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ORIGINAL RESEARCH

Metabolic Syndrome and Menopause: The Impact of Menopause Duration on Risk Factors and Components

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Purpose: This study was undertaken to investigate the impact of menopause duration on the risk factors and components of metabolic syndrome (MetS).

Patients and Methods: Women aged between 45 and 60 years participated in the study. Participants were split into two groups based on the duration of menopause. Women who had been menopausal for 1 to ≤5 years constituted Group 1, while women with 6–10 years of menopause duration formed Group 2.

Results: Significant differences were observed between the two groups for various factors associated with MetS, including anthropometric measurements, biochemical markers, and blood pressure. The conicity index, weight-to-hip ratio, waist-to-height ratio, visceral adiposity index (VAI), and menopause duration were associated with increased risk of MetS. Our multivariate logistic regression model showed that women with elevated VAI had a 2.073-fold (95% CI: 1.73–2.48, p<0.001) increased risk of MetS, while women with menopause duration more than 5 years had a 6.44-fold (95% CI: 3.336–12.45, p<0.001) increased risk of MetS.

Conclusion: The duration of menopause was found to be linked to a higher risk of MetS. Our results emphasize the importance of monitoring and managing metabolic health in women during the menopausal period, particularly those with extended menopause duration.

Keywords: metabolic syndrome, menopause, anthropometric measurements

Introduction

Menopause is defined as the end of female reproductive capacity and occurs at approximately 45–55 years of age.[1] Estrogen declines during menopause, resulting in changes in the body that may include bone loss, increased abdominal fat, and a more unfavorable cardiovascular risk profile, although not all women experience obvious symptoms. Menopausal status also significantly increases the likelihood of developing cardiovascular diseases, type 2 diabetes mellitus, and metabolic syndrome (MetS).[2] MetS is also known as Reaven syndrome, insulin resistance syndrome, and syndrome X. It is defined according to various parameters specified by organizations including the World Health Organization (WHO), National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III), and International Diabetes Federation (IDF).[3] Hypertension, hypertriglyceridemia, central obesity, hyperglycemia, and low high-density lipoprotein cholesterol (HDL-C) are among the diagnostic criteria for MetS.[4]

Menopause is also accepted as an indicator of MetS in women regardless of age. The risk of developing MetS increases with years after menopause, but the full impact of duration of menopause remains unclear.[5] The prevalence of MetS also varies according to the characteristics of the population such as genetic profile, eating habits, and lifestyle. The MetS prevalence among postmenopausal women in Turkey was reported as 15.5%.[6]

In postmenopausal women, weight gain and obesity are particularly effective in increasing the prevalence of MetS. Due to the increase in visceral fat, the functions of the adipose tissue deteriorate, resulting in chronic low-grade inflammation and

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lipotoxicity. The inflammation and altered circulating adipokines promote angiogenesis and have been implicated as risk factors for colorectal, endometrial, and postmenopausal breast cancer. Furthermore, adipocyte-cancer cell crosstalk leads to morphological and functional changes in adipose tissue, resulting in the proliferation, invasion, and metastasis of tumor cells.[7]

Central obesity is characterized by increased visceral adipose tissue and contributes more to MetS risk than general adiposity.[8] Increased visceral fat and waist circumference (WC) are powerful independent predictors of metabolic change.[9] Furthermore, the waist-to-height ratio (WHtR), visceral adiposity index (VAI), and conicity index (C-index) are commonly applied parameters that have significant correlations with central obesity. The VAI is a mathematical index for evaluating visceral fat and the C-index is used for assessing the distribution of body fat, both of which are reliable predictors of MetS risk.[10,11] Considering the impact of the aforementioned parameters, this study was conducted to evaluate the relationship between MetS and the duration of menopause.

Patients and Methods

The study included 705 women aged between 45 and 60 years. The study design was cross-sectional and the participants were volunteers selected from the general population of women in Turkey in 2020–2021. Ethical approval of the study protocol was granted by the local ethics committee of Ankara Medipol University (08.27.2021/31). Menopause was defined as the lack of menstrual periods for more than 1 year.[1] Participants were split into two groups based on the duration of menopause; women who had been menopausal for 1 to ≤5 years constituted Group 1 (n=438), while women with 6–10 years of menopause formed group 2 (n=267). Women who were undergoing hormone replacement therapy, experienced surgical menopause, underwent chemotherapy or radiotherapy, or had liver disease, kidney disease, or a history of cardiac failure or thyroid surgery were excluded from the study. Participants were informed about the research protocol and they provided their informed consent. The questionnaire used in this study was administered to the participants in face-to-face interviews.

