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ARTICLE

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The Relationship between Obesity and Cardiovascular Risk in Postmenopausal Women

ABSTRACT

Objective: The aim of this study was to investigate the relationship between obesity and cardiovascular risk in postmenopausal women.

Methods: The study included 43 postmenopausal women who were admitted to Dicle University Medical School Family Medicine Outpatient Clinic. Body mass index (BMI), waist and hip circumferences, body fat mass and percentage, 24-hour arterial tension measurements, homocysteine (Hcy), lipid and vitamin B12 levels, and Framingham risk score (FRS) were compared between obese (BMI \geq 30 kg/m²) and non-obese (BMI<30 kg/m²) patients.

Results: The patients included 25 (58.1%) obese and 18 (41.9%) non-obese patients. Abdominal obesity was seen in 29 (67.4%) and truncal obesity in 18 (41.9%) participants. Family history of cardiac disease was seen in 25 (58.1%) women, most of whom were obese. Based on FRS, moderate cardiovascular risk was assessed in 21.6%, but none of the participants were at high risk. FRS was positively correlated with Hcy and waist/hip ratio.

Conclusions: The results of this study indicate that age- and gender-dependent differences must be taken into consideration for cardiovascular risk assessments and postmenopausal women should be informed about obesity and hypertension in order to improve their quality of life.

Keywords: Obesity, Homocysteine, Blood Pressure Monitoring, Framingham Risk Score.

Postmenopozal Kadınlarda Obesite ve Kardiyovasküler Risk İlişkisi

ÖZET

Amaç: Bu çalışmada postmenopozal kadınlarda obesite ve kardiyovasküler risk ilişkisinin incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya Dicle Üniversitesi Tıp Fakültesi Aile Hekimliği Polikliniğine başvuran 43 postmenopozal kadın dahil edilmiştir. Beden kitle indeksi (BKİ), bel ve kalça çevresi, vücut yağ kitle ve yüzdesi, 24-saatlik kan basıncı ölçümleri, homosistein (Hcy), lipid ve vitamin B12 düzeyleri ve Framingham risk skorlaması (FRS) obez olan (BKİ \geq 30 kg/m²) ve obez olmayan (BKİ<30 kg/m²) kadınlarda ölçülerek karşılaştırılmıştır.

Bulgular: Kadınların 25'i (%58.1) obez ve 18'i (%41.9) non-obezdi. Abdominal obesite 29 (%67.4), trunkal obesite 18 (%41.9) katılımcıda görüldü. Kardiyak hastalık aile öyküsü, çoğu obez olan 25 (%58.1) kadında tespit edildi. FRS'ye göre orta düzeyde kardiyovasküler risk %21.6 oranında saptanırken hiçbir kadın yüksek risk grubunda değildi. FRS, Hcy ve bel-kalça oranı ile pozitif olarak korele idi.

Sonuç: Bu çalışma kardiyovasküler risk değerlendirmesinde yaş ve cinsiyete bağlı farklılıkların göz önünde bulundurulması ve postmenopozal kadınların, yaşam kalitelerini arttırmak için obesite ve hipertansiyon konusunda bilgilendirilmeleri gerektiğini göstermektedir.

Anahtar Kelimeler: Obesite, Homosistein, Kan Basıncı Monitorizasyonu, Framingham Risk Skorlaması.

INTRODUCTION

Recent technological advancements in diagnostic and treatment methods in medicine have resulted in an increased life expectancy as well as a longer postmenopausal period which makes women more prone to diseases such as obesity, hypertension, and cardiovascular disease (CVD) (1). Contrary to popular belief, CVD mortality in women is higher than the sum of all deaths caused by malignancies and is the leading cause of death in postmenopausal women (2-4). Globally, 33.3% of women deaths were due to cardiovascular reasons (2,4). Even though it has been well documented that most deaths are caused by cardiovascular diseases and their complications in both genders, there are major differences between women and men with regard to the risk factors for CVD (2,5,6). The risk factors for cardiovascular disease have remarkable gender-dependent differences and the effects of traditional risk factors are not the same in women and men (2,7). Moreover, common presentations, treatment responses and results of CVDs are gender-specific (7). Although the rates of cardiovascular disease have significantly decreased for men over the past decades, there has been no similar decline for women (8).

Global cardiovascular risk is defined as the probability of encountering an acute coronary event or stroke within a specific time interval which is reported as a percentage over a ten-year time period and is defined as an absolute risk (9). The main cardiovascular risk factors for women include smoking, diabetes mellitus (DM), obesity, hypertension, hyperlipidemia and physical inactivity (10). Postmenopausal state, however, is worsening the risk profile by alteration fat distribution and causing obesity (7). In addition, cardiovascular mortality was found to be higher in postmenopausal women (11).

