) measurement obtained over a 5-minute interval was recorded.

FBG, total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and insulin levels were determined from morning pre-prandial blood. The homeostasis model index (HOMA) was used to evaluate insulin resistance. The HOMA insulin resistance (HOMA-IR) value was calculated using the following formula: [FBG (mg/dl)/18 x fasting serum insulin (mU/L)]/22.5.

MS was diagnosed and determined according to the classification system established in 2005 by the International Diabetes Federation. These criteria consist of central obesity (defined as WC ≥80 cm) and two of the following components: TG ≥150 mg/dL, HDL <50 mg/dL, systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, and FBG ≥100 mg/dL.

Ultrasonographic evaluation

Ultrasonographic measurements were performed with a high-resolution ultrasonographic system (Aplio 500; Toshiba, Toshigi, Japan). The measurements were conducted with the PLT-704SBT (4.8-11.0 MHz) linear transducer in abdominal mode with an ultrasonography device to obtain measures of VFT and subcutaneous fat thickness (SFT); the device was used in carotid mode to obtain C-IMT measurements. ET was measured with a PLT-661VT (3.6-8.8 MHz) endovaginal transducer in vaginal mode.

All patient measurements were performed in the supine position; values collected after respiration were used to exclude abdominal wall-based respiratory tension. Both the preperitoneal VFT (maximal) and SFT(minimal) were longitudinally examined by scanning along the linea alba from the xiphoid to the umbilicus using a linear probe. Fat thickness for VFT and SFT was classified as the distance from the liver surface to the linea alba and between the skin and the linea alba, respectively [18] (Figure 1a).

For the C-IMT measurement, the probe was placed parallel to the carotid artery, and the measurement was performed while the artery was prolonging the longitudinal plane with the front and rear walls of the artery visible. The distance from the beginning of the hyperechogenic line (lumen-intima interface), which was closest to the lumen in the rear wall of the artery, to the end of next hypoechogenic line (media-adventitia interface) was measured [19] (Figure 1b).

The ET measurements were performed with the patient in the dorsal lithotomic position. Double-layer thickness from the thickest part in the longitudinal plane was accepted as ET (Figure 1c).

The ET measurement was performed by the same gynecologist (F.E.), while the VFT, SFT, and C-IMT measurements were routinely performed by the same experienced radiologist