This questionnaire was specifically designed to collect relevant data from postmenopausal women; a validated scale was not used in this study.

The questionnaire was organized within the following sections:

Demographic Characteristics

This section was intended to obtain data related to the participant's age, education level, occupation, and general health status.

Anthropometric Measurements

The body composition, height, body weight, hip circumference (HC), and WC of all participants were measured by a researcher. Body mass index (BMI) was calculated as weight (kg)/height squared (m^2). BMI values of ≥30.0 kg/m^2 were considered as signifying obesity, while BMI values of 25–29.9 kg/m^2 were categorized as overweight, 18.5 to 24.9 kg/m^2 as normal or healthy weight, and <18.5 kg/m^2 as underweight.[12] The weight-to-hip ratio (WHR) was calculated as WC/HC. A previous study confirmed that women were at high risk of MetS in the event of WC of ≥88 cm or WHR of >0.85. In the present study, WHR, WHtR, VAI, and C-index values were calculated to facilitate the evaluation of central obesity.[13,14] The following equations were applied:

$$\mathrm{VAI_{Female}} = [\mathrm{WC\,(cm)}/(36.58+(1.88 \times \mathrm{BMI})] \times (\mathrm{Triglycerides\,(TG)}/0.81) \times (1.52/\mathrm{HDL-C})$$

$$\mathrm{C-index_{female}} = \mathrm{WC\,(m)}/[0.109 \times \mathrm{body\,weight\,(kg)}/\mathrm{height\,(m)}]$$

MetS

MetS was identified according to the NCEP-ATP III and IDF criteria. For that purpose, systolic blood pressure and diastolic blood pressure were measured after participants had rested for 10 min in a sitting position. Three consecutive measurements of blood pressure were taken from both arms. Blood tests included fasting blood glucose (FBG), total cholesterol (TC), HDL-C, low-density lipoprotein cholesterol (LDL-C), and TG.[15,16]

The primary outcome of the study was determining the association between duration of menopause and MetS. The secondary outcome of the study was defining the predictive power of anthropometric measurements for MetS.

Statistical Analysis

All statistical analyses conducted in this study were performed using IBM SPSS Statistics 20.0 (IBM Corp., Armonk, NY, USA). Continuous variables were described as means and standard deviations, and categorical variables were presented as frequencies and percentages. Independent samples *t*-tests and chi-square tests were performed for comparisons of the groups. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive power of the variables for MetS. A multivariate logistic regression model was established. Values of $p<0.001$ were accepted as significant with 95% confidence intervals.

Results

Table 1 presents the comparisons of anthropometric measurements, biochemical data, and MetS components between the groups. There were no differences in BMI values or HDL-C levels between the groups.

Table 1 Comparison of Descriptive Statistics and Anthropometric Measurements of the Groups

Variables	Group 1 (n = 438) (1 - ≤ 5 years)		Group 2 (n= 267) (6–10 years)		Total		p-*value*
	Mean	SD	Mean	SD	Mean	SD	
Age (y)	52.04	4.74	53.44	4.82	52.57	4.81	0.067
BMI (kg/m^2)	29.6	5.2	30.4	5.14	29.6	5.8	0.071
Menopause Duration (y)	3.2	1.3	7.6	1.71	5	2.6	<0.001*
WC (cm)	94.0	13.8	100.3	13.5	96.4	14.0	<0.001*
HC (cm)	108.0	10.8	109.7	11.3	108.6	11.0	0.041*
WHR	0.86	0.07	0.91	0.08	0.9	0.1	<0.001*
NC (cm)	35.4	2.9	35.9	2.7	35.6	2.8	0.016*
WHtR	0.60	0.09	0.65	0.09	0.62	0.09	<0.001*
BFP (%)	36.3	6.6	39.0	6.4	37.3	6.7	<0.001*
BWP (%)	44.7	4.3	42.9	4.7	44.0	4.5	<0.001*
LBM (kg)	42.5	5.5	42.7	5.7	42.5	5.6	0.662
AF (kg)	8.0	3.2	10.5	3.4	8.9	3.5	<0.001*
SBP (mmHg)	121.0	17.5	125.9	16.0	122.8	17.1	<0.001*
DBP (mmHg)	74.7	12.9	76.8	11.7	75.5	12.5	0.037*
FBG (mg/dL)	99	29.9	104.7	35.4	101.1	32.2	0.022*
TG (mg/dL)	131.4	57.2	139.7	63.4	134.6	59.7	0.001*
HDL-C (mg/dL)	53.3	13.0	53.0	12.7	53.2	12.9	0.762
LDL-C (mg/dL)	114.9	32.4	121.2	32.6	117.3	32.6	0.015*
TC (mg/dL)	193.7	41.2	201.5	41.0	196.7	41.3	0.015*
CI	1.61	0.13	1.66	0.14	1.63	0.13	<0.001*
VAI	2.25	1.40	2.52	1.78	2.35	1.56	0.029*

Note: *p-value of less than 0.05 was considered to be statistically significant.