Obesity, which causes a series of metabolic changes in human body, increases the risk of cardiovascular diseases in both genders (12). It increases the risk more in women (64%) than men (46%) (2,13). It is more common in middle aged women, particularly after menopause, due to the estrogen depletion that resulting in altered body composition and therefore central adiposity (14). Physical inactivity, dyslipidemia, hypertension and insulin resistance are quite relevant with obesity but during the past three decades, the increasing rate of obesity was higher than both of them (2,13). During menopause, physical activity decreases as body mass index (BMI) increases (13).

Hypertension, one of the strong risk factors, is highly prevalent in women with CVD (1). In developed countries, 30% of women are hypertensive and this ratio is rising up to 53% in low or middle income countries (3). The CVD mortality is doubled with every 20 mmHg systolic and 10 mmHg diastolic blood pressure increase for the patients aged 40-89 years (3). Hypertension is

more lethal in women, since the target value achievements of the treatment, so the control of hypertension is more difficult in aging women than in aging men (13,15). Although their mechanisms have not been fully described, the factors that are thought to play a role in the pathogenesis of postmenopausal hypertension include hormonal changes, activation of the renin-angiotensin-endothelin systems and sympathetic nervous systems, weight gain, inflammation, increased vasoconstrictors, and psychological mood (15,16). In obese individuals, the accumulation of intraabdominal fat plays an important role in the pathogenesis of hypertension (17).

Dyslipidemia is among the most prevalent risk factors for CVDs. After menopause, triglyceride (TG), total cholesterol and low density lipoprotein (LDL) cholesterol increase while high density lipoprotein (HDL) cholesterol decreases (13). However, low HDL cholesterol is more predictive than high LDL cholesterol in women in terms of CVDs (1,3). Smoking also has more harmful effects, for example, it triples the risk of myocardial infarction in women (2,7). When compared with men, smoking women have 25% more increased CVD risk (13). In addition, the effects of excessive smoking in women have been shown to be 2-4 times higher than in men (12).

Although the factors mentioned above have been confirmed as risk factors for cardiovascular diseases, the mechanisms by which they influence and in what extent they contribute to this risk remain unclear. Furthermore it is not possible to explain 25% of CVDs by classical risk factors; therefore, new studies are being carried out to understand the mechanisms and to identify new risk factors (18). In recent studies, Hcy, a sulfur-containing amino acid which is formed during the methionine metabolism, has been defined as a strong and independent risk factor for cardiovascular diseases, particularly for coronary heart disease, stroke, and atherosclerosis (18-23). Hiperhomocysteinemia-induced endothelial dysfunction has a critical role in vascular pathology (22). There is a positive correlation between Hcy and blood pressure and this correlation is prominent in women (18). The concentration of Hcy decreases with increasing serum folate and vitamin B12 levels, whereas it increases with smoking and increasing BMI so its concentration is affected from demographic features, lifestyle, and dietary habits (24).

In spite of the estimation that the prevalence of CVD will increase by 15-20% until 2020 and that the CVD mortality of the women will increase by 120% in developing countries, many articles reported that women, especially at postmenopausal state, are not adequately represented in trials with regard to CVD and its risk factors (1,2,4,5,13). The limited data of CVD risk assessment of

postmenopausal women reveal that the risks are not evaluated thoroughly in women and the misperception that women are protected against the CVDs, make the management of these diseases more difficult. For this reason, the aim of this study is to evaluate the CVD risks of postmenopausal women in terms of obesity.

MATERIAL AND METHODS

The cross-sectional and descriptive study included 43 postmenopausal women who applied to Dicle University Medical School Family Medicine Outpatient Clinic and agreed to participate in the study. The following parameters were recorded for each participant and compared between obese and non-obese patients: BMI, waist circumferences (WC), Hip circumferences (HC), body fat mass and fat percentage measured by bioelectric impedance analysis (BIA), 24-hour ambulatory blood pressure measurements, plasma Hcy, vitamin B12 and lipid levels, and FRS. The study was approved by Dicle University Medical Faculty Ethics Committee (decision number: 596).

A written consent was obtained from each participant; however, the uneducated women gave their consent with the help of their relatives. For each participant, socio-demographic features, physical activity status (30 minutes per day or not), cardiovascular disease history, menopause duration (years), anthropometric measurement values, and smoking status were recorded. The women with the history of treatment for metabolic disorders and folate or vitamin B12 intake within the last 6 months, and have oncological problems were not included to the study.

