Adherence to a Mediterranean diet and cardio-metabolic risk in postmenopausal women by body composition

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ABSTRACT

Background and Objectives: To evaluate whether cardio-metabolic risk data in obese postmenopausal women are affected by adherence to the Mediterranean diet. **Methods and Study Design:** This cross-sectional study was conducted in 89 pre-obese and obese postmenopausal women (PMW) aged 40-75 years with a Body Mass Index (BMI) value ≥ 25 kg/m^2. Demographic characteristics, health status, anthropometric measurements, physical activity status, nutritional habits, lipid profile, some biochemical results and cardiovascular risk predictor (CVRP) data were collected by face-to-face interviews. **Results:** In this study, a negative correlation was found between CVRP and a Mediterranean diet score (MEDI-LITE) scores in pre-obese and obese PMW (p=0.008, p=0.02, respectively). Total cholesterol levels of the obese women were found to be negatively correlated with MEDI-LITE scores (p=0.002). VLDL-cholesterol (p=0.04, p=0.008, respectively) and triglyceride levels (p=0.002, p=0.003, respectively) of the pre-obese and obese women were negatively correlated with MEDI-LITE scores. According to the logistic regression analysis, the variables affecting CVRP negatively in our study were age, smoking, and salt use, while the variables affecting CVRP positively were MEDI-LITE score and omega 3 fatty acid consumption. **Conclusions:** In this study, it was observed that the increase in the Mediterranean diet (MedDiet) adherence score of the pre-obese and obese women in the postmenopausal period had favourable effect on lipid profile and CVRP. It is considered that adhering to the MedDiet in pre-obese and obese PMW can be recommended as an effective strategy to prevent the increased risk of cardiovascular disease due to advanced age, menopause, and high BMI values.

Key Words: postmenopause, cardio-metabolic risk, obesity, MEDI-LITE score, mediterranean diet

INTRODUCTION

One of the main factors increasing morbidity and mortality in the postmenopausal period is the increase in cardiovascular disease incidences. The increase in cardiovascular diseases is partly associated with advancing age and partly with the fact that cardiovascular risk factors are adversely affected by the disappearance of the protective effects of estrogen.[1] Postmenopausal women have higher blood pressure and low-density lipoprotein (LDL) cholesterol levels than men and also they have higher and more often multiple concurrent atherosclerotic risk factors.[2] Weight gain is one of major concern in this lifespan and it has been reported that menopause is associated to approximately 2 kg of weight gain.[3] Although the increase in body mass index (BMI) during this period is probably more related to women's age than to menopause itself, increased abdominal subcutaneous and visceral fat with menopause is associated with an increased incidence of metabolic syndrome, diabetes mellitus, and cardiovascular disease.[2] In postmenopausal women compared to premenopausal women, it has been observed that there is an increase in total body fat, especially in the distribution of android fat.[4] During menopause, a decrease in estrogen levels has been associated with the loss of lean body mass and an increase in fat mass.[5] The longitudinal Study of Women's Health Across the Nation study showed that the mean lean body mass loss during menopause is 0.5% per year and fat mass increases 1.7% per year.[6] Body composition changes in this population are associated with an increased risk of coronary heart disease, potentially affecting women's health as a whole. According to data from the National Health and Nutrition Examination Survey (NHANES), participants with low lean body mass and high fat mass have been shown to have the highest risk of mortality due to cardiovascular diseases.[7] The Framingham heart study evaluated the relationship between the degree of obesity and cardiovascular disease in a total of 5,209 men and women who were followed for 26 years. In this study, it was stated that obesity is an independent risk factor, and it was shown that body weight is a determining factor for the presence of coronary artery disease due to its association with age, blood pressure, smoking, serum cholesterol, and glucose intolerance.[8] In the Framingham heart study, it was reported that the most effective dietary profile in reducing serum cholesterol levels in postmenopausal women was higher intake of plant-derived protein and complex carbohydrates, and less fat intake.[9]

