Hindawi Publishing Corporation
Journal of Obesity
Volume 2012, Article ID 969124, 9 pages
doi:10.1155/2012/969124

Research Article

The Impact of Abdominal Obesity Status on Cardiovascular Response to the Mediterranean Diet

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Received 4 July 2012; Revised 10 September 2012; Accepted 18 September 2012

Academic Editor: Robert Ross

We investigated the impact of abdominal obesity status on the cardiovascular response to a fully controlled 4-week isoenergetic Mediterranean diet (MedDiet). Thirty-eight abdominally obese individuals (waist circumference >102 cm in men and >88 cm in women) and thirty-one nonabdominally obese individuals were recruited and studied before and after the MedDiet. All analyses were adjusted for the slight decrease in body weight, which occurred during the MedDiet (mean: 0.9 ± 1.2 kg). A group by time interaction was noted for waist circumference ($P = 0.02$), abdominally obese subjects showing a significant decrease and nonabdominally obese subjects a nonsignificant increase (resp., −1.1 and +0.3%). The MedDiet resulted in decreases in total cholesterol, LDL-C, HDL-C, apolipoprotein B, A-1, and A-2, total cholesterol/HDL-C ratio, LDL-C/HDL-C ratio, and systolic and diastolic blood pressure (time effect: $P < 0.05$). For all variables related to glucose/insulin homeostasis, no change was observed except for a decrease in 2 h glucose concentrations (time effect: $P = 0.03$). No group by time interaction was observed in any of the metabolic variables studied. Results from our study suggest that the adoption of the MedDiet leads to beneficial metabolic effects, irrespective of the abdominal obesity status.

1. Introduction

Nowadays, it is well known that obesity is an important predictor of morbidity and mortality related to cardiovascular disease and type 2 diabetes [1]. More precisely, excess abdominal fat, especially abdominal visceral fat, has been identified by some as a marker of metabolic disorders such as the atherogenic dyslipidemia (elevated triglyceride (TG) and reduced high-density lipoprotein-cholesterol (HDL-C) concentrations), hypertension, and hyperglycemia [2, 3]. Waist circumference is a simple anthropometric measurement frequently used in clinical practice to assess abdominal obesity and it has been shown to correlate with the amount of visceral fat in men and in women [4]. The most frequently used cut points for waist circumference are 102 cm in men and 88 cm in women [5, 6]; beyond these values, individuals are at increased risk of cardiometabolic disorders [7, 8]. For these at-risk individuals, the adoption of a healthy lifestyle is strongly recommended [5, 9].

Some evidence suggests that the adoption of healthy dietary habits may lead to beneficial effects on cardiometabolic risk factors even if body weight remains stable [10, 11]. Using dietary approaches that do not rely on weight loss to successfully improve the metabolic profile is particularly relevant considering the very low proportion of subjects who can achieve and maintain weight loss [12]. In this regard, one model of healthy eating is the Mediterranean diet (MedDiet). Both epidemiological and interventional studies conducted in different countries have demonstrated that the adherence to the MedDiet is associated with reduced rates of cardiovascular events [13, 14] and cardiometabolic risk factors such as dyslipidemia, hypertension, and insulin resistance [15]. Although only few studies have investigated the effects of the MedDiet in an isoenergetic context, results from fully controlled nutritional studies showed beneficial effects of the MedDiet on lipid profile [10, 16] and blood pressure [16] even when body weight remained stable.