Abbreviations: AF, Abdominal Fat; BFP, Body Fat Percentage; BMI, Body Mass Index; BWP, Body Water Percentage; CI, Conicity Index; DBP, Diastolic Blood Pressure; FBG, Fasting Blood Glucose; HC, Hip Circumference; HDL-C, High Density Lipoprotein Cholesterol; LBM, Lean Body Mass; LDL-C, Low Density Lipoprotein Cholesterol; NC, Neck Circumference; SBP, Systolic Blood Pressure; TC, Total Cholesterol; TG, Triglycerides; VAI, Visceral Adiposity Index; WC, Waist Circumference; WHtR, Waist-to-Height Ratio; WHR, Waist-to-Hip Ratio.

Looking at the prevalences of metabolic abnormalities and MetS among the participants, there were differences between the groups in terms of FBG, WC, elevated blood pressure, and MetS. Group 2 had a higher frequency of abnormalities in FBG, higher WC values, and elevated blood pressure compared to Group 1 (44.9% vs 31.4%, 94.3% vs 87.1%, and 48.7% vs 35.1%, respectively; p<0.001). The number of women who met the criteria for MetS was higher in Group 2 than in Group 1 (87 vs 137 participants; p=0.001) (Table 2).

Univariate logistic regression analysis revealed that WHR, WHtR, C-index, VAI, and menopause duration were associated with an increased risk of MetS. Multivariate logistic regression analysis was then performed, and it was found that women with elevated VAI values had a 2.073-fold (95% CI: 1.73–2.48, p<0.001) increased risk of MetS, while women with menopause duration more than 5 years had a 6.44-fold (95% CI: 3.336–12.45, p<0.001) increased risk of MetS (Table 3).

A flowchart of this study is shown in Figure 1. The study comprised 805 patients initially, with the final analysis conducted on 705 women.

Figure 2 demonstrates the ROC analysis results for the ability of WHR, WHtR, C-index, VAI, and menopause duration to predict MetS. The ROC analysis revealed that although all of these variables had statistical significance, the area under the curve (AUC) value was highest for the VAI, followed by menopause duration.

Table 2 Prevalence of Metabolic Abnormalities and MetS Among Groups

Variables	Group 1 (1 - ≤ 5 years) (n=438)		Group 2 (6–10 years) (n=267)		p-*value*
	n	%	n	%	
WHtR (≥0.50)	377	87.1	254	96.6	<0.001*
FBG (≥100 mg/dL)	136	31.4	118	44.9	<0.001*
WC (≥80 cm)	377	87.1	248	94.3	0.002*
Elevated blood pressure (SBP ≥130 and/or DBP ≥85 mmHg)	152	35.1	128	48.7	0.001*
TG (≥150 mg/dL)	127	29.3	105	39.9	0.062
HDL-C (<50 mg/dL)	181	41.8	114	43.3	0.689
MetS	87	38.8	137	52.1	0.001*

Notes: *p-value of less than 0.05 was considered to be statistically significant.
Abbreviations: BMI, Body Mass Index; DBP, Diastolic Blood Pressure; FBG, Fasting Blood Glucose; HDL-C, High-Density Lipoprotein Cholesterol; Diastolic Blood Pressure; TG, Triglycerides; WC, Waist Circumference; WHtR: Waist-to-Height Ratio.