There is a long-held understanding that diet plays an important role in the etiology of many chronic diseases, thus contributing to geographic differences in morbidity and mortality rates caused by chronic diseases in different countries and populations worldwide.[10] Diet can regulate inflammation, a process involved in all stages of atherothrombosis.[11] In particular, starting with ecological data in the context of the Seven Countries study in the 1960s, the Mediterranean diet (MedDiet) has long been studied for its potential beneficial effects on a variety of chronic disease outcomes.[12] In a cohort study of elderly people in rural Greece they found that a one unit increase in a diet score, devised a priori on the basis of eight desirable key features of the traditional common diet in the Mediterranean region, was associated with a statistically significant 17 % reduction in overall mortality.[13] With greater adherence to the MedDiet, various observational studies have demonstrated longer lifespan and good quality of life, as well as reduced mortality and morbidity caused by cardiovascular diseases and other nutrition-related diseases.[14,15] In a study evaluating the relationship between adherence to the

MedDiet and dyslipidemia in a cohort of adults in the Mediterranean area in Italy, it was shown that the incidence of dyslipidemia decreased as the higher adherence to the MedDiet.[16] The essential concept of the MedDiet is that this is not a set of changes to our usual diet dictated by scientific experiments. It is a set of food habits and recipes enjoyed traditionally by the ordinary people of Mediterranean countries who have been found to have lower rates of coronary and other chronic diseases than the most scientifically developed countries, for example, USA, UK and Germany.[17] In the study of Truswell and Noah, in which they evaluated the traditional eating habits of 18 countries with a coast on the Mediterranean, including Turkey, they emphasized that there are differences as well as similarities in the traditional eating habits of the countries, and that nutritionists should consider these differences when defining MedDiet modules.[18] Adherence to the principles of the traditional MedDiet, as operationalized in the diet score used, is likely to be associated with lower overall mortality.[19] The traditional MedDiet involves a high intake of plant-based foods, predominantly fruits and vegetables, cereals and whole grain breads, beans, nuts, and seeds. It includes locally grown, fresh, and seasonal unprocessed foods. While fresh vegetables and fruits are consumed daily and in large amounts, concentrated sugars or honey are consumed in lower amounts several times a week. The MedDiet includes olive oil as the main course ingredient and source of fat, low to moderate amounts of cheese and yogurt, low amounts of red meat and higher amounts of fish, and low to moderate amounts of red wine with main meals.[20]

In peri- and post-menopausal women, long-term high adherence to MedDiet may reduce cardiovascular risk, and the incidence of cardiovascular events and deaths. Short-term high adherence to MedDiet may improve vasomotor symptoms, improve cardiovascular risk factors such as blood pressure and cholesterol levels.[21]

The aim of this study was to evaluate whether cardio-metabolic risk data in obese postmenopausal women are affected by adherence to the MedDiet.

MATERIALS AND METHODS

This cross-sectional study was conducted in a hospital (identifiers were removed for blind peer review) in 89 pre-obese and obese women aged 40-75 years with a BMI score of 25 kg/m^2 or over, and who were postmenopausal (amenorrhea lasting more than one year). Women who were pregnant and lactating, those with heart failure, chronic kidney failure, and liver disease, those with bowel disease (Crohn's, irritable bowel syndrome, and short bowel syndrome), those not in an age range of 40-75 years, those with BMI < 25 kg/m^2, and those who did not accept to participate in the study were not included. Data were collected using a questionnaire administered via face-to-face interviews. The following data were analyzed: women’s demographic characteristics, health status (diagnosed disease, co-morbidities, menopausal status, medicine used), anthropometric measurements (height, weight, BMI), physical activity status, information on nutritional habits, lipid profile and some biochemical results (serum total cholesterol, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol, triglyceride, vitamin D, calcium, phosphorus, parathyroid hormone (PTH)), and the cardiovascular risk predictor (CVRP) (triglyceride/HDL cholesterol ratio).[22]