Some evidence showed that the acute effects of the diet on lipid profile and glucose/insulin homeostasis are influenced by the degree of abdominal obesity. In fact, some studies have demonstrated that the visceral adipose tissue accumulation is linked to increased postprandial TG [17–19], glucose [20], and insulin [18, 20] concentrations. Mechanistically, the link between abdominal adipose tissue and these cardiovascular disorders may be partly explained by the high lipolytic action of visceral adipose tissue [21]. In fact, an excess of free fatty acids released by abdominal visceral adipose tissue into the portal vein contributes directly to dyslipidemia, via an increase in TG availability with a subsequent increase in the catabolism of HDL-C, and hyperglycemia. In line with these facts, one could therefore hypothesize that, in an isoenergetic context, the increased free fatty acids flux to the liver found with an excess of abdominal adipose tissue may interfere with dietary effects associated with the adoption of the healthy MedDiet, resulting in a less beneficial metabolic response to the MedDiet in abdominally obese individuals than in nonabdominally obese individuals. However, the impact of abdominal obesity status on the response to the adoption of healthy dietary habits is unknown. Thus, the aim of this study is to verify whether the now widely used dietary recommendation in clinical practice to adhere to the traditional MedDiet leads to similar beneficial cardiovascular effects in abdominally obese and in nonabdominally obese individuals characterized by a slightly deteriorated lipid profile. In this case, a well-controlled approach in an isoenergetic context was essential in order to isolate the metabolic effects of the MedDiet in these two groups with a maximum of control over confounding variables.

2. Methods

2.1. Subjects. Subjects were men and premenopausal women, between 24 and 53 years of age, recruited from the Quebec City metropolitan area (Canada). To be included in the study, subjects must have slightly elevated LDL-C concentrations (between 3.4 and 4.9 mmol/L) or total cholesterol to HDL-C ratio $\geq$5.0 and at least one of the four following inclusion criteria: waist circumference >94 cm in men and >80 cm in women [22]; TG > 1.7 mmol/L; fasting glycemia between 6.1 and 6.9 mmol/L and/or blood pressure levels $\geq$130/85 mm Hg. The participants were recruited according to the following exclusion criteria: significant weight change (>2.5 kg) in the three months before the study, cardiovascular events, use of medication that could affect dependent variables under study (namely, lipid-lowering, hypoglycemic, insulin sensitizers and antihypertensive medication), smoking, pregnancy, and use of systemic hormonal contraceptives. One hundred and forty-four volunteers were invited to a screening visit and seventy-five subjects met the inclusion criteria. Among this initial group, five subjects dropped out during the run-in period for personal reasons. Therefore, seventy participants were included in the study.

Table 1: Servings of key foods of the Mediterranean pyramid consumed daily during the Mediterranean diet intervention for a 10460 kJ/d (2500 kcal/d) menu.

Key foods*	MedDiet (servings/d)
Olive oil (mL)	43.3
Whole grains products	5.7
Fruits and vegetables	16.1
Legumes	0.5
Nuts	0.9
Cheese and yogurt	2.0 Mostly low in fat
Fish	1.3
Poultry	0.9
Eggs	0.3
Sweets	0.3
Red meat	0.2
Red wine	1.3

MedDiet: Mediterranean diet.
*Extra virgin and virgin olive oils were used. Serving size for whole grains products = 125 mL (rice, pasta, bulgur, and couscous), one bread piece or 30 g cereal; serving size for fruits and vegetables = 125 mL; serving size for legumes = 175 mL and for nuts = 30 g; serving size for fish, poultry and red meat = 75 g; serving size for egg = 100 g; serving size for dairy products (mostly low fat cheese and yogurt) = 50 g cheese, 175 g yogurt, and 250 mL milk; serving size for red wine = 150 mL.

The present study was conducted according to the guidelines laid down in the Helsinki Declaration of 1964. All subjects provided written informed consent for their participation. The study protocol was approved by the Laval University Research Ethics Committee on human experimentation.

2.2. Study Design. A detailed description of the nutritional intervention has been published elsewhere [16]. Before the controlled MedDiet intervention, participants went through a 4-week run-in period in order to control for the inter- and intraindividual variability in dietary intakes. During the run-in period, all participants had to comply with healthy eating according to the Canada's Food Guide [23] as instructed by a registered dietitian. Briefly, the Canada's Food Guide is an educational tool indicating the recommended number servings per day for four different food groups (vegetables and fruits, grain products, milk and alternatives, and meat and alternatives) according to the age and sex of individuals. Moreover, in addition to these quantitative recommendations, this tool includes recommendations about the nutritional quality of selected food. Participants had to maintain constant their body weight and physical activity level during the run-in period.