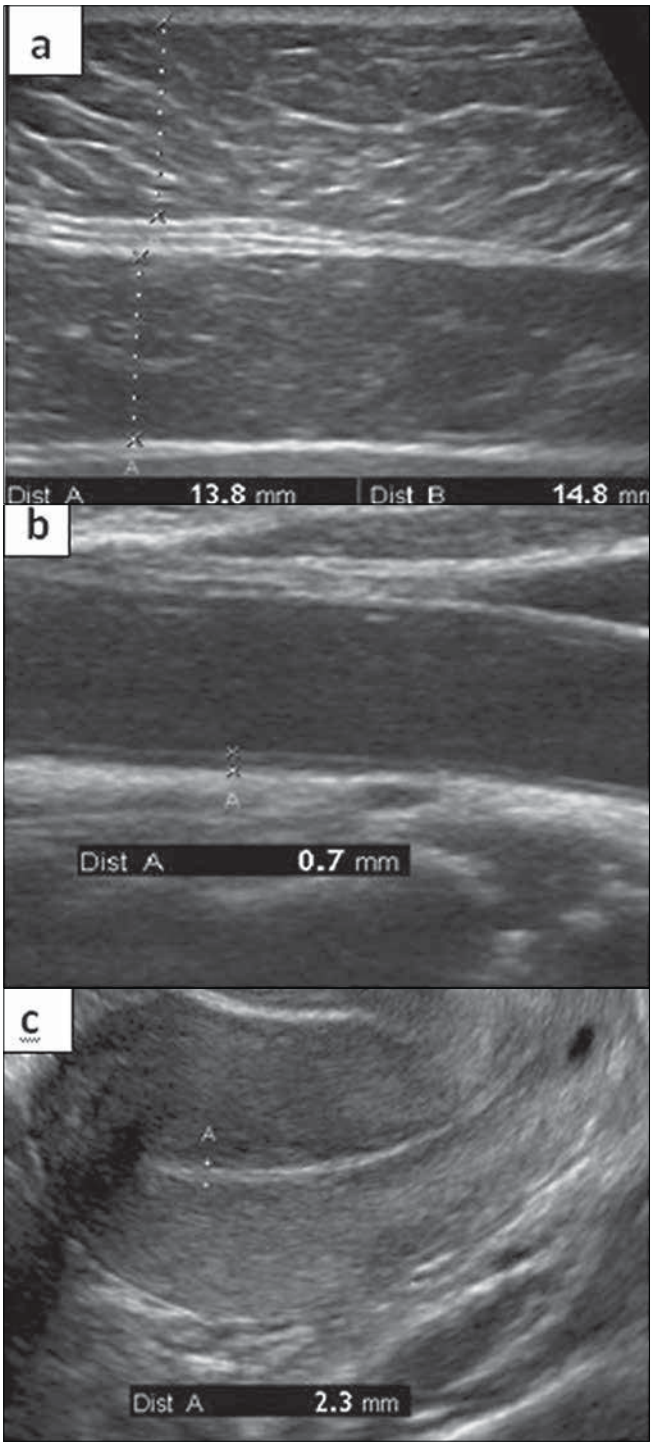

Figure 1. Representative examples of measurements of VFT (Dist A) – SFT (Dist B) in a, C-IMT in b and ET in c.

(M.S.E.). For study reliability, 20 of the 63 patients were blindly evaluated by two observers with no prior knowledge or information about the other's analysis and/or measurements. The intra-observational reproducibility of the ultrasonographic estimations for M.S.E. was r = 0.960 for SFT; r = 0.923 for VFT; and r = 0.921 for C-IMT (p <0.001). The reproducibility for F.E. in ET was r = 0.991 (p <0.001). The reproducibility between the two observers was r = 0.952 for SFT; r = 0.904 for VFT; r = 0.926 for C-IMT; and r = 0.989 for ET (p <0.001).

Table I. Baseline characteristics and ultrasonographic findings of women with an ET≤5 mm and women with an ET>5 mm, as well as women with and without MS, in the postmenopausal period. Categorical variables were presented as the mean±SD (standard deviation). p<0.05 was considered statistically significant.

	ET ≤5mm (n=54) mean±SD	ET >5mm (n=9) mean±SD	*P*	METABOLIC SYNDROME (-) (n=37) mean±SD	METABOLIC SYNDROME (+) (n=26) mean±SD	*P*
Age (years)	56,90±6.31	55.33±7.68	0.37	56.35±5.88	55.15±7.33	0.15
Pregnancy	5.11±3.13	5.33±3.77	0.49	4.75±2.89	5.69±3.57	0.10
Term parity	3.81±2.67	4.88±3.68	0.28	3.54±2.29	4.57±3.41	0.09
Age at menopause (years)	48.81±3.30	45.77±3.96	**0.01**	48.62±3.31	48.03±3.88	0.15
Time since menopause (years)	8.09±6.33	9.55±6.42	0.22	7.72±5.93	9.11±6.85	0.12
BMI (kg/m²)	31.79±5.67	33.3±2.63	0.11	30.96±4.90	33.48±5.71	**0.01**
WC (cm)	91.03±9.72	64.11±5.84	0.16	89.00±8.90	95.00±8.84	**0.005**
WC/HC	0.84±0.06	0.83±0.04	0.30	0.83±0.07	0.85±0.48	**0.01**
Systolic blood pressure (mmHg)	123.23±21.36	121.11±16.15	0.25	116.38±23.80	131.96±9.74	**<0.001**
Dyastolic blood pressure (mmHg)	78.15±7.78	74.44±13.33	0.19	75.05±7.65	81.15±9.08	**0.001**
Blood Chemistry Analysis						
FBG (mg/dL)	93.20±10.14	96.11±11.12	0.30	91.70±7.34	96.4±13,11	**0.005**
TC (mg/dL)	218.56±35.96	229.44±30.11	0.19	220.72±42.00	219.23±22.94	0.24
TG (mg/dL)	142.44±64.60	142.22±52.90	0.33	120.59±41.16	173.46±74.80	**<0.001**
HDL-C (mg/dL)	56.42±14.84	50.11±8.41	0.11	59.18±13.90	50.30±13.25	**0.001**
LDL-C (mg/dL)	134.09±32.40	148.62±32.41	0.10	138.25±38.97	132.76±20.22	0.19
İnsulin (mU/L)	10.09±5.36	13.10±4.88	**0.03**	10.26±6.09	10.95±4.23	0.05
HOMA-IR	2.33±1.36	3.16±1.42	**0.02**	2.34±1.54	2.63±1.15	0.40
Ultrasonographic Findings						
C-IMT (mm)	0.67±0.15	0.80±0.24	**0.03**	0.67±0.13	0.72±0.20	0.07
SFT (mm)	17.46±5.50	18.52±4.19	0.20	17.3±5.48	17.99±5.15	0.21
VFT(mm)	12.28±5.24	15.58±4.37	0.06	11.8±4.46	14.07±5.99	0.38
EMT (mm)				3.41±2.69	4.16±2.57	0.17