Women’s body weight was measured and recorded with a weighing instrument with an accuracy of ±0.1. Women’s height was measured and recorded by the dietitian with a stadiometer. While taking height measurements, the women’s feet were together and their heads were in the Frankfurt plane (bottom border of the eye and the top border of the ear canal were on the same line).[23] BMI values were calculated with the formula of body weight (kg)/height $(m)^2$. According to the ranges determined by the World Health Organization, BMI values were classified as 25-29.9 kg/m^2 as pre-obese and 30 kg/m^2 and over as obese.[24] In order to determine the food consumption status, one-day food consumption records taken with the 24-hour recall method. Energy and nutritional elements taken with the daily diet were analyzed using the "Computer Assisted Nutrition Program, Nutrition Information Systems Package Program (BEBIS)" developed for the Turkish population. MedDiet adherence were assessed using the Mediterranean diet score (MEDI-LITE), a validated food frequency questionnaire.[25] Food consumption frequency and MedDiet adherence as assessed by the MEDI-LITE score, have been widely used, approved, and recommended for use in clinical studies.[26,27]

With the MEDI-LITE score, daily and weekly food intakes are assessed with nine questions about the foods recommended in the MedDiet. The highest consumption of fruits, vegetables, grains, legumes, fish, and olive oil is expressed with 2 points, the moderate consumption with 1 point, and the lowest consumption with 0 points. On the other hand, 2 points correspond to the lowest consumption of meat and meat products, dairy products and alcohol, while 1 point represents the moderate consumption, and 0 points the highest consumption. The final score obtained ranges from 0 (low adherence to the MedDiet) to 18 (high adherence to the MedDiet). Especially milk and dairy product consumption should not exceed 180 g per day, and meat and meat products should not exceed 80 g per day.[26]

The type of exercise (endurance, balance, strength and flexibility), frequency (per week, per day), and duration were questioned in determining the physical activity status of the individuals.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Turkey's Health Ministry (Approval number: 2020-05-19T13_15_24) and Toros University Clinical Research Ethics Committee (Approval number: (≠66, 18/05/2020). Informed consent was obtained from all individual participants included in the study.

Statistical analysis

The data obtained in the study were evaluated with the SPSS 15.0 package program. Appropriate descriptive values are given for qualitative and quantitative variables. Qualitative variables are expressed as numbers (n) and percentage (%), while quantitative variables are expressed as mean and standard deviation ($\bar{X}\pm SD$). The conformity of the variables to the normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Between two independent groups, a difference test between two means (Student's t-test or non-parametric Mann-Whitney-U test) was used for continuous variables, and non-parametric Spearman correlation analysis was used to determine correlations between numerical variables. A logistic regression analysis test was used to evaluate the variables thought to affect the cardiovascular risk factor. A value of $p<0.05$ was considered statistically significant.

RESULTS

In this study, 46.1% of the postmenopausal women were classified as pre-obese and 53.9% as obese. Demographic and clinical characteristics of the women are shown in Table 1.

There was no statistically significant difference between the cardiovascular risk predictor (CVRP) values of pre-obese and obese women. On the other hand, obese women had higher serum PTH values ($p=0.005$) and lower vitamin D levels ($p=0.01$) than pre-obese women (Table 2).

In order to evaluate the relationship of low vitamin D and high PTH levels with nutritional habits in obese women, the women's 24-hour food consumption data were assessed. In terms of the BMI classification, there was a difference between women in terms of daily energy (kcal/day) ($p=0.001$), carbohydrate (gr/day) ($p=0.002$), and fat (gr/day) ($p=0.001$) intakes, and there was no difference in terms of the consumption of other nutrients (vitamins soluble in fat or water, minerals, fiber, and cholesterol). There was no statistically significant difference between MEDI-LITE scores of the women according to the BMI classification. (Table 2).

When the lipid profile of the women was evaluated, a negative correlation was found between the CVRP values of the pre-obese and obese women and the MEDI-LITE scores (r=-0.411, *p*=0.008, r=0.327, *p*=0.02, respectively). While the total cholesterol levels of the obese women were negatively correlated with the MEDI-LITE score (r=-0.443, *p*=0.002), the VLDL cholesterol levels of the pre-obese and obese women (r=-0.321, *p*=0.04, r=0.379, *p*=0.008, respectively) and their triglyceride levels (r=-0.462, *p*=0.002, r=0.416, *p*=0.003, respectively) showed a negative correlation with the MEDI-LITE score. No correlation was found between age, BMI, blood pressure, and biochemical parameter measurements (serum calcium, vitamin D, and PTH) and CVRP values of the women (*p*>0.05) (Table 3).