After the run-in period, subjects were assigned to a 4-week experimental diet formulated to be concordant with characteristics of the traditional MedDiet [24]. Key foods included in the experimental MedDiet are shown in Table 1. Moreover, the nutritional composition of the experimental MedDiet is presented in Table 2. The percentages of energy derived from lipids, carbohydrates, proteins, and alcohol were, respectively, of 32%, 46%, 17%, and 5%. All foods and drinks were prepared by food technicians at the Clinical

Table 2: Daily nutritional composition of the Mediterranean diet intervention for a 10 460 kJ/d (2500 kcal/d) menu.

	MedDiet For 10460 kJ/d (2500 kcal/d)
Energy (kJ)	10460
Carbohydrate (% of total energy)	46.0
Fiber (g)	42.3
Protein (% of total energy)	17.0
Fat (% of total energy)	32.0
SFA (% of total energy)	6.7
MUFA (% of total energy)	18.1
PUFA (% of total energy)	4.7
Cholesterol (mg)	289.7
Alcohol (% of total energy)	5.0
MUFA to SFA ratio	2.7
Sodium (mg)	3039

MedDiet: Mediterranean diet.

Investigation Unit (CIU) of the Institute of Nutraceuticals and Functional Foods (INAF; Laval University) and provided to participants according to a 7 d cyclic menu. Participants were instructed to consume entirely meals provided. On weekdays, participants came to the CIU to consume their noon meal under supervision, at which time they picked up their evening meal and next day's packaged breakfast. Weekend meals were prepared, packaged, and provided at Friday's visits. Compliance was measured with a checklist on which participants noted foods consumed and, if needed, the amount of foods not consumed for each day of the controlled MedDiet intervention.

Since the controlled MedDiet intervention aimed at being isoenergetic, the habitual energy intake of each participant was established by averaging energy intakes estimated by a validated food frequency questionnaire (FFQ) [25] and energy needs as determined by the Harris-Benedict formula. Body weight was measured on weekdays and foods and energy provided were adjusted to keep each subject's body weight as constant as possible throughout the study. Participants were also instructed to maintain their usual physical activity level during this controlled intervention. In women, all tests were carried out in the early follicular phase of their menstrual cycle (from the third to the ninth day of the menstrual cycle) since fluctuations in female hormones may influence some metabolic variables [26].

2.3. Dietary Intakes. Each participant completed a validated quantitative FFQ [25] administrated by a registered dietitian which inquires on food habits during the last month just before the controlled MedDiet intervention in order to evaluate dietary intakes before the controlled MedDiet intervention (i.e., during the entire 4-week run-in period). A Mediterranean score (MedScore) derived from the FFQ was calculated as described by Goulet and colleagues [27]. The MedScore can vary between zero and forty-four points. A MedScore of forty-four would imply a food pattern which is perfectly concordant with the traditional MedDiet.

2.4. Biochemical Measurements. Blood samples were collected from an antecubital vein into vacutainer tubes after a 12 h overnight fast. Assessment of the basic lipid profile and of lipoprotein-lipid concentrations was performed according to previously described methods [27]. A blood sample was also collected into a vacutainer tube containing EDTA for the assessment of glucose and insulin concentrations. Glucose and insulin concentrations were measured in a fasting state and 2 h after an oral administration of 75 g glucose as previously described [16]. Insulin sensitivity was determined by the homeostasis model assessment (HOMA) approach index ($1/[\text{fasting glucose} \times \text{fasting insulin}/22.5]$).

2.5. Anthropometric and Blood Pressure Measurements. Body weight, height, and waist and hip circumferences were measured using standardized methods [28]. The waist circumference measurement was taken at the end of a normal expiration with a tape placed horizontally directly on the skin at the middistance between the last rib and the top of the iliac crest. Hip circumference was taken as the widest protrusion of the hip. Waist and hip circumferences were determined as the mean of three measurements. Systolic and diastolic blood pressures were measured on the right arm using an automated blood pressure monitor (BPM 300-BpTRU: Vital Signs Monitor, VSM MedTech Ltd., Coquitlam, Canada) after a 10-minute rest in the sitting position. Blood pressure was computed as the mean of three readings.

