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ORIGINAL ARTICLE

Mediterranean diet improves sexual function in women with the metabolic syndrome

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In the present study, we tested the effect of a Mediterranean-style diet on sexual function in women with the metabolic syndrome. Women were identified in our database of subjects participating in controlled trials evaluating the effect of lifestyle changes and were included if they had a diagnosis of female sexual dysfunction (FSD) associated with a diagnosis of metabolic syndrome, a complete follow-up in the study trial and an intervention focused mainly on dietary changes. Fifty-nine women met the inclusion/exclusion criteria; 31 out of them were assigned to the Mediterranean-style diet and 28 to the control diet. After 2 years, women on the Mediterranean diet consumed more fruits, vegetables, nuts, whole grain and olive oil as compared with the women on the control diet. Female sexual function index (FSFI) improved in the intervention group, from a mean basal value of 19.7 ± 3.1 to a mean post-treatment value of 26.1 ± 4.1 ($P = 0.01$), and remained stable in the control group. C-reactive protein (CRP) levels were significantly reduced in the intervention group ($P < 0.02$). No single sexual domain (desire, arousal, lubrication, orgasm, satisfaction, pain) was significantly ameliorated by the dietary treatment, suggesting that the whole female sexuality may find benefit from lifestyle changes. A Mediterranean-style diet might be effective in ameliorating sexual function in women with metabolic syndrome.
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Introduction

The metabolic syndrome consists of a constellation of factors that increases the risk of cardiovascular disease and type 2 diabetes. Recent estimates indicate that the metabolic syndrome is highly prevalent in the United States, with an estimated 24% of the adult population affected.[1] Its clinical identification is based on measures of abdominal obesity, atherogenic dyslipidemia, raised blood pressure and glucose intolerance.[2] The etiology of this syndrome is largely unknown, but presumably represents a complex interaction between genetic, metabolic, and environmental factors, including diet.[3,4] Several recent studies also suggest that a proinflammatory state and an endothelial dysfunction are also associated with the metabolic syndrome.[5–7]

Interestingly enough, each component of the metabolic syndrome is associated with an increased risk of female sexual dysfunction (FSD), including diabetes mellitus,[8] hypertension,[9] dyslipidemia[10] and obesity.[11] We have recently shown that women with the metabolic syndrome had increased prevalence of sexual dysfunction;[12] moreover, there was an increase in sexual dysfunction prevalence as the number of components of the metabolic syndrome increased, suggesting that the cumulative burden of cardiovascular risk may play a role in FSD.[13] Although lifestyle changes are strongly recommended as first-line therapy for the metabolic syndrome as a whole and each of its component separately,[14] to our knowledge there are no reported study investigating the role of dietary interventions in women with FSD and associated metabolic risk factors. In this context, a Mediterranean-style diet rich in whole grain, fruits, vegetables, legumes, walnut and olive oil might be effective in reducing

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both the prevalence of the metabolic syndrome and the cardiovascular risk associated with it.[15] In the present study, we analyzed the effect of Mediterranean diet on FSD in women with the metabolic syndrome.

Subjects and methods

Women were identified in our database of subjects participating in randomized controlled trials evaluating the effect of lifestyle changes.[15,16] To be included in the present analysis, women must have the following: a diagnosis of metabolic syndrome, a diagnosis of FSD, a complete follow-up in the study trial, and an intervention focused mainly on dietary changes. Metabolic syndrome was diagnosed as recommended by the Adult Treatment Panel III:[2] (1) abdominal adiposity as defined by a waist circumference of >102 cm in men and >88 cm in women; (2) low serum high-density lipoprotein (HDL)-cholesterol (<40 mg/dl or <50 mg/dl in men and women, respectively); (3) hypertriglyceridemia as defined by an elevated triglyceride of $\geqslant 150$ mg/dl; (4) elevated blood pressure as defined by a blood pressure of at least 130/85 mm Hg; and (5) abnormal glucose homeostasis as defined by a fasting plasma glucose concentration of $\geqslant 110$ mg/dl. Women were excluded if they had clinical or instrumental signs or symptoms of cardiovascular disease, psychiatric problems, a history of alcohol abuse (at least 500 g alcohol/week in the last year), or if they smoked or took any medication. Informed written consent was obtained from all women participating in the study that was approved by the Institutional Review Board.