The measured and recorded parameters were as follows:

a) Bioelectric Impedance Analysis (BIA): Patients underwent BIA after ≥ 8 h of night rest with empty stomach and an empty bladder. A Tanita Body Composition Analyzer [TANITA BC 418 MA©] was used for measurements. Body fat mass (kg) and body fat ratio (%) are recorded.

b) Body Mass Index (BMI): BMI has been used for more than a century (25), which is calculated by dividing the body weight (kg) by the square of height (m²). In our study, the weight measurements were obtained from a TANITA BC 418 MA scale and the height measurements were performed with bare feet while the patient was in an upright position, so that the gluteal and back regions of the patient could touch the wall tangentially. Patients with a BMI of ≥ 30 kg/m² were considered to be obese (26).

c) Waist and hip circumferences, waist-hip ratio: The complications of obesity are mostly associated with abdominal obesity. Central obesity is known as android-type obesity and lower-body obesity is known as gynoid-type obesity. The waist-hip ratio is used to distinguish these two types of obesity. WC was measured horizontally at the "belly-level" by a tape measure. In women, a WC of >88 cm indicates that the patient is at risk for cardiac disease and metabolic complications (26). HC was measured horizontally, passing through the pubis and the most protruding point of the gluteus maximus muscle. The waist-hip ratio, was calculated by dividing the waist circumference (cm) by the hip circumference (cm). The values greater than 0.85, called truncal or central obesity (26).

d) 24-hour ambulatory blood pressure monitoring (ABPM): Ambulatory blood pressure monitoring is used to determine blood pressure fluctuations over a 24-hour period and is used to avoid the "white coat" effect. ABPM was achieved using a Mobil-O-Graph NG version 20 brand holter device. The device was set to measure the blood pressure at 30-minute intervals during the day and at 1-hour intervals at night. Mean systolic and diastolic measurements were recorded and evaluated.

e) Blood sampling: Blood samples were obtained from the antecubital vein by applying minimal tourniquet force after 10 hours of fasting. Four cc of blood were collected in a heparinized tube, and 7 mL of blood were collected in a gel tube with silica particles on the wall. The samples were centrifuged at 1,500 g for 10 min. The serums and plasmas were separately placed into 2 mL Eppendorf tubes and stored at -80 °C until analysis.

f) Homocysteine, vitamin B12 and lipid measurements: Serum vitamin B12 levels were determined using a Roche cobas 601 analyzer with an ECLIA (Electrochemiluminescence Immunoassay) method. Vitamin B12 levels between 191 and 663 pg/mL were considered to be normal. Plasma Hcy was measured by high-performance liquid chromatography (HPLC) (HP 1100 Series HPLC, Agilent Technologies, CA, USA). Although there is no specific cut-off value for Hcy, the values less than 15 μ mol/L were considered to be normal (27). Lipid (total cholesterol, triglyceride, HDL and LDL cholesterol) levels were measured by Architect C8000-C16000 (Abbott Lab) devices using enzymatic process and formula calculation methods.

g) The Framingham Risk Score (FRS): FRS was originated from the Framingham Heart Study (28,29) and calculated using the parameters of age, gender, LDL and HDL cholesterol, blood pressure, diabetes, and smoking status (30). 10-year risk displayed as percentage and grouped as low (<10%), intermediate (10-19%) and high (\geq 20%) risk of CVD.

Statistical Analysis: SPSS 18.0 for Windows (SPSS, Chicago, IL, USA) was used for statistical evaluation. Since the numbers of women were less than 30 in each groups, nonparametric Mann-Whitney U test was used for comparisons. Chi-square test (Fisher's exact, if necessary) was used for categorical data. To determine the relationships between the parameters, Spearman's

rho (correlation coefficient) was used. The results were expressed as mean \pm standard deviation and median with minimum and maximum values, and a p value of <0.05 was considered significant.

RESULTS

The 43 participants included 24 (58.1%) obese and 19 (41.9%) non-obese women with a mean age of 56.3 ± 10.2 (range, 42-86) years. Of these, 79.1% (n=34) were housewives and 53.5% (n=23) were uneducated. Four (9.3%) of them were smokers and 17 (39.5%) were using antihypertensive drugs due to hypertension. Mean duration of menopause was 8.2 ± 8.2 (range, 1-30) years. No participant was taking regular physical activity. Positive family history rate of CVD was 58.1%. Mean anthropometric and biochemical values are shown in Table 1.

Table 1. Mean-Median values anthropometric and biochemical parameters of the participants