2.6. Statistical Analyses. Data were collected before (i.e., immediately after the run-in period) and after the controlled MedDiet intervention and results are expressed as means and standard deviation (SD) or standard error of the mean (SEM). For our analyses, men and women with a waist circumference of, respectively, >102 cm and >88 cm were considered as having abdominal obesity while men and women with a waist circumference of, respectively, ≤102 cm and ≤88 cm were considered as nonabdominally obese individuals as previously suggested [5, 6]. Data were analyzed by using SAS statistical package version 9.2 (SAS Institute Inc., Cary, NC, USA). A $P \leq 0.05$ (two sided) was judged to be statistically significant. For variables not normally distributed, a transformation was performed in order to obtain a normal distribution. Differences between abdominally obese and nonabdominally obese participants before the controlled MedDiet intervention were assessed using the General Linear Model procedure and were adjusted for sex. MIXED procedures for repeated measurements were used to evaluate time and group by time interaction effects on anthropometric and metabolic variables in response to the MedDiet. Tukey-Kramer tests were used to determine precisely the location of significant differences. Pearson correlations were performed in all participants to quantify the relationships of waist circumference before the controlled MedDiet intervention and changes in metabolic variables.

Although the controlled MedDiet intervention aimed at being isoenergetic, both abdominally obese and nonabdominally obese subjects experienced a small but significant weight loss (1.1 kg or 1.2% of initial body weight in

Table 3: Characteristics of subjects before the 4-week controlled Mediterranean diet intervention[1].

Variables	Nonabdominally obese individuals ($n = 31$)		Abdominally obese individuals ($n = 38$)	
	Mean	SD	Mean	SD
Men (n, (%))	22 (71.0)		15 (39.5)*	
Age (years)	42.6	6.6	41.4	7.9
Body weight (kg)	78.4	10.5	91.1*	17.2
BMI (kg/m^2)[2]	26.6	1.6	31.6*	4.6
Waist circumference (cm)				
Total	92.8	6.2	105.3*	10.9
Men	96.0	4.3	112.3*	10.0
Women	85.1	1.5	100.8*	9.0
TG (mmol/L)[2]	1.64	0.88	1.62	1.08
Total cholesterol (mmol/L)	5.61	0.71	5.38	0.83
LDL-C (mmol/L)	3.66	0.59	3.45	0.66
HDL-C (mmol/L)	1.20	0.34	1.18	0.27
Apo B (g/L)[2]	1.11	0.22	1.08	0.17
Apo A-1 (g/L)	1.37	0.20	1.36	0.17
Apo A-2 (g/L)	0.36	0.06	0.34	0.04
Systolic blood pressure (mmHg)	112.1	13.8	114.0	11.1
Diastolic blood pressure (mmHg)	75.5	8.9	78.4*	10.0
Fasting glucose (mmol/L)	5.68	0.35	5.89*	0.60
2 h glucose (mmol/L)	6.08	1.70	7.14	2.38
Fasting insulin (pmol/L)[2]	64.5	30.4	113.4*	81.8
2 h insulin (pmol/L)[2]	365.4	326.6	621.4*	604.1
HOMA index[2,3]	0.0927	0.1148	0.0757*	0.1505

BMI: body mass index; TG: triglycerides; LDL-C: low-density lipoprotein-cholesterol; HDL-C: high-density lipoprotein-cholesterol; Apo: apolipoprotein; HOMA index: homeostasis model assessment index.

[1]Data represent characteristics of participants after the run-in period.

Men and women with a waist circumference of, respectively, >102 cm and >88 cm were considered as having abdominal obesity. Analyses were performed after adjustment for sex.

Mean values were significantly different between groups before the controlled Mediterranean diet by the General Linear Model procedure; *$P < 0.05$.

[2]Analysis was performed on transformed values.