According to the logistic regression analysis, the variables affecting CVRP negatively in our study were age, smoking, and salt use, while the variables affecting CVRP positively were MEDI-LITE score and omega 3 fatty acid consumption (Table 4).

DISCUSSION

Menopause is a process defined as the permanent end of the menstrual cycle. Estrogen level, which decreases with the end of the menstrual cycle, is also listed among the factors that cause both body weight gain and an increased risk of cardiovascular disease in women.[28]

In postmenopausal women, with increasing age, there is a decrease in muscle mass and an increase in body fat tissue, and this causes an increase in the prevalence of obesity.[29] Although it has been reported in large-scale studies that the main predictor of the increase in body weight and obesity is aging and that menopause has an indirect effect, it has been suggested that decreasing estrogen levels in this period may be associated with increased visceral adipose tissue and cause obesity.[30,31] In a study conducted by Sowers et al in postmenopausal women for a period of 6 years, it was shown that there was a 10% increase in body fat mass and a 1% decrease in skeletal muscle mass in postmenopausal women compared to their premenopausal periods, after the adjustment for chronological age.[32] Obesity is an independent risk factor for cardiovascular diseases. In addition, it is argued in some studies that the decrease in estrogen, which helps to prevent the atherothrombotic process in cardiovascular diseases, may also be a risk factor.[33] however, there exist studies claiming otherwise.[34,35] In the Framingham heart study, which is one of the important studies evaluating the risk of cardiovascular disease in obesity, it is emphasized that each 1 kg/m^2

increase in BMI increases the cardiovascular risk by 7% in postmenopausal women.[36] Serum triglyceride and cholesterol values are widely used as predictors of the cardiovascular risk, and generally increased LDL-cholesterol and fasting triglyceride levels are taken as a basis. It is argued that the triglyceride and HDL-cholesterol ratio is a superior atherogenic index compared to other lipid parameters and ratios.[37] It was found that 53.9% of the postmenopausal women participating in this study were obese, and 46.1% were pre-obese. The CVRP values of the women in the obese group were higher than the that of the other group; however, this difference was not statistically significant.

In this study, it was determined that, as the BMI value of the individuals participating in the study increased, serum vitamin D levels decreased in accordance with the literature. Obesity, which is an important risk factor for cardiovascular diseases, often occurs together with vitamin D deficiency.[38] The relationship between obesity and vitamin D is bidirectional and it is not certain which mechanism affects the other.[39] The increased amount of adipose tissue in obesity prevents the activation of vitamin D by increasing the amount of stored vitamin D, and in this case, there is an increase in body weight with the stimulation of lipogenesis caused by the increase in intracellular calcium in adipocytes.[40] In a study conducted in obese and pre-obese adults in New Zealand, a relationship was found between decreased serum $25(OH)D_3$ level and increased body weight and waist circumference.[41] Similarly, Lagunova et al conducted a study in 2126 individuals and found a negative correlation between BMI values and serum $25(OH)D_3$ levels.[42]

In this study, according to the logistic regression analysis, it was found that advanced age, smoking, and salt use negatively affected the CVRP values, whereas omega 3 fatty acid consumption positively affected it. Inflammatory, oxidative, thrombotic, and vascular factors play an important role in cardiovascular diseases and lipoprotein metabolism.[43] Omega 3 fatty acids reduce the risk of cardiovascular disease by lowering plasma triacylglycerols and blood pressure, improving vascular reactivity, and reducing inflammation.[44] Observational and clinical studies have shown that consumption of omega 3 fatty acids, which have an anti-inflammatory effect, has a negative effect on cardiovascular risk.[45,46] Contrary to these studies, it was found that the use of omega 3 fatty acids did not cause a change in the incidence of cardiovascular events in the STRENGTH study, which was conducted in 4 years with participants from different countries.[47] Smoking is associated with increased levels of multiple inflammatory markers, including C-reactive protein, interleukin-6, and tumor necrosis factor alpha.[48]