Assessment of sexual function

A validated 19 items self-report instrument for assessing key dimensions of female sexual function, as previously described by Rosen *et al*.[17] was used, and a total of six domains was analyzed. Briefly, the specific domains analyzed in the female sexual function index (FSFI) included sexual desire, arousal, lubrication, orgasm, satisfaction and pain during sexual intercourse. Sexual desire was assessed as frequency and desire level with two questions. Arousal was assessed as frequency, level, confidence and satisfaction with four questions. Lubrication was assessed as frequency, difficulty, frequency of maintaining and difficulty in maintaining with four questions. Orgasm was assessed as frequency, difficulty and satisfaction with three questions. Satisfaction was assessed as the amount of closeness with partner, sexual relationship and overall sex life with three questions. Pain was assessed as pain frequency during vaginal penetration and pain frequency following vaginal penetration with three questions. Each domain was scored on a scale of zero or 1–6, with higher score indicating better function. For each six domains, a score was calculated and the total score was obtained by adding the six domain scores. The total score range was 2–36: a score of 23 or lower indicated sexual dysfunction. The tool was administered during the follicular (days 5–8) phase of the menstrual cycle.

Interventional trial

Fifty-nine women with the metabolic syndrome who met the inclusion/exclusion criteria were to be enrolled in the study; 31 out of them were assigned to the intervention diet and 28 to the control diet. Women in the intervention diet were given detailed advice about the usefulness of the experimental diet. The program involved education on reducing, if needed, dietary calories, personal goal setting, and self monitoring (food diaries) through a series of monthly small-group sessions. Behavioral and psychological counseling was also offered. The dietary advice was tailored to each subject on the basis of 3-day food records. The recommended composition of the dietary regimen was the following: carbohydrates 50–60%, proteins 15–20%, total fat <30%, saturated fat <10% and less than 300 mg of cholesterol consumed per day. Moreover, subjects were advised to consume at least 250–300 g of fruits, 125–150 g of vegetables and 25–50 g of nuts per day; in addition, they were also encouraged to consume 400 g of whole grains daily (legumes, rice, maize and wheat) and to increase the consumption of olive oil. Women were also advised to increase consumption of fish and to reduce intake of red or processed meat. Women were in the program for 24 months and had monthly sessions with the nutritionist for the first year, and bimonthly sessions for the second year. Compliance with the program was assessed by attendance at the meetings and completion of the diet diaries. Women in the control diet were given general oral and written information about healthy food choices at baseline and at subsequent visits, but no specific individualized program was offered to them. Women for both groups also received guidance on increasing their level of physical activity, mainly walking for a minimum of 30 min per day, but also swimming or aerobic ball games.

Anthropometric measures, nutrient intakes and laboratory analyses

Height and weight were recorded with participants wearing lightweight clothing and no shoes using a Seca 200 scale with attached stadiometer (Seca, Hamburg, Germany). Twenty-four hour nutrient intakes were calculated with food-composition tables and patients' weekly diet diaries. All women

were asked to keep a record of food intake for 3 days, and to record occupational, household and leisure time physical activity, to assess dietary adherence and exercise activity. Foods were measured using standard measuring cups and spoons and weight-approximation diagrams.

Estimation of insulin sensitivity in the fasting state was assessed with homeostasis model assessment (HOMA) and calculated with the formula: fasting plasma glucose (mmol/l) $\times$ fasting serum insulin (μU/ml)/25, as described by Matthews *et al*.[18] With such a method, high HOMA scores denote low-insulin sensitivity (insulin resistance). Assays for serum total and HDL cholesterol, triglyceride and glucose levels were performed in the hospital's chemistry laboratory. Plasma insulin levels were assayed by radioimmunoassay (Ares, Serono, Italy). Serum samples for C-reactive protein (CRP) levels were stored at -80°C until assay. High-sensitivity CRP was assayed by immunonephelometry on Behring Nephelometer 2 (Dade Behring, Marburg, Germany).