[3]Calculated as (1/[fasting glucose (mmol/L) × fasting insulin (pmol/L)/22.5]) for measuring insulin sensitivity.

abdominally obese subjects and 0.6 kg or 0.8% in nonabdominally obese subjects). Thus, all analyses linked to waist circumference, waist-to-hip ratio, and metabolic variables are presented with adjustments for body weight change occurring during the controlled MedDiet intervention. Body mass index (BMI) change was highly correlated to body weight change ($r = 0.99$; $P < 0.0001$). Therefore adjustment for BMI change provided similar results as those obtained after adjustment for body weight change (results not shown). One nonabdominally obese subject was excluded from our analyses due to illness which led to a significant reduction in food intake during several days just before the end of the controlled MedDiet intervention. Thirty-eight abdominally obese subjects and thirty-one nonabdominally obese subjects were included in the analyses. A sample size of 69 participants allowed to detect a difference of 13% in the changes in LDL-C concentrations between groups, considering a standard deviation of 0.66 mmol/L (19% of the mean), an alpha risk of 0.05, and a beta risk of 0.20 in two-sided contrasts in this parallel-design study.

3. Results

3.1. Baseline Characteristics. Before the controlled MedDiet intervention (i.e., at the end of the run-in period), body weight, BMI, and waist circumference (by study design) were different between abdominally obese and nonabdominally obese subjects, abdominally obese individuals having higher baseline values than nonabdominally obese individuals (Table 3). Except for 2 h glucose concentration, all variables related to glucose/insulin homeostasis were also different between the two groups, abdominally obese subjects having higher baseline values for fasting glucose and insulin concentrations as well as for 2 h insulin concentration and lower insulin sensitivity as measured by HOMA index than nonabdominally obese individuals. Variables related to the lipid profile as well as systolic blood pressure were similar between the two groups. Diastolic blood pressure was higher for abdominally obese individuals than for nonabdominally obese individuals. For dietary variables, there was no significant difference in energy intake, macronutrient intakes, and the monounsaturated fatty acids (MUFA) to saturated fatty

Table 4: Dietary intakes of subjects before the 4-week controlled Mediterranean diet intervention[1].

Variables	Non-abdominally obese individuals ($n = 31$)		Abdominally obese individuals ($n = 38$)	
	Mean	SD	Mean	SD
Energy (kJ)[2]	10910	2222	11174	3507
Carbohydrate (% of total energy)	49.5	6.0	47.6	7.8
Protein (% of total energy)	16.8	2.9	18.0	3.1
Fat (% of total energy)[2]	33.7	6.2	33.7	5.9
SFA (% of total energy)	10.5	1.9	11.1	2.8
MUFA (% of total energy)[2]	14.8	5.1	14.1	2.7
PUFA (% of total energy)[2]	5.7	1.5	5.8	1.4
Alcohol (% of total energy)[2]	2.5	2.0	2.9	2.9
MedScore (arbitrary units)	26.3	5.2	23.5*	5.0
MUFA to SFA ratio[2]	1.44	0.55	1.32	0.26

SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids; MedScore: Mediterranean score.
[1]Values are presented as mean and standard deviation (SD). Data represent dietary intakes during the run-in period. Men and women with a waist circumference of, respectively, >102 cm and >88 cm were considered as having abdominal obesity.
Analyses were performed after adjustment for sex.
*Mean values were significantly different between groups before the Mediterranean diet by the General Linear Model procedure; $P = 0.03$.
[2]Analysis was performed on transformed values.

acids (SFA) ratio between the two groups during the run-in period. (Table 4). However, abdominally obese subjects had a lower MedScore than nonabdominally obese subjects.

3.2. Effects of the MedDiet on Anthropometric Variables. No group by time interaction effect was observed for body weight and BMI in response to the MedDiet (Table 5). After adjustments for body weight change during the controlled MedDiet intervention, a group by time interaction was noted for waist circumference ($P = 0.02$), abdominally obese subjects having a significant decrease whereas subjects without abdominal obesity having a nonsignificant increase (−1.1% in abdominally obese subjects and +0.3% in nonabdominally obese subjects, resp., $P = 0.03$ and $P = 0.91$). No change in waist to hip ratio was observed.