The MedDiet is a diet model characterized by consumption of fruits, vegetables, whole grain breads and cereals, legumes, oilseeds, and processed products, reduced consumption of sweet and red meat, increased consumption of fish and olive oil, and moderate consumption of wine.[49] The MedDiet has lower calories and higher antioxidant content than other diet models.[50,51] A general analysis of the studies involving individuals consuming the MedDiet shows that the MedDiet prevents obesity,[52,53] but it is not clear whether this positive effect is due to low calorie intake or the nutrients contained in the diet.[53,54] In this study, it was observed that the MedDiet adherence assessed by MEDI-LITE scores in pre-obese and obese postmenopausal women participating in the study did not differ between the groups (p>0.05). This result, which is different from the literature, can be interpreted as the fact that this study is an observational study without energy restriction. In clinical studies, it has been shown that the consumption of these nutrients that make up the MedDiet together and in recommended amounts has a protective effect on cardiovascular diseases by reducing inflammation, which is effective in all atherothrombotic processes, thanks to the high antioxidant content it contains.[15,55] According to the 5-year-long PREDIMED study, which had a high participation rate and 57% of the participants were postmenopausal women, it was observed that the MedDiet was superior to the low-fat diet in protection against cardiovascular diseases, and it was determined that those who consumed the MedDiet had a lower incidence of cardiovascular disease than those who consumed the low-fat diet.[56] The Lyon diet heart study showed that increased adherence to the MedDiet is consistently associated with lower cardiovascular risk.[57] Adherence to the MedDiet has been shown to be associated with lower serum triglyceride, total, and LDL-cholesterol levels in a cross-sectional study and an intervention study in healthy middle-aged women.[58,59] In another study conducted with postmenopausal women in Sicily, the women participating in the study were taught the MedDiet and cooking methods suitable for this diet, and they were asked to practice it at home for one year. At the end of the study, it was emphasized that women who adopted the MedDiet had a clear tendency towards loss of body weight, a strong decrease in serum cholesterol levels, and an increase in quality of life.[60] A systematic review of 30 randomized controlled trials indicated that data on the efficacy of the MedDiet in reducing and managing the risk of cardiovascular disease contained uncertainty in terms of statistical heterogeneity; however, it was emphasized that it is a diet that can be recommended to improve health and reduce the burden of cardiovascular disease in women.[61] In this study, it was determined that the score of adherence to the MedDiet was negatively correlated with serum triglyceride, total cholesterol, VLDL cholesterol levels, and CVRP, supporting the literature, and it was an important variable that positively affected CVRP according to the logistic regression analysis.

Our study has some limitations that should be acknowledged. First of all, because it is a cross-sectional study, its causality could not be evaluated. Second, we had a small and heterogeneous study population. Randomized controlled studies with more participants are warranted.

Conclusion

In this cross-sectional study, it was seen that the increase in the MedDiet adherence score in pre-obese and obese women in the postmenopausal period had a favourable effect on the lipid profile and the CVRP values. Based on the present results, it is thought that adherence to the MedDiet in pre-obese and obese postmenopausal women can be recommended as an effective strategy to prevent the increased risk of cardiovascular disease caused by advanced age, menopause, and high BMI values.

AUTHOR DISCLOSURE

The authors state no conflict of interest. There are no financial supports provided.

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Table 1. Demographic and clinical results

Variable	Value
Age, (mean±SD), year	55.07±6.14
BMI, (mean±SD) kg/m^2	31.23±4.28 (25.15-44.12)
BMI Classification, kg/m^2 (%)	
Pre-obese (25 - < 29.99 kg/m^2)	41 (%46.1)
Obese (≥ 30 kg/m^2)	48 (%53.9)
Systolic blood pressure (mmHg), (mean±SD),	12.78±1.22
Diastolic blood pressure (mmHg), (mean±SD),	8.77±1.08
Current smokers, (%)	1.3
Cigarette (mean±SD), count/day	2.21±6.52
Duration of smoking (mean±SD), year	2.99±8.10
Physically active, (%)	14.6
Activity duration, (mean±SD), hour/week	0.84±2.12
Activity frequency, (mean±SD), day/week	0.21±0.73
Prescription medicine use, (%)	61.8
Family history of heart disease, (%)	57.3
Co-morbidity, n	
Diabetes mellitus	24
Hypertension	13
Other	6

SD: standard deviation.