Statistical analysis

Data are presented as mean $\pm$ s.d. unless otherwise indicated. We compared baseline data using a *t*-test for continuous variables and a Wilcoxon test for CRP. We compared risk factors and nutrient intakes after 2 years using a test based on the values at the end of follow-up and a *t*-test based on differences from baseline. The effects of intervention on FSFI score and CRP levels were tested by means of paired *t*-tests and a Wilcoxon-matched test. The χ^2-test was used for comparing proportions of women in the two groups that obtained normal sexual function after treatment. Multivariate regression analysis tested the independent association and contribution of changes in nutrient intake, body mass index (BMI), waist, physical activity and plasma CRP concentrations with the dependent variable (changes in FSFI score), also including baseline FSFI score as covariate. A value of $P<0.05$ was considered significant. All analyses were conducted using SPSS 11.5 for Windows.

Results

The clinical and metabolic characteristics of women participating in the study are shown in Table 1: there was no significant difference between groups in any of the parameters evaluated, including the FSFI score. Moreover, there was no need for any medication for chronic diseases, such as hypertension, diabetes or dyslipidemia in the course of the study in both groups.

Baseline data showed no important difference in the nutrient intake between the two groups (Table 2). After 2 years, women on the Mediterranean diet consumed a greater percentage of calories from polyunsaturated and monounsaturated fat; had a greater intake of Ω-3 fatty acids; and lower saturated fat than controls had. Total fruit, vegetable, nuts and whole grain intakes, and olive oil consumption were also significantly higher in the intervention group. The level of physical activity increased in both groups (intervention group: 27 min/week; control group: 30 min/week) without any difference between them.

After 2 years, women on the intervention diet had a significant decrease in glucose, insulin, HOMA, triglycerides and blood pressure (Table 3). Nine women in the intervention group had impaired fasting glucose (IFG, between 110 and 125 mg/dl) at baseline and four had frank diabetes (fasting glucose >126 mg/dl); the corresponding numbers after diet were 4 and 3, respectively ($P<0.05$). There was no significant change in any of these parameters in the control group, nor in the prevalence of IFG or diabetes (six women with IFG and three women with diabetes). Serum concentrations of CRP were significantly reduced in women on the Mediterranean-style diet compared with controls.

Female sexual function score improved in the intervention group, from a mean basal FSFI value of 19.7 ± 3.1 to a mean post-treatment value of 26.1 ± 4.1 ($P=0.01$). The improvement was significant for the whole FSFI score, but not for any of the six domains (Table 4).

In the intervention group, changes in FSFI score were related to a dietary pattern characterized by an

Table 1 Characteristics of the study participants[a]

Characteristic	*Mediterranean diet* (n = *31*)	*Control diet* (n = *28*)	P-*value*
Age (years)	42.3 $\pm$ 4.5	415 $\pm$ 3.9	NS
Body mass index (kg/m^2)	28.8 $\pm$ 2.8	29.2 $\pm$ 3.1	NS
Waist circumference (cm)	89 $\pm$ 8	90 $\pm$ 9	NS
Plasma glucose (mg/dl)	109 $\pm$ 10	112 $\pm$ 11	NS
Serum insulin (μU/ml)	20 $\pm$ 7	18 $\pm$ 6	NS
HOMA	4.1 $\pm$ 0.7	4.0 $\pm$ 0.7	NS
Serum lipids (mg/dl)			
Total cholesterol	224 $\pm$ 32	216 $\pm$ 28	NS
HDL-cholesterol	46 $\pm$ 8	47 $\pm$ 8	NS
LDL-cholesterol	145 $\pm$ 16	134 $\pm$ 21	NS
Triglycerides	165 $\pm$ 53	180 $\pm$ 60	NS
Blood pressure (mmHg)			
Systolic	132 $\pm$ 9	134 $\pm$ 8	NS
Diastolic	84 $\pm$ 5	85 $\pm$ 7	NS
FSFI score	19.7 $\pm$ 3.1	20.1 $\pm$ 2.9	NS
CRP (mg/l)[b]	2.1 (0.7/4.6)	2.0 (0.6/4.7)	NS

Abbreviations: CRP, C-reactive protein; FSFI, female sexual function index; HDL, high-density lipoprotein; HOMA, homeostasis model assessment; LDL, low-density lipoprotein; NS, not significant.