Statistical analysis

The statistical package SPSS for Windows 16.0 (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) was used to analyze the data. A Mann-Whitney U test was applied for MS (+) and (-) groups as well as the EM >5 mm and EM ≤5 mm groups. Mean and standard deviations were used to describe the data. A Chi-squared test was used to determine the differences between the ET >5 and ET ≤5 groups in terms of MS. The relationships between ultrasonographic measurements and metabolic risk factors as well as anthropometric measurements were analyzed by Pearson's correlation coefficient. Linear regression was used for multivariate analysis. Receiver operating characteristic (ROC) curve analysis was used to determine the discriminating cut off value in order to predict ET. A *p*-value of 0.05 or less was considered statistically significant.

Results

A total of 64 women were included in the study. One woman with an ET of more than 5 mm was found to have an endometrial polyp as a result of fractional explorative curettage and histopathological examination and was thus excluded from the study.

An ET of greater than 5 mm was present in 9 of 63 women in the study. The number of women with MS criteria was 26.

The basic characteristics of the groups with an ET ≤5 mm and >5 mm and postmenopausal women with and without MS criteria are presented in Table 1.Age at menopause was statistically lower in the ET >5 mm group than the ET ≤ 5 mm group (p = 0.01). Insulin and HOMA-IR levels were significantly higher in the EM >5 mm group (p = 0.03 and p =0.02, respectively). MS was detected in 4 (44.4%) women with an ET >5 mm and in 22 (40.7%) women with an ET ≤5 mm, with no significant difference between groups (p =0.83). Considering the ultrasonographic

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Table II. Correlations between ultrasonographic measurements and metabolic parameters, anthropometric measurements, and demographic data. r=Pearson correlation coefficient. p<0.05 was considered statistically significant.

	ET *r*	*P*	C-IMT *r*	*P*	VFT *r*	*P*	SFT *r*	*P*
Age (years)	0.056	0.66	0.41	**0.001**	-0.22	0.07	0.084	0.51
Pregnancy	-0.009	0.94	0.39	**0.002**	-0.25	**0.04**	-0.023	0.86
Term parity	0.061	0.63	0.34	**0.006**	-0.18	0.15	-0.073	0.57
Age at menopause (years)	-0.20	0.11	-0.09	0.47	-0.08	0.49	0.21	0.86
Time since menopause (years)	0.17	0.18	0.47	**<0.001**	-0.18	0.14	0.75	0.56
BMI (kg/m²)	0.249	**0.04**	0.096	0.45	0.467	**<0.001**	0.618	**<0.001**
WC (cm)	0.232	0.06	0.168	0.18	0.399	**0.001**	0.581	**<0.001**
WC/HC	-0.109	0.39	0.090	0.48	0.020	0.87	0.214	0.09
Systolic blood pressure (mm Hg)	0.04	0.72	0.05	0.68	-0.01	0.93	0.017	0.89
Diastolic blood pressure (mmHg)	0.17	0.16	-0.13	0.30	0.006	0.96	0.104	0.42
Blood Chemistry Analysis								
FBG (mg/dL)	0.12	0.32	0.005	0.96	-0.09	0.45	0.182	0.15
TC (mg/dL)	0.06	0.59	0.11	0.36	0.14	0.27	0.03	0.17
TG (mg/dL)	0.07	0.54	0.10	0.41	0.43	**<0.001**	0.000	1.0
HDL-C (mg/dL)	-0.18	0.13	-0.14	0.24	-0.26	**0.03**	-0.03	0.78
LDL-C (mg/dL)	0.09	0.46	0.13	0.29	0.07	0.58	0.06	0.63
İnsulin (mU/L)	0.22	0.08	0.01	0.90	0.32	**0.01**	0.31	0.14
HOMA-IR	0.23	0.07	0.02	0.85	0.31	**0.01**	0.33	**0.01**
Ultrasonographic Findings								
CIM-T (mm)	0.230	0.06	-	-	0.037	0.77	0.103	0.421
VFT (mm)	0.286	**0.02**	-	-	-	**-**	0.342	**0.006**
SFT (mm)	0.157	0.22	-	-	-	-	-	-

measurements, there was no difference between groups in terms of VFT and SFT; however, the CIM-T value was higher in the ET >5 mm group (p = 0.03).