Anthropometric and biochemical Values	Mean \pm SD	Median (min-max)
<i>Age (years)</i>	56.3 \pm 10.2	53.0 (42-86)
<i>Height (cm)</i>	155.1 \pm 5.3	155.0 (137-171)
<i>Weight (kg)</i>	75.0 \pm 16.4	76.9 (45-120)
<i>Waist circumference (cm)</i>	97.3 \pm 22.5	95.0 (70-119)
<i>Hip circumference (cm)</i>	111.2 \pm 12.3	109.0 (85-145)
<i>Waist-Hip ratio</i>	0.84 \pm 0.07	0.84 (0.69-1.03)
<i>Fat Mass (kg)</i>	29.8 \pm 10.8	27.6 (11-60)
<i>Fat Percentage</i>	38.5 \pm 6.6	38.2 (22-51)
<i>Menopause duration (years)</i>	8.2 \pm 8.2	3.0 (1-30)
<i>Hcy (μmol/L)</i>	13.5 \pm .4	11.3 (5.5-33.4)
<i>Vitamin B12 (pg/mL) level</i>	330.8 \pm 254.9	264.7 (114.5-1215.0)
<i>Systolic Blood Pressure (mmHg)</i>	123.5 \pm 17.1	122.0 (94-169)
<i>Diastolic Blood Pressure (mmHg)</i>	77.3 \pm 10.1	77.0 (60-101)
<i>Triglyceride (mg/dL)</i>	156.3 \pm 60.7	141.5 (63-292)
<i>Total Cholesterol (mg/dL)</i>	207.2 \pm 38.5	209.0 (125-291)
<i>LDL Cholesterol (mg/dL)</i>	125.6 \pm 30.2	124.0 (64-192)
<i>HDL Cholesterol (mg/dL)</i>	49.9 \pm 12.0	48.0 (22-79)
<i>BMI</i>	30.9 \pm 6.2	30.8 (20.5-47.0)
<i>FRS (%)</i>	6.7 \pm 4.1	5.0 (2-17)

The waist circumferences ranged from 70 to 119 cm and 67.4% of the measurements (n=29) were >88 cm. Truncal obesity (W/H $>$ 0.85) was observed in 18 (41.9%) patients. Thirty one (73.8%) of the women had a fat percentage of $>34\%$ (reference range, 23-34%). Five women (11.6%) had blood pressure values greater than 140/90 mmHg and 14 women (32.6%) had Hcy values greater than 15.0 μ mol/L. Eight women (18.6%) had vitamin B12 values lower than 191 pg/mL and 3 (7.0%) had values greater than 663 pg/mL.

The 25 women (58.1%) who had a BMI of ≥ 30 , had a higher family history of cardiac diseases (p=0.018), but there was no significant relationship between BMI and other socio-demographic features (p $>$ 0.05). None of our patients had high risk level of FRS. In spite of the significantly higher FRSs in obese patients (p=0.024), there was no significant difference between BMI and low and intermediate risk of FRSs (p=0.754). Mean anthropometric and biochemical values in comparison with BMI and FRS are shown in Tables 2 and 3, respectively.

Table 2. Anthropometric and biochemical values in comparison with BMI scores

Anthropometric and Biochemical Values	BMI		p
	< 30 (n=18)	≥ 30 (n=25)	
Age (years)	55.9±12.4	56.6±8.5	0.414
Height (cm)	155.2±5.8	155.0±5.1	0.570
Weight (kg)	63.0±12.5	83.6±13.2	<0.001
Waist circumference (cm)	86.1±12.0	105.4±24.9	<0.001
Hip circumference (cm)	102.3±8.4	117.8±10.5	<0.001
Waist-Hip ratio	0.84±0.08	0.85±0.07	0.579
Fat Mass (kg)	21.9±7.1	35.1±9.5	<0.001
Fat Percentage	33.6±5.5	41.8±5.1	<0.001
Menopause duration (years)	7.9±9.2	8.4±7.6	0.960
Hcy (µmol/L)	13.2±8.3	13.6±4.9	0.218
Vitamin B12 (pg/mL) level	361.3±309.6	308.8±211.1	0.825
Systolic Blood Pressure (mmHg)	118.4±18.3	127.2±15.6	0.082
Diastolic Blood Pressure (mmHg)	74.9±10.2	79.0±9.9	0.078
Triglycerides (mg/dL)	166.8±69.8	150.4±55.7	0.598
Total Cholesterol (mg/dL)	208.9±40.9	206.1±37.8	0.863
LDL Cholesterol (mg/dL)	124.5±34.1	126.2±28.3	0.876
HDL Cholesterol (mg/dL)	49.6±10.9	50.1±12.8	0.950
FRS (%)	5.0±3.0	7.7±4.4	0.024

The women who had >4 years of menopause duration had higher HDL cholesterol levels and FRS (p=0.029 and p=0.006, respectively) (Figure 1); however, no relation was established between menopause duration and any other parameters. Similarly, no significant relationship was observed

between FRS and familial cardiac disease history or obesity. FRS was lower in women with Hcy levels of <15.0 µmol/L when compared to those with Hcy levels of ≥15.0 µmol/L (8.4±4.1% and 5.8±3.9%, respectively) but this wasn't statistically significant.