Table 2. Biochemical parameters and evaluation of nutrient intakes of postmenopausal women

Biochemical parameters	Pre-obese (n=41)	Obese (n=48)	*p*
BMI (kg/m^2)			
Cardiovascular Risk Predictor (triglyceride/HDL-cholesterol ratio)	3.35±2.89	4.28±3.37	0.06
Total Cholesterol (mg/dL)	206.61±41.96	200.27±34.69	0.39
LDL Cholesterol (mg/dL)	118.40±35.70	111.39±30.52	0.50
HDL Cholesterol (mg/dL)	56.30±14.27	50.92±10.51	0.11
VLDL Cholesterol (mg/dL)	30.99±37.81	18.82±22.77	0.14
Triglyceride (mg/dL)	165.27±106.46	194.29±115.10	0.15
$25(OH)D_3$ (ng/dL)	27.08±14.03	19.80±12.36	0.01*
Parathyroid hormone level (pg/mL)	53.04±23.63	71.09±30.65	0.005**
Daily consumption of nutrients calculated via 24-hour food consumption			
Energy (kcal/day)	1493.99±374.95	1774.98±390.84	0.001**
Protein (g/day)	59.44±16.41	63.07±17.35	0.52
Carbohydrate (g/day)	177.17±43.15	210.24±52.42	0.002**
Fat (g/day)	58.25±72.73	21.37±20.69	0.001**
Fiber (g/day)	17.72±8.57	18.69±4.99	0.10
Cholesterol (mg/day)	352.08±215.61	375.03±251.44	0.93
MEDI-LITE score	10.12±2.01	10.14±1.96	0.79

Mann-Whitney-U test, *$p<0.05$, ** $p<0.01$.

Table 3. Correlation between the MED-LITE score and lipid profile in postmenopausal women

Variables	Pre-obese (n=41)		Obese (n=48)	
MEDI-LITE Score	r	*p*	r	*p*
Cardiovascular Risk Predictor (triglyceride/HDL-cholesterol ratio)	-0.411	0.008**	-0.327	0.02*
Total cholesterol (mg/dL)	-0.009	0.95	-0.443	0.002**
VLDL cholesterol (mg/dL)	-0.321	0.04*	-0.379	0.008**
Triglyceride (mg/dL)	-0.462	0.002**	-0.416	0.003*

Spearman's correlation analyses, *$p<0.05$, ** $p<0.01$.

Table 4. Regression analysis between CVRP and other determinants in postmenopausal women

Variables	Regression analysis (Adjusted R^2 value=0.445, p=0.001**)		
	Coeff.	%95CI	*p*
Age, (year)	0.242	0.223 to 0.027	0.01*
MEDI-LITE score	-0.275	-0.756 to -0.130	0.006**
Smoking, n	0.288	0.859 to 4.304	0.004**
Yes (13)			
No (76)			
Salt consumption behavior, n	0.190	0.074 to 1.281	0.02*
None (18)			
Little use (17)			
Normal use (48)			
Over-use (6)			
Diastolic Blood Pressure, (mmHg), **(mean**±SD)	-0.193	-1.149 to 0.019	0.06
Comorbidity, n	-0.173	-2.35 to 0.163	0.08
Tea consumption behavior (count/day), n	0.059	-1.44 to 2.92	0.5
None (5)			
1-4 tea cups (47)			
5-10 tea cups (34)			
≥10 tea cups (14)			
Energy, kcal	-1.89	-0.092 to 0.062	0.7
Carbohydrate, g	0.741	-0.268 to 0.361	0.77
Protein, g	0.067	-0.296 to 0.321	0.93
Fat, g	1.777	-0.438 to 0.950	0.46
Omega 3 fat acid, g	-0.243	-1.60 to -0.186	0.01*
Cholesterol, g	0.119	-0.002 to 0.005	0.35
Soluble fiber, g	-0.239	-0.501 to 0.030	0.08
Insoluble fiber, g	0.179	-0.072 to 0.357	0.18

*p<0.05, ** p<0.01.