For the comparison between the MS+ and MS- groups, the BMI, WC, WC/HC, and systolic and diastolic blood pressure were significantly higher in the MS+ group (p = 0.01, p = 0.005, p = 0.01 and p < 0.001, respectively). The FBG (p = 0.005) and TG (p < 0.001) were higher, while the HDL (p = 0.001) was lower, in the MS+ group. Ultrasonographic measurements were not affected by the presence of MS.

Considering all postmenopausal women in the study, the C-IMT value showed a positive correlation with age (p = 0.001), pregnancy (p = 0.002), term parity (p = 0.006) and time since menopause (p < 0.001).

The VFT showed a negative correlation with pregnancy and HDL (p = 0.04 and p = 0.03) and a positive correlation with TG (p = 0.001), insulin (p = 0.01), and HOMA-IR (p = 0.01). The SFT showed a positive correlation only with the HOMA-IR from biochemical values (p = 0.01). ET demonstrated a positive correlation only with BMI (p = 0.04) and VFT (p = 0.02). VFT and SFT presented a positive correlation with both BMI and WC from the anthropometric measurements (p <0.001). Among CIM-T, VFT, and SFT, a significant correlation was found only between VFT and SFT (p = 0.006) (Table II).

BMI, WC, and WC/HC showed a positive correlation with both insulin (p = 0.01, p = 0.001, and p = 0.001, respectively) and HOMA-IR (p = 0.01, p = 0.001, and p = 0.001, respectively). In addition, WC/HC showed a positive correlation with age (p = 0.001), term parity (p = 0.03), and age at menopause (p = 0.007) (Table III).

To determine the risk factors for pathologic endometrial thickening in the postmenopausal period, we utilized linear regression analysis. In particular, we performed correlation analysis with the variables related to pathologic endometrial thickening. Among the variables showing a strong correlation, those that were strongly correlated with pathologic endometrial thickening were included in the regression analysis. As such, SFT, VFT, and C-IMT were included in the regression model. Moreover, CIM-T was associated with significant pathologic endometrial thickening in the postmenopausal period (p = 0.04) (Table IV).

The prognostic value of CIM-T was determined using ROC curves. The ROC curve analysis for CIM-T revealed an area under the curve (AUC)of 68.2%. Using a cut-off value of 0.65 mm for CIM-T, the sensitivity was 88.9% and the specificity was 44.4% for an ET greater than 5 mm. In comparison, for a 0.75 mm cut-off for C-IMT, the sensitivity and specificity were 55.6% and 72.2%, respectively. For an ET >5 mm, the

Table III. Correlation between anthropometric measurements and metabolic parameters and demographic data. r= Pearson correlation coefficient. p<0.05 was considered statistically significant.

	BMI *r*	*P*	WC *r*	*P*	WC/HC *r*	*P*
Age (years)	0.032	0.80	0.174	0.17	0.414	**0.001**
Pregnancy	0.017	0.89	0.13	0.29	0.216	0.08
Term parity	0.59	0.64	0.20	0.10	0.273	**0.03**
Age at menopause (years)	-0.04	0.70	0.008	0.95	0.15	0.22
Time since menopause (years)	0.06	0.63	0.17	0.17	0.33	**0.007**
Systolic blood pressure (mmHg)	0.13	0.31	0.89	0.49	0.003	0.98
Diastolic blood pressure (mmHg)	0.18	0.16	0.07	0.55	0.11	0.36
Blood Chemistry Analysis						
FBG (mg/dL)	0.09	0.48	0.11	0.39	0.016	0.90
TC (mg/dL)	0.03	0.8	-0.008	0.95	-0.11	0.35
TG (mg/dL)	0.20	0.11	0.23	0.07	0.13	0.29
HDL-C (mg/dL)	-0.16	0.21	0.19	0.12	-0.09	0.45
LDL-C (mg/dL)	0.004	0.97	0.03	0.80	-0.12	0.33
Insulin (mU/L)	0.31	**0.01**	0.41	**0.001**	0.41	**0.001**
HOMA-IR	0.31	**0.01**	0.41	**0.001**	0.40	**0.001**

sensitivity and specificity were 77.8% and 51.9% (AUC: 66%), respectively, using a cut-off value of 13.0 mm for VFT. While the sensitivity and specificity were 66.7% and 61.1% (AUC: 62.6%), respectively, at cut-off value of 32.7 for BMI, the sensitivity was 55.6% and specificity was 63% (AUC: 60.1%) at a cut-off value of 94.5 mm for WC (Figure 2).