Table 3. Anthropometric and biochemical values in comparison with FRS

Anthropometric and Biochemical Values	Framingham Risk Score		p
	<10% (n = 33)	≥ 10% (n = 10)	
Age (years)	53.1±6.3	64.1±10.9	0.003
Height (cm)	155.7±3.9	158.3±5.7	0.404
Weight (kg)	76.2±16.6	77.4±8.2	0.645
Waist circumference (cm)	94.6±13.2	97.4±8.3	0.506
Hip circumference (cm)	113.1±12.5	109.5±8.2	0.675
Waist-Hip ratio	0.83±0.07	0.89±0.07	0.076
Fat Mass (kg)	30.6±11.6	30.7 ± 6.2	0.768
Fat Percentage	39.0±6.6	39.4±5.6	0.971
Menopause duration (years)	6.0±6.3	14.5±8.4	0.013
Hcy (µmol/L)	13.1±6.8	15.0±5.1	0.238
Vitamin B12 (pg/mL) level	288.6±193.6	370.0±328.6	0.461
Systolic Blood Pressure (mmHg)	117.8±15.2	138.6±18.7	0.005
Diastolic Blood Pressure (mmHg)	74.7±9.2	86.1±12.0	0.025
Triglycerides (mg/dL)	154.0±60.2	164.3±66.3	0.732
Total Cholesterol (mg/dL)	208.6±32.9	201.9±57.1	0.658
LDL Cholesterol (mg/dL)	126.4±26.1	122.6±44.1	0.740
HDL Cholesterol (mg/dL)	51.3±10.7	44.6±15.4	0.177
BMI	31.1±6.2	31.0±3.7	0.754

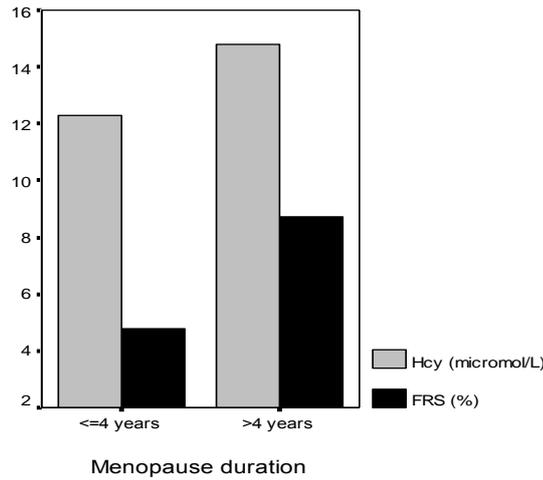


Figure 1. Hcy levels and FRSs in comparison with menopause duration (p=0.171 and p=0.006, respectively)

HDL cholesterol established negative correlation with diastolic blood pressure (r=-0.397, p=0.015) and positive correlation with LDL cholesterol (r=-0.494, p=0.002). Triglyceride had a positive correlation with waist-hip ratio (r=0.420,

p=0.011). FRS was positively correlated with Hcy and waist/hip ratio (r=0.336, p=0.042 and r=0.367, p=0.025, respectively). The correlation of all parameters with each other is shown in Table 4.

Table 4. Correlations of the parameters with each other

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. Age																
2. Menopause Duration	0.834**															
3. Homocysteine	0.291	0.332*														
4. Vitamin B12	0.063	0.087	-0.309*													
5. Systolic Blood Pressure	0.041	0.054	0.060	0.001												
6. Diastolic Blood Pressure	-0.064	-0.037	-0.023	-0.058	0.814**											
7. Fat %	0.022	0.030	0.080	-0.099	0.115	0.077										
8. Fat Mass	-0.084	-0.116	0.116	-0.132	0.182	0.152	0.945**									
9. Triglyceride	-0.264	-0.199	-0.189	0.012	-0.007	-0.023	0.244	0.243								
10. Total Cholesterol	0.037	0.122	-0.028	0.228	-0.160	-0.201	0.012	-0.115	0.215							
11. LDL Cholesterol	0.044	0.101	0.069	0.197	-0.115	-0.166	-0.020	-0.117	0.156	0.966**						
12. HDL Cholesterol	0.237	0.236	-0.163	0.229	-0.305	-0.397*	-0.019	-0.121	-0.323	0.577*	0.494**					
13. Waist Circumference	0.054	0.035	-0.010	-0.010	0.290	0.179	0.719**	0.725**	0.296	-0.176	-0.166	-0.225				
14. Hip Circumference	-0.126	-0.118	0.032	-0.141	0.119	0.148	0.856**	0.874**	0.142	-0.122	-0.103	-0.096	0.735**			
15. W-H Ratio	0.256	0.230	0.045	0.044	0.289	0.096	0.247	0.243	0.420*	0.041	0.013	-0.160	0.561**	0.025		
16. BMI	-0.169	-0.271	-0.014	-0.035	0.279	0.252	0.811**	0.857**	0.244	-0.061	-0.054	-0.142	0.790**	0.875**	0.173	
17. FRS	0.509**	0.431**	0.336*	-0.025	0.593**	0.440**	0.309	0.354*	0.183	-0.106	-0.053	-0.286	0.394*	0.243	0.367*	0.311

* p<0.05 level
**p<0.01 level

DISCUSSION

The present study investigated the relationship between obesity and cardiovascular risk factors in postmenopausal period. Of the 43 women, 58.1% were obese and 79.1% were housewives. It was remarkable that 58.1% had a family history of cardiovascular diseases and most of them were obese. The high prevalence of obesity in our participants may be explained by lack of physical activity, since they declared no regular physical activity; additionally, most of the women were housewives and did not have regular jobs outside the home. Similarly, Kara et al. (31) indicated that most of their reproductive-age participants with metabolic syndrome and higher BMI were housewives. Another reason of obesity might be unhealthy diet but it didn't evaluated in this study.