[a]Data are presented as mean $\pm$ s.d. except where otherwise indicated.

[b]Median (interquartile range).

Table 2 Nutrient indices at entry to study and after 2 years

Nutrient	*Mediterranean diet* (n = *31*)		*Control diet* (n = *28*)		P-*value at 2 years*
	Baseline	*2 years*	*Baseline*	*2 years*	
Total energy (kcal/day)	2024±270	1967±245	1996±259	1980±243	NS
Carbohydrates (%)	54±6	53±6	54±5	54± 5	NS
Protein (%)	15±2	15±2	15±2	15±2	NS
Fat (%)	31±4	32±4	31±3	31±3	NS
Saturated	13±2.8	8±1.4	13±2.7	13±2.8	<0.001
MUFA	9±1.2	14±1.7	10±1.1	10±1.2	<0.001
PUFA	9±1.0	10±1.0	7±0.8	7±0.9	NS
Ω-3 fatty acids (g/day)	0.5±0.1	1.1±0.2	0.5±0.1	0.5±0.1	<0.001
Olive oil (g/day)	14±2.2	23±3.7	14±2.3	15±2.6	<0.001
Fruits, vegetables, nuts and legumes (g/day)	187±43	385±87	178±46	197±42	<0.001

Abbreviations: MUFA, monounsaturated fat; NS, not significant; PUFA, Polyunsaturated fat.
P value at 2 years indicates difference between the two interventions (Med-diet vs control diet).

Table 3 Changes in assessed variables after 2 years

Variable	*Mediterranean diet* (n = *31*) *Mean change*	*Control diet* (n = *28*) *Mean change*	P-*value*
Body mass index (kg/m^2)	−0.2±0.2	0±0.1	NS
Waist circumference (cm)	−1±0.5	0±0.5	NS
Plasma glucose (mg/dl)	−4±3	0±0.4	<0.05
Serum insulin (μU/ml)	−3±0.9	0.5±0.4	<0.05
HOMA	−0.6±0.2	0.1±0.2	<0.05
Serum lipids (mg/dl)			
Total cholesterol	−7±4	−2±2	NS
HDL-cholesterol	+2±2	0±0.5	NS
LDL-cholesterol	−8±4	−2±2	NS
Triglycerides	−18±8	−2±2	<0.05
Blood pressure (mm Hg)			
Systolic	−3±1	0±0.3	<0.05
Diastolic	−2±1	−1±1	NS
CRP (mg/l)	−0.7±0.3	0.1±0.1	<0.02

Abbreviations: CRP, C-reactive protein; FSFI, female sexual function index; HDL, high-density lipoprotein; HOMA, homeostasis model assessment; LDL, low-density lipoprotein; NS, not significant.

Table 4 Changes in overall FSFI score and each sexual domain score

Sexual function parameter	*Mediterranean diet* (n = *31*) *Mean change*	*Control diet* (n = *28*) *Mean change*	P-*value*
FSFI	6.4±3.8	0.3±0.7	<0.01
Desire	1.0±1.5	0.2±0.5	NS
Arousal	0.8±1.4	−0.2±0.8	NS
Lubrication	1.1±1.9	0.2±0.7	NS
Orgasm	1.0±1.7	0.1±0.7	NS
Satisfaction	1.1±1.6	−0.2±0.8	NS
Pain	0.9±1.6	0.3±0.8	NS

Abbreviations: FSFI, female sexual function index; NS, not significant.

increased in intake of fruits, vegetables, nuts and legumes, and in the ratio of polyunsaturated to saturated lipids ($P<0.02$); however, no individual dietary component was associated with changes in FSFI. The associations between changes in FSFI and dietary patterns remained significant after performing a multivariate analysis in which FSFI score was the dependent variable and BMI, waist, level of physical activity, baseline FSFI score and serum CRP concentrations were the independent variables: BMI (38% of the variance, $P=0.01$), nutrient intake (20% of the variance, $P=0.02$) and CRP (12% of the variance, $P=0.04$) were independent predictors of FSFI score and explained near 70% of the variability in its changes.