3.3. Effects of the MedDiet on Metabolic Variables. After adjustment for body weight change, the controlled MedDiet intervention resulted in decreases in total cholesterol, LDL-C, HDL-C, apolipoprotein (apo) B, apo A-1, and apo A-2 concentrations (Table 5). Total cholesterol to HDL-C ratio, LDL-C to HDL-C ratio, and systolic and diastolic blood pressure also decreased in response to the MedDiet. No significant change was observed for TG concentrations. No change was observed for variables related to glucose and insulin homeostasis, except for 2 h glucose concentrations, for which a decrease was found. No group by time interaction was observed for any of the metabolic variables studied.

Similar results were obtained for anthropometric and metabolic variables when statistical analyses were performed after adjustments for age, sex. MedScore during the run-in period and metabolic baseline values measured at the end of the run-in period (results not shown).

Waist circumference before the controlled MedDiet intervention was not associated with changes in metabolic variables ($P > 0.05$), except for change in diastolic blood pressure, which was negatively associated with waist circumference before the controlled MedDiet intervention ($r = -0.32$, $P = 0.008$). However, this association was no longer significant after adjustment for diastolic blood pressure value before the MedDiet intervention.

4. Discussion

Results from this fully controlled-feeding study showed for the first time that, in a sample of men and women characterized by a slightly deteriorated lipid profile, abdominally obese individuals had similar cardiovascular benefits from the adoption of an isoenergetic MedDiet than nonabdominally obese individuals. Since slightly elevated LDL-C and/or total cholesterol to HDL-C ratio are indicators of the need of initiating interventions aiming at improving health behaviors to prevent cardiovascular disease [9], our results are clinically relevant since they suggest that, among these at-risk individuals, the adoption of an isoenergetic MedDiet brings some beneficial effects on lipid and lipoprotein concentrations and blood pressure levels regardless of abdominal obesity status.

Our results showed that abdominally obese individuals responded differently to the isoenergetic MedDiet than nonabdominally obese individuals with respect to waist circumference changes. In fact, after adjusting for the slight body weight loss, abdominally obese individuals displayed a decrease in waist circumference in response to the MedDiet, whereas subjects without abdominal obesity had a nonsignificant increase. This small but significant decrease in waist circumference in abdominally obese individuals even in an isoenergetic context may be explained by some dietary components of the MedDiet which have been shown to influence adipose tissue distribution, such as its high content in whole grains, dietary fibers, and MUFA. Indeed, some studies have shown that whole grain [29], fiber [30, 31] and MUFA [32] intakes were inversely linked to abdominal

Table 5: Effects of the 4-week controlled Mediterranean diet intervention on anthropometric and metabolic variables associated with cardiovascular risk in abdominally obese and non-abdominally obese individuals[1].