Abdominal and truncal obesity were seen in majority of our participants (67.4% and 41.9%,

respectively) and hypertension was seen in 39.5%. The body composition indices established positive correlations with one another. A study which aimed to determine the prevalence of metabolic syndrome in Chinese postmenopausal women reported that both BMI and WC were highly correlated with body fat (32). In another study, the prevalence of truncal and abdominal obesity in postmenopausal women were found to be 68% and 60%, respectively, and hypertension was seen in 56% of them (33). In their research regarding the hormonal and biochemical parameters of pre- and postmenopausal women, Tufano et al. (34) reported that the postmenopausal obese women had higher values of WC compared to the premenopausal obese ones. In African American women, Warren et al. (35) detected that WC was independently associated with a 5-fold risk of hypertension and DM. Another study regarding the impacts of

visceral fat, blood pressure, and insulin sensitivity in hypertensive obese women revealed that there was a significant correlation between visceral fat and 24-hour ambulatory blood pressure measurements and these values were significantly higher in postmenopausal women (36). Also, Kanai et al. (17) found that intraabdominal fat accumulation plays an important role in the pathogenesis of hypertension in obese patients. In a study examining the relationship between hypertension and cardiovascular risk factors in women, obesity and dyslipidemia were shown to be associated with hypertension (37). In their study with 377 Portuguese women, Machado et al. (38) reported that hypertension was associated with obesity and being postmenopausal.

Although, there wasn't any significant difference in lipid parameters in terms of BMI or FRS in our study, some studies indicate higher levels in postmenopausal women with high CVD risk and pointed out that in women, HDL cholesterol was a better marker for CVD than LDL cholesterol (3,39).

In our study, based on FRS, 23.3% of the women were at intermediate risk for cardiovascular disease and none of them were at high risk. The reason may be that, as Wenger pointed out, FRS does not adequately explain the risk of CV in women (13). Also, there was a significant correlation between FRS and Waist-Hip ratio. In an American study on abdominal obesity and cardio metabolic risk, women had abdominal obesity at a rate of 62.5%, and the cardiovascular risk increased with an increase in WC (40). In a study conducted in USA, android fat as well as BMI is found to be the determinant of arterial stiffness and the changes of android fat over time was related to changes in vascular function (41). On the other hand, in a postmortem evaluation, any significant association couldn't be shown between Waist-Hip ratio and severe coronary atherosclerosis or sudden cardiac death (42).

In the present study, HDL established a negative correlation with diastolic blood pressure, whereas a positive correlation was found between triglycerides and Waist-Hip ratio. Cognacci et al. (43) studied menopausal symptoms and risk factors for cardiovascular disease and revealed that HDL-cholesterol was negatively correlated both with BMI and menopause duration, the triglycerides were positively correlated with WC, and the FRS was directly and independently correlated with BMI. In our study, FRS was positively correlated with Waist-Hip ratio and Hcy. It was revealed that the duration of menopause also increased with an increase in Hcy values, which was attributed to aging. The increase in Hcy in older people was explained by Kocabalkan et al. (20), who found that the Hcy levels increased with a decrease in kidney functions and age-related vitamin B12 deficiency but we can't explain the correlation between Hcy

and FRS only by aging. A study investigated the cardiovascular disease (CVD) risk factors for serum Hcy levels and indicated that the Hcy levels increased with increasing age and were significantly higher in patients with CVD (19). In addition, the study also indicated that the optimal cut-off point for Hcy in patients with CVD should be $<15 \mu\text{mol/L}$ for patients with either metabolic or non-metabolic syndrome. The Homocysteine Slovakia Study found a very high prevalence of hyperhomocysteinemia in patients with stable ischemic heart disease (44). In the USA, Park et al. (21) reported that the participants with high 10-year risk for coronary heart disease had low-grade systemic inflammation and hyperhomocysteinemia. Similarly, after using the adjusted cox-proportional hazard analysis in the Multiethnic Study of Atherosclerosis (MESA) study and the National Health and Nutrition Examination Survey (NHANES) III, Veeranna et al. (45) suggested that the Hcy levels of $\geq 15 \mu\text{mol/L}$ significantly predicted cardiovascular disease. The authors also reported that the addition of Hcy levels to FRS significantly improved the prediction of FRS, especially in the subjects at intermediate risk for coronary heart diseases.

In conclusion, in the assessment of obesity and CVD risk, not only BMI but also body fat mass and body fat ratio should be used as well. Additionally, it was found that the Hcy levels can also be used for cardiovascular risk assessments, but further epidemiologic studies are needed to identify the mechanisms involved. Moreover, gender-related differences in the assessment of cardiovascular disease risks should be taken into greater consideration.