Discussion

Our results show that consumption of a Mediterranean-style diet in women with the metabolic syndrome and FSD at baseline significantly improved sexual functions, together with a significant reduction of systemic vascular inflammation, as indicated by the reduced levels of CRP. As a whole, these findings suggest that a Mediterranean-style diet may be a safe strategy for amelioration of sexual function in women with the metabolic syndrome.

FSD is characterized by disturbances in the psychophysiological changes associated with the sexual response cycle in women, including disorders of sexual desire, arousal, orgasm and pain.[19] Sexual difficulties in women appear to be widespread in society, influenced by both health-related and psychosocial factors, and are associated with impaired quality of life and interpersonal relationships.[20] Older data reveal that up to 76% of women

had some type of sexual dysfunction.[21] Data from the National Health and Social Life Survey (NHSLS), a study of adult sexual behavior, showed that 43% of women in the United States had at least one of sexual problem, in relation with age, marital status, education, race or ethnicity.[22] These figures have recently been confirmed by the results of Global Study of Sexual Attitudes and Behaviors (GSSAB), an international survey of various aspects of sex and relationships among adults aged 40–80 years.[23]

The mechanism by which a Mediterranean-style diet can improve sexual function in women with the metabolic syndrome is unclear. Macronutrient intake produces oxidative stress that leads to a proinflammatory state.[24] Moreover, modulation of the fiber content of the meal may influence cytokine concentrations, and hence the proinflammatory milieu.[25] As dietary fiber may have anti-inflammatory roles,[26] it may be that the fiber content of the Mediterranean diet, eventually magnified by some other components with antioxidant capability, may influence the transient oxidative stress that occurs after macronutrient ingestion. Our data support this interpretation, as consumption of foods that are rich in dietary fiber and antioxidants remained significant determinants of FSF changes in multivariate analysis. Further supporting this interpretation was the significant decrease of CRP levels after diet, which correlated with improved sexual function. However, from a public health perspective, it may be unnecessary to elucidate every mechanism of single nutrient or food: current recommendations for disease prevention emphasize the simultaneous change of several dietary behaviors, such as decreasing fat and increasing whole grains and greens.[27]

To the best of our knowledge, these results represent the first demonstration that a Mediterranean-style diet rich in whole grain, fruits, vegetables, legumes, walnut and olive oil might be effective in ameliorating sexual function in women with the metabolic syndrome. However, no single sexual domain was significantly ameliorated by the dietary treatment; on the other hand, the FSFI score, which represent the algebraic sum of each domain, significantly improved, indicating that the overall effect on female sexuality is more than the sum of its parts. As the diagnosis of FSD is still based on the composite FSFI score, and not on how many domains are affected by diet, we must rely with the overall score saying that FSD shows significant amelioration after long-term dietary changes. Interestingly enough, this aspect is mirrored by the inability to say which particular component of the diet can account for the changes observed in FSFI score. This is not new, as in a recent population-based study involving 22 043 apparently healthy adults in Greece, adherence to a traditional Mediterranean diet was associated with significantly lower total mortality.[28] Despite a robust inverse association between the overall Mediterranean-diet score and mortality, no appreciable associations were seen for most of the individual dietary components, leading to suggest that the cumulative effects (synergistic or interactive) of multiple dietary components may be substantial. So, multiple dietary interventions, as in the present study, render difficult the assessment of the effect of each one separately; however, the clinical utility of a whole-diet approach in the prevention of cardiovascular disease has been emphasized.[29] Improvement of sexual function in women can be added to the list of potential benefits associated with consumption of a traditional Mediterranean-style diet.[24]

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