Variables	Non-abdominally obese individuals ($n = 31$)			Abdominally obese individuals ($n = 38$)			P value	
	Change	SEM	Δ%	Change	SEM	Δ%	Time	Group*time
Body weight (kg)[2]	−0.62	0.16	−0.79	−1.12	0.21	−1.23	**<0.0001**	0.1481
BMI (kg/m^2)[2]	−0.20	0.05	−0.76	−0.38	0.07	−1.21	**<0.0001**	0.2947
Waist circumference (cm)	0.31	0.32	0.33	−1.20*	0.49	−1.14	0.1526	**0.0174**
Waist to hip ratio	0.01	0.01	0.99	−0.01	0.01	−0.85	0.8763	0.0586
TG (mmol/L)[2]	−0.25	0.10	−15.45	−0.15	0.13	−9.02	0.0724	0.0888
Total cholesterol (mmol/L)	−0.40	0.11	−7.21	−0.49	0.10	−9.02	**<0.0001**	0.6021
LDL-C (mmol/L)	−0.26	0.10	−7.17	−0.36	0.08	−10.52	**<0.0001**	0.4323
HDL-C (mmol/L)	−0.03	0.02	−2.12	−0.05	0.02	−4.63	**0.0154**	0.3678
Total cholesterol/HDL-C ratio	−0.30	0.10	−6.05	−0.23	0.11	−4.80	**0.0010**	0.6273
LDL-C/HDL-C ratio	−0.26	0.08	−7.82	−0.16	0.08	−5.34	**0.0009**	0.4271
Apo B (g/L)[2]	−0.09	0.03	−8.41	−0.11	0.02	−9.99	**<0.0001**	0.6961
Apo A-1 (g/L)	−0.06	0.02	−4.03	−0.07	0.02	−5.39	**<0.0001**	0.4856
Apo A-2 (g/L)	−0.020	0.005	−5.58	−0.021	0.006	−6.21	**<0.0001**	0.8916
Systolic blood pressure (mmHg)	−3.50	1.46	−3.12	−3.45	1.12	−3.03	**0.0003**	0.9629
Diastolic blood pressure (mmHg)	−2.64	0.90	−3.49	−4.03	1.04	−5.14	**<0.0001**	0.3281
Fasting glucose (mmol/L)	0.02	0.06	0.40	−0.06	0.08	−1.07	0.6884	0.3977
2-h glucose (mmol/L)	−0.33	0.29	−5.47	−0.51	0.24	−7.15	**0.0263**	0.6323
Fasting insulin (pmol/L)[2]	−1.2	3.3	−1.83	−14.1	6.9	−12.44	0.1533	0.2687
2-h insulin (pmol/L)[2]	−33.9	48.9	−9.28	−139.2	62.7	−22.41	0.0839	0.8845
HOMA index[2,3]	−0.009	0.018	−10.20	−0.016	0.017	−21.38	0.5681	0.5813

Δ%: percentage of change; BMI: body mass index; TG: triglycerides; LDL-C: low-density lipoprotein-cholesterol; HDL-C: high-density lipoprotein-cholesterol; Apo: apolipoprotein; HOMA index: homeostasis model assessment index.

[1]All analyses concerning waist circumference, waist-to-hip ratio, and metabolic variables are adjusted for weight change during the MedDiet. Values are presented as means with their standard errors (SEM). Men and women with a waist circumference of, respectively, >102 cm and >88 cm were considered as having abdominal obesity.

[2]Analysis was performed on transformed values.

[3]Calculated as (1/[fasting glucose (mmol/L) × fasting insulin (pmol/L)/22.5]) for measuring insulin sensitivity.

*Abdominally obese individuals significantly decrease their waist circumference in response to the MedDiet, $P = 0.03$.

adipose tissue, independently of body weight. However, previous well-controlled study did not find a significant change in waist circumference in response to the adoption of the MedDiet [10, 33], whereas uncontrolled studies gave conflicting results [15, 34]. These conflicting results between studies may be explained by the inclusion of both abdominally obese and nonabdominally obese individuals in previous studies. In fact, our results add to the previous literature as they show that, when considered as a whole, the adoption of the MedDiet in a well-controlled nutritional intervention context leads to adipose tissue distribution changes, but these changes seem to be influenced by the abdominal obesity status. The underlying mechanisms of these changes in adipose tissue distribution observed only in abdominally obese individuals in response to the isoenergetic MedDiet will require further investigation.

A decrease in waist circumference is usually associated with improvements in metabolic factors related to cardiovascular disease [3, 35]. Further analyses performed within our sample showed that waist circumference changes were not associated with any metabolic changes in abdominally obese individuals after adjustment for weight change (results not shown). These results suggest that beneficial changes in lipid profile and blood pressure occurred because of the adoption of the isoenergetic MedDiet, independently of waist circumference changes in abdominally obese individuals. Considering that the MedDiet is a MUFA-rich diet, these results are consistent with those from a study by Archer and collaborators which showed that changes in lipid profile were independent of waist circumference changes in response to a high-MUFA diet [36].