Limitations and Implications: Because the patients in our study were selected from an outpatient clinic and not from the community, the number of patients in our study was limited. However, the high prevalence of postmenopausal obesity in our study highlights the fact that a lack of physical activity and unhealthy dietary habits are higher among women but regrettably any information about dietary habits were not obtained. Besides, special risks for women such as polycystic ovary, oral contraceptives, hormonal infertility treatment, pregnancy induced hypertension, gestational diabetes and psychological problems (especially depression) didn't discussed here.

Since, CVD risk assessment regarding postmenopausal women requires more evidence, women's participation into trials should be increased. Accordingly, in order to improve the quality of life in postmenopausal women, they should be informed about the effects of obesity, smoking, physical activity and diet, after all, women need further educations regarding these issues because the prevention is more cost-effective than treatment.

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REFERENCES

1. Miller P. Women and cardiovascular disease: what can health providers do to reduce risks? *N C Med J*. 2016;77(6):406-409.
2. Wenger NK. Transforming cardiovascular disease prevention in women: time for the Pygmalion construct to end. *Cardiology*. 2015;130:62-68.
3. Collins P, Webb CM, de Villiers TJ, et al. Cardiovascular risk assessment in women-an update. *Climacteric*. 2016;19(4):329-336.
4. Mehran R, Vogel B, Ortega R, et al. The Lancet Commission on women and cardiovascular disease: time for a shift in women's health. *Lancet*. 2019;393(10175):967-968.
5. The Lancet. Cardiology's problem women. *Lancet*. 2019;393(10175):959.
6. Duenas C KA. Women's cardiology. The essence chapter dedicated to women's cardiology. *Rev Colomb Cardiol*. 2018;25(6):e29-e31.
7. Ketepe-Arachi T, Sharma S. Cardiovascular disease in women: understanding symptoms and risk factors. *European Cardiology Review*. 2017;12(1):10-13.
8. Lee LV, Foody JM. Cardiovascular disease in women. *Curr Atheroscler Rep* 2008 Aug;10(4):295-302.
9. Vanuzzo D, Pilotto L, Mirolo R, Pirelli S. Cardiovascular risk and cardiometabolic risk: an epidemiological evaluation. *Ital Cardiol (Rome)* 2008 Apr;9(4) Suppl:6-17.
10. Banks AD. Women and heart disease: missed opportunities. *J Midwifery Womens Health* 2008 Sep-Oct;53(5):430-9.
11. Lomeli C, Rosas M, Mendoza-González C, et al. Hypertension in women. *Arch Cardiol Mex* 2008 Apr-Jun;78 Suppl 2:S2-98-103.
12. Sclavo M. Cardiovascular risk factors and prevention in women: similarities and differences. *Ital Heart J Suppl* 2001 Feb;2(2):125-41.
13. Wenger N. Tailoring cardiovascular risk assessment and prevention for women: one size does not fit all. *Global Cardiology Science and Practice*. 2017;2017(1):e201701.
14. Atapattu PM. Obesity at Menopause: an expanding problem. *J Pat Care* 2015;1(1):103 doi: 10.4172/2573-4598.1000103
15. Yanes LL, Reckelhoff JF. Postmenopausal hypertension. *Am J Hypertens* 2011 Jul;24(7):740-749.
16. Barua L, Faruque M, Banik PC, et al. Cardiovascular risk assessment among postmenopausal women: a review. *Preprints* 2018, 2018060135 (doi: 10.20944/preprints201806.0135.v1).
17. Kanai H, Matsuzawa Y, Kotani K, et al. Close correlation of intra-abdominal fat accumulation to hypertension in obese women. *Hypertension* 1990 Nov;16(5):484-90.
18. Ganguly P, Alam SF. Role of homocysteine in the development of cardiovascular disease. *Nutr J* 2015;14:6.
19. Kang JY, Park IK, Lee JY, et al. Use of serum homocysteine to predict cardiovascular disease in Korean men with or without metabolic syndrome. *J Korean Med Sci* 2012;27(5):500-505.
20. Kocabalkan F, Baykal Y, Bozoglu E. Homocysteine as a cardiovascular risk factor in the elderly. *Turk Geriatri Derg* 2000;3(2):69-73.
21. Park CS, Ihm SH, Yoo KD, et al. Relation between c-reactive protein, homocysteine levels, fibrinogen, and lipoprotein levels and leukocyte and platelet counts, and 10-year risk for cardiovascular disease among healthy adults in the USA. *Am J Cardiol* 2010 May 1;105(9):1284-8.
22. Wu X, Zhang L, Miao Y, et al. Homocysteine causes vascular endothelial dysfunction by disrupting endoplasmic reticulum redox homeostasis. *Redox Biology*. 2019;20:46-59.
23. Chrysant SG, Chrysant GS. The current status of homocysteine as a risk factor for cardiovascular disease: a mini review. *Expert Review of Cardiovascular Therapy*. 2018;18(8):559-565.
24. Aksoy SN, Geyikli I, Saygili EI. Determinants of plasma homocysteine levels in healthy people. *Turk J Biochem* 2006;31(4):175-181.
25. Han TS, Lean MEJ. Anthropometric indicators of obesity and regional distribution of fat stores. In: Björntorp P, ed. *International Textbook of Obesity*. Turkish, 1st ed. by Dursun AN. Istanbul: And Publisment; 2002; 51-67.
26. World Health Organization. Waist circumference and waist-hip ratio: report of a WHO expert consultation. Geneva, 8-11 December, 2008. https://www.who.int/nutrition/publications/obesity/WHO_report_waistcircumference_and_waisthip_ratio/en/ (Access Date: 02 February 2019)
27. Antoniadou C, Antonopoulos AS, Tousoulis D, et al. Homocysteine and coronary atherosclerosis: from folate fortification to the recent clinical trials. *Eur Heart J* 2009 Jan;30(1):6-15.
28. Dawber TR, Meadors GF, Moore FE Jr. Epidemiological approaches to heart disease: the Framingham Study. *Am J Public Health Nations Health* 1951 Mar;41(3):279-81.