Table 3 Univariate and Multivariate Logistic Regression Analysis of the Variables for MetS

Metabolic Variables (n=705)	OR (95% CI)		P-*value*	OR (95% CI)		P-*value*
WHtR	51.146	(9.534–274.382)	<0.001*	1.494	(0.095–23.539)	0.775
VAI	70.66	(1.695–2.336)	<0.001*	2.073	(1.732–2.481)	<0.001*
WHR	90.68	(12.247–67.445)	<0.001*	0.433	(0.10–19.595)	0.667
C-index	19.96	(5.642–70.61)	<0.001*	1.473	(0.120–18.157)	0.762
Menopause Duration (y)	1.264	(1.186–1.347)	<0.001*	0.961	(0.854–1.082)	0.515
Menopause 1-≤ 5 years (n= 438) 6–10 years (n=267)	4.813	(3.432–6.748)	<0.001*	6.444	(3.336–12.450)	<0.001*

Note: *p-value of less than 0.05 was considered to be statistically significant.
Abbreviations: CI, Conicity Index; VAI, Visceral Adiposity Index; WHR, Waist-to-Hip Ratio; WHtR: Waist-to-Height Ratio.

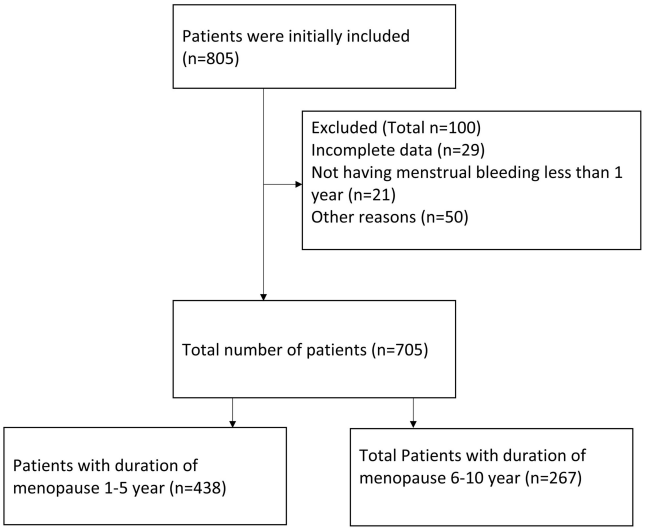

Figure 1 Flow Chart of the Study.

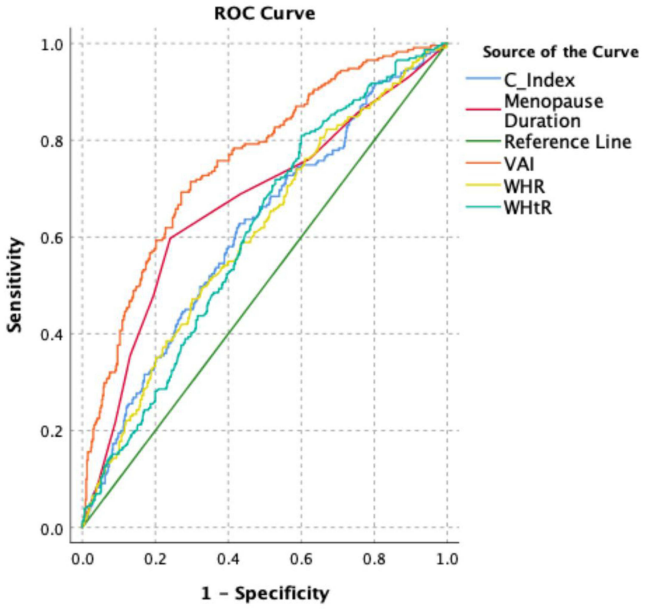

Figure 2 ROC analysis of C-index, Menopause Duration, VAI, WHR and WHtR for predictability of MetS (AUC of C-index:0.612, cut off point: 1.632 sensitivity:60.6%, specificity:58.1%; AUC of VAI:0.755, cut off point:2.19, sensitivity:71.4%, specificity:70.3%, AUC of WHtR:0.607, cut off point:0.61, sensitivity:57.1%, specificity:56.8%, AUC of WHR:0.755, cut off point:0.89, sensitivity:58%, specificity:57.1%, AUC of Menopause Duration: 0.667, cut off point:5, sensitivity:68.8%, specificity:62.4%).

Discussion

The occurrence of MetS varies between 10% and 84% worldwide according to the diagnostic criteria that are applied.[17,18] These diagnostic criteria include various physiological, biochemical, clinical, and metabolic factors, together with anthropometric measurements. Advanced age is a crucial risk factor for developing MetS, as reported by the NHANES III study conducted with data from 2011–2016, which showed a 39.4% risk in the age group of 40–59 years and a 48.6% risk in the age group of >60 years.[19]

In our study, in Group 2, abnormalities in FBG, higher WC values, and elevated blood pressure were found more frequently. While WHR, WHtR, C-index, VAI, and menopause duration were all associated with an increased risk of MetS, the AUC value of the VAI was highest, followed by menopause duration.