We initially hypothesized that the increased lipolysis from visceral adipose tissue could interfere with dietary effects of the MedDiet in an isoenergetic context, resulting in an overall lower responsiveness to dietary modifications for abdominally obese individuals compared to nonabdominally obese individuals. However, results from our study do not support this hypothesis since we showed that the adoption of an isoenergetic MedDiet globally improves cardiovascular health outcomes related to lipid profile in a similar manner in abdominally obese and in nonabdominally obese individuals. Moreover, waist circumference before the MedDiet intervention was not associated with changes in any of the variables related to the lipid profile. One possible explanation is that, in our study, abdominally obese individuals had initially a similar lipid profile than nonabdominally obese individuals. Indeed some previous studies have suggested that the postprandial lipid response to a meal was closely linked to fasting lipid concentrations that are usually altered among subjects with abdominal obesity [18]. Therefore similarities in lipid profile between groups at baseline may have perhaps contributed to the similar metabolic response to diet between our two groups.

In concordance with the literature, abdominally obese individuals in our study were characterized by a more deteriorated glucose/insulin homeostasis than nonabdominally obese individuals. Despite this fact, no group by time interaction was noted in response to the MedDiet. Moreover, for variables related to glucose/insulin homeostasis, significant improvements were only found for 2 h glucose concentrations. Our results are in line with previous well-controlled studies in which it was shown that the adoption of a MedDiet in an isoenergetic context did not affect insulin sensitivity compared to a diet rich in saturated fatty acids or to a Canadian diet [10, 33].

A major strength of this study is the strict controlled design of the nutritional MedDiet intervention ensuring an optimal control over energy intake and diet quality. Since obese individuals are usually found as underreporting their energy intake [37], this well-controlled context permits to avoid this bias which could have influenced the interpretation of results. However, few limitations of our study need to be mentioned. The short duration of the study may be viewed as a limitation. However, it has been shown in the literature that, after only two weeks of feeding under controlled conditions, changes in many cardiometabolic variables were already maximized [38], suggesting that the duration of our study was sufficient to obtain significant changes in cardiometabolic variables. The small sample size due to the controlled nutritional nature of our intervention did not provide the power required to perform analyses in men and women separately. However, statistical analyses adjusted for the sex gave similar P values for all metabolic variables studied, suggesting that the sex did not influence the results obtained. Moreover, a previous paper from this controlled nutritional study showed that men respond similarly to women to our controlled MedDiet intervention, except for apo A-2 and 2 h insulin concentrations, men experiencing more important decreases than women [16]. These previous results suggest that, for almost all metabolic variables studied, there was no difference between both sexes in response to the MedDiet. Our findings are limited to a population of men and women with a slightly deteriorated cardiometabolic profile. Thus, this limitation prevents us from generalizing our results to the overall population. Another limitation is that the nonabdominally obese individuals in our study had relatively high average waist circumference (i.e., 96.0 cm in men and 85.1 cm in women). These values are higher than cutoff points for abdominal obesity suggested by other organizations, such as the International Diabetes Federation [22] and the Canadian Heart Health Surveys [39]. However, the average waist circumference in our two groups was significantly different before the controlled MedDiet intervention which allowed comparing two different groups on the basis of waist circumference.

In summary, results from this controlled-feeding study suggest that, in a sample of men and women characterized by slightly elevated LDL-C and/or total cholesterol to HDL-C ratio, abdominally obese individuals have similar cardiometabolic benefits from the MedDiet in an isoenergetic context than nonabdominally obese individuals. These results highlight that, in these individuals, abdominal obesity status does not seem to influence dietary effects associated with the adoption of the MedDiet. Altogether, results obtained provide additional useful information in order to elaborate effective nutritional strategies in prevention of cardiovascular disease in clinical practice. However, since only few data exist on the impact of excess abdominal adipose tissue on the response to dietary manipulations, further studies are needed to address this issue.

Conflict of Interests

The authors declare no conflict of interests.

Disclosure

This clinical trial was registered at http://www.clinicaltrials.gov/ as NCT01293344.

Acknowledgments

The authors would like to thank the metabolic kitchen staff and nurses from the INAF, Laval University. They thank all the participants for their cooperation and their enthusiasm. This paper was supported by the Canadian Institutes of Health Research (MOP 84568) and the Heart and Stroke Foundation of Quebec (2007-180). A. Bedard is a recipient of a studentship from Canadian Institutes of Health Research.

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