29. Dawber TR, Kannel WB. An epidemiologic study of heart disease: the Framingham study. *Nutr Rev* 1958 Jan;16(1):1-4.
30. Wilson PW, D'Agostino RB, Levy D, et al. Prediction of coronary heart disease using risk factor categories. *Circulation*. 1998;97(18):1837-47.
31. Kara IH, Baltaci D, Sayin S, et al. Investigation of hematologic and biochemical parameters in obese women in reproductive age. *Konuralp Tıp Dergisi [Konuralp Medical Journal]* 2012;4(1):1-7.
32. Ruan X, Jin J, Hua L, et al. The prevalence of metabolic syndrome in Chinese postmenopausal women and the optimum body composition indices to predict it. *Menopause* 2010 May-Jun;17(3):566-70.
33. Tandon VR, Mahajan A, Sharma S, et al. Prevalence of cardiovascular risk factors in postmenopausal women: A rural study. *J Midlife Health* 2010 Jan;1(1):26-9.
34. Tufano A, Marzo P, Enrini R, et al. Anthropometric, hormonal and biochemical differences in lean and obese women before and after menopause. *J Endocrinol Invest* 2004 Jul-Aug;27(7):648-53.
35. Warren TY, Wilcox S, Dowda M, et al. Independent association of waist circumference with hypertension and diabetes in African American women, South Carolina, 2007-2009. *Prev Chronic Dis* 2012 May;9:E105.
36. Faria AN, Ribeiro Filho FF, Gouveia Ferreira SR, et al. Impact of visceral fat on blood pressure and insulin sensitivity in hypertensive obese women. *Obes Res* 2002 Dec;10(12):1203-6.
37. Shimomura T, Wakabayashi I. Associations of cardiovascular risk factors with prehypertension and hypertension in women. *Blood Press* 2012 Dec;21(6):345-51.
38. MachadoVde S, Valadares AL, Costa-Paiva L, et al. Morbidity and associated factors in climacteric women: a population based study in women with 11 or more years of formal education. *Rev Bras Ginecol Obstet* 2012 May;34(5):215-20.
39. Pardhe BD, Ghimire S, Shakya J, et al. Elevated cardiovascular risks among postmenopausal women: a community based case control study from Nepal. *Biochemistry Research International* 2017;2017:3824903. Doi: 10.1155/2017/3824903.
40. Ghandehari H, Le V, Kamal-Bahl S, et al. Abdominal obesity and the spectrum of global cardiometabolic risks in US adults. *Int J Obes (Lond)* 2009 Feb;33(2):239-48.
41. Corrigan FE, Kelli HM, Dhindsa DS, et al. Changes in truncal obesity and fat distribution predict arterial health. *Journal of Clinical Lipidology*. 2017;11:1354-1360.
42. Kocovski L, Lee JD, Parpia S, et al. Association of waist-hip ratio to sudden cardiac death and severe coronary atherosclerosis in medicolegal autopsies. *Am J Forensic Med Pathol* 2017;38:226-228.
43. Cagnacci A, Cannoletta M, Palma F, et al. Menopausal symptoms and risk factors for cardiovascular disease in postmenopause. *Climacteric* 2012 Apr;15(2):157-62.
44. Lietava J, Vocnout B, Dukat A, et al. Homocysteine Slovakia study: study design and occurrence of hyperhomocysteinaemia and other risk factors. *Bratisl Lek Listy* 2012;113(2):80-6.
45. Veeranna V, Zalawadiya SK, Niraj A, et al. Homocystein and reclassification of cardiovascular disease risk. *Am Coll Cardiol* 2011 Aug 30;58(10):1025-33.