Central obesity is associated with increased rates of insulin resistance, hypertension, diabetes, impaired lipid profile, and elevated blood glucose. It is also a cornerstone of MetS and leads to increased cardiometabolic risk.[20] In our study, both Group 1 and Group 2 had significantly higher TG and FBG levels and lower HDL-C levels among overweight women compared to those with normal body weight. Bhosale et al reported no difference in HDL-C levels between the control and MetS groups, but they determined significant differences for TG, LDL-C, and FBG.[21] In the present study, we found that women in Group 2 had higher FBG, TC, TG, and LDL-C values than those in Group 1 ($p<0.001$). The severity of overweight was associated with an increased risk of MetS. Overweight women with metabolic disorders have twice the risk of developing cardiovascular diseases and diabetes compared to individuals with normal body weight without MetS. Furthermore, individuals with normal weight and MetS have a threefold increased risk of cardiovascular diseases and fourfold increased risk of diabetes.[22] Excessive abdominal weight, which is more closely related to central obesity than BMI,[16] is a pivotal factor contributing to MetS.[17] Changes in body fat mass occur during menopause. A one-year follow-up study revealed a significant increase in women's WC, fat mass, and fat percentage values after menopause, while lean mass decreased considerably.[23] Another 5-year study reported substantial increases in total fat mass, body fat percentage, body fat mass, and visceral fat values in postmenopausal women.[24] Recently, WHtR has been suggested as a better indicator of MetS than BMI and WC.[25] WHR and WC are parameters used to measure visceral and abdominal fat distribution, providing better results than BMI.[26] Previous studies evaluating MetS have shown that WHtR values above 0.5 are associated with increased cardiometabolic risk, surpassing BMI and WHR in terms of its power as a discriminating marker.[27,28] In a study conducted with young adults in the United States, a WHtR cutoff point of 0.58 was found to predict the presence of MetS.[29] In our study, we found that the WHR, WHtR, VAI, and C-index were valuable in predicting the presence of MetS, consistent with the relevant literature indicating increased body mass and BMI values in menopausal women.

The emergence of metabolic risk factors in the postmenopausal period may directly result from estrogen deficiency and ovarian failure.[30] Ovarian hormones have cardioprotective effects, and decreased levels of endogenous estrogen, especially in cases of early menopause, may lead to imbalanced lipid profiles and a higher risk for the development of cardiovascular diseases.[31]

Estrogen is involved in processes of gluteofemoral fat deposition, and its loss during menopause is associated with increased abdominal fat. In addition, the loss of ovarian function causes negative changes in lipoprotein profile, glucose and insulin metabolism, vascular endothelial dysfunction, and body fat distribution.[32]

In our study, the most important risk factor for MetS was found to be the duration of menopause. Yu et al found that women with menopause duration of more than 20 years were more likely to experience MetS and increased blood pressure compared to those with menopause duration of less than 10 years.[33] Cho et al showed that the risk of developing MetS increased with the duration of menopause in postmenopausal women. They also found that it reached peak levels at 10–14 years.[34] Zhou et al obtained similar results in a Chinese population. They revealed a relationship between years since menopause and MetS, and the highest risk of MetS was reported for patients with menopause duration of 5–9 years.[35] Variations in the impact of menopause duration among these studies may be attributed to differences in ethnic backgrounds. Regarding the metabolic abnormalities associated with MetS, our study showed that women who had been menopausal for more than 5 years had a significantly higher risk of MetS than women who had been menopausal for ≤5 years.

There are several limitations of this study that need to be considered. First, the participants were volunteers selected from the general population of women in Turkey. The non-random sampling method may have introduced selection bias and the results may not be generalizable to the extended population or other ethnic groups. Furthermore, the study relied on self-reported data, including information on nutritional habits and behaviors, which may have affected the accuracy of the data.

Conclusion

This study highlights the impact of menopause on metabolic health in women. The duration of menopause emerged as a significant risk factor, indicating the progressive nature of metabolic changes during this period. Targeting alterable risk factors such as central obesity may potentially mitigate the risk of MetS and its associated complications. Larger studies are warranted to explore the underlying mechanisms of menopausal MetS and develop tailored interventions for this high-risk population.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Ankara Medipol University (08.27.2021/31).

Author Contributions

All authors made significant contributions to the work reported, whether in the conception, study design, execution, acquisition of data, analysis and interpretation, or all of these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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