Discussion

Menopause is the natural termination of menstruation and reproduction due to the loss of ovarian function [20]. Irrespective of the reproductive or menopausal period, the estrogen receptors on the endometrium respond to circulating estrogens, and the increased abundance of estrogen can result in endometrial overgrowth. ET has been suggested to be proportional to estrogen status and may be a predictor of estrogen levels, even in postmenopausal women [21].

While the source of estrogen is the ovaries in the premenopausal period, adipose tissue is known to produce estrogen from androgen precursors in the postmenopausal period [3-5]. Indeed, an increase in BMI is known to increase ET [13]. Abdominal adiposity is typical in the postmenopausal period, and this type of adiposity is associated with increased ET and CVD risk [5, 22]. While peripheral fat tissue consists of subcutaneous fat only, abdominal fat consists of both subcutaneous and visceral fat tissue [5]. Warming et al. [5] found that visceral fat tissue was the source of estrogen formed by the conversion of androgen precursors; after assessing the body fat distribution of 531 healthy postmenopausal women with dual energy x-ray absorptiometry, these authors concluded that VFT was the most relevant fat component for ET. Studies conducted in subsequent years have also supported the notion that subcutaneous fat tissue and visceral fat tissue have different endocrine functions [17]. This functional difference can be explained by the distribution of body fat,

Table IV. Evaluation of multivariate analysis for ultrasonographic measurements. β: Beta coefficient. CI: confidence interval. p<0.05 was considered statistically significant.

	β	95% CI for β	*P*
SFT	-0.03	-0.02 - 0.01	0.80
VFT	0.22	-0.002 - 0.03	0.80
C-IMT	0.25	0.01 - 1.03	0.04

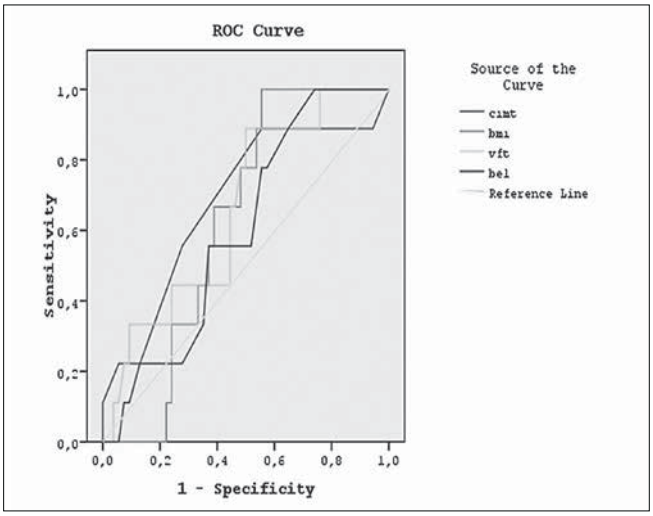

Figure 2. ROC plot to predict the presence of an ET>5 mm during the postmenopausal period. The optimal cut off points for predicting an ET>5 mm were a C-IMT of 0.65 mm (AUC=68.2%, p= 0.082), VFT of 13 mm (AUC=66%, p= 0.126), WC of 94.5 cm (AUC=60.1%, p=0.336) and BMI of 32.7 (AUC=62.6, p= 0.231).

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which may affect circulating sex hormone levels or may change the plasma concentrations of these hormones. Sex hormone binding protein (SHBG) levels are lower in abdominal adiposity compared to other types of adiposity, which may increase the free estrogen levels and ET [23]. The high insulin levels due to insulin resistance also lead to decreased SHBG levels [24]. In our study, we observed a positive correlation between ET with VFT and BMI.

Abdominal adiposity, which is typical in menopause, leads to an increased risk of CVD and MS [22]. We found that VFT decreased as HDL increased and that VFT increased as TG and insulin resistance increased. Insulin resistance also showed a positive correlation with WC and BMI. The fact that VFT showed a positive correlation with BMI and WC supports these findings. Again, we observed that BMI, WC, and WC/HC were higher in women with MS criteria. Accordingly, adipokine secretion and the levels of free fatty acids are increased due to increased visceral fat tissue and can cause insulin resistance [25]. Increased insulin levels have been shown to result in not only increased free estrogen but also increased insulin growth factor (IGF)-1 and IGF binding protein-1, which may activate endometrial cell growth [26]. Furthermore, adipose tissue may affect ET by providing a location to convert androgen precursors to estrogen and thus contributing to insulin resistance.

Visceral fat tissue is responsible for metabolic side effects. Previous reports have suggested that cytokines released from the visceral component increase oxidative stress and cause endothelial damage by triggering low-level inflammation [27]. C-IMT has been reported as a systemic marker of inflammation and was also associated with endothelial damage [10]. C-IMT was also shown to be a useful marker for CVD and MS [11, 12]. Age is an independent and significant factor for CVD. Furthermore, the influence of premenopausal hormones has been shown to be protective against CVD, although this effect is diminished after menopause [28]. C-IMT also gradually increases with age [29], and changes in the cardiovascular system during pregnancy have been documented and manifest their effects later in life [30]. Wolff et al. [31] found a positive relationship between an increased number of children and increased C-IMT. We also identified a positive relationship between C-IMT and age, duration of menopause, pregnancy and term parity number. In particular, multiple publications have demonstrated an inverse relationship between ET and pregnancy and term parity. Gull et al. [32], found an inverse association between the number of completed pregnancies and endometrial disease and suggested that endometrial hyperplasia and cancer occurred less frequently with increased pregnancies. Albrektsen et al. [33] and Lambe et al. [34] suggested that each delivery stimulates the mechanical shedding of malignant precursor cells and prevents a thickened endometrium. Similarly, progesterone may contribute antimitotic properties and reduce the growth of the endometrial lining. We observed that VFT showed a positive correlation with ET and was inversely proportional to the number of pregnancies. However, we could not show this correlation with ET. Pregnancy, term parity numbers, and the duration of menopause may affect C-IMT and ET in different ways. However, these parameters showed no difference between the ET >5 mm and ≤ 5 mm groups. Therefore, our results were unaffected by these parameters.

We observed a positive correlation between increased ET and abnormal endometrial conditions. Using 5 mm as the cut off value for ET, endometrial cancers and typical endometrial hyperplasia could be determined with 80.5% sensitivity and 86.2% specificity [16]. Although we could not show a statistically significant relationship between C-IMT and ET, considering clinically significant ET, we observed a significant increase only in the CIM-T value in women with an ET > 5 mm. Insulin and insulin resistance were also elevated in these women, and insulin resistance seemed to lead to the activation of endometrial growth and increased ET independent of increased free estrogen levels [26]. We observed that the age at menopause was younger in women with an ET >5 mm. However, this variable was not considered useful because there was no significant associated between an ET > 5 mm and time since menopause and age, which is closely related to the age at menopause (age at menopause = age - time since menopause).

The limited number of postmenopausal women with an ET >5 mm was one limitation of our study. However, when diabetes mellitus and hypertension are used as exclusion criteria, it is less likely that postmenopausal women with an ET>5 mm will be included in the study. Therefore, studies including a higher number of participants are needed to determine the accuracy of the C-IMT cut-off value, which will help identify potentially deleterious ET in postmenopausal women.

In conclusion, ultrasonography is an easy-to-access, simple and inexpensive method to determine the relationship between body fat distribution and ET in women during the postmenopausal period. We observed a positive relationship between ET and VFT, and CIM-T was significantly higher in postmenopausal women with an ET > 5 mm. Therefore, C-IMT may be a predictor of pathological ET, and postmenopausal women with high VFT and C-IMT values should be evaluated in terms of ET. Taking into account these conclusions, we could only stronger suggest the need of cooperation between cardiologists, endocrinologists and gynecologists in prediction and defining risk of endomtrial hyperplasia and endometrial cancer.

Authors' contribution:

1. Fatma Eskicioğlu – concept, study design, acquisition of data, analysis and interpretation of data, article draft, corresponding author.
2. Muhammet Sakıp Eskicioğlu – interpretation of data.
3. Alper Tunga Özdemir – analysis and interpretation of data, revised critically article.
4. Beyhan Özyurt – data analysis.

Authors' statement

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