Short-Term Benefits of an Unrestricted-Calorie Traditional Mediterranean Diet, Modified With a Reduced Consumption of Carbohydrates at Evening, in Overweight-Obese Patients.

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Supplemental Table 1. Adherence to Mediterranean Diet in the study population before nutritional intervention.

		Legend					
ITEMS	MEAN±SEM	Never	1-4	5-8	9-12	13-18	>18
Full fat dairy products	1.3±0.3	5	4	3	2	1	0
Red meat and meat products	1.4±0.3	5	4	3	2	1	0
Poultry	2.5±0.3	5	4	3	2	1	0
Potatoes	1.2±0.2	0	1	2	3	4	5
Non-refined cereals	1.6±0.4	0	1	2	3	4	5
Vegetables	4.6±0.2	0	1	2	3	4	5
Fruits	4.8±0.2	0	1	2	3	4	5
Legumes	2.4±0.3	0	1	2	3	4	5
Fish	2.2±0.3	0	1	2	3	4	5
Olive oil (times/week)	MEAN±SEM	Never	Rare	<1	1-3	3-5	Daily
	5.0±0.0	0	1	2	3	4	5
Alcoholic beverages (ml/day)	MEAN± SEM	<300	300	400	500	600	>700 or 0
	4.5±0.2	5	4	3	2	1	0
Total	33.9±0.3						

Data are reported as a means $\pm$ SEM. Eleven main components of the Mediterranean diet (non-refined cereals, fruits, vegetables, potatoes, legumes, olive oil, fish, red meat, poultry, full fat dairy products and alcohol) were considered. In detail, we used monotonic functions (with the exception of alcohol intake) in order to score the frequency consumption of these foods. In particular, we assigned individual ratings (from 0 to 5 or the reverse) in each of the 11 food groups according to their position in the Mediterranean diet pyramid. For the consumption of items presumed to be close to this pattern (non-refined cereals, fruits, vegetables, legumes, olive oil, fish, and potatoes) we assigned score 0 when someone reported no consumption, score 1 when they reported consumption of 1-4 servings/month, score 2 for 5-8 servings/month, score 3 for 9-12 servings/month, score 4 for 13-18 servings/month and score 5 for more than 18 servings/month. On the other hand, for the consumption of foods presumed to be outside of this diet (meat and meat products, poultry and full fat dairy products) we assigned the scores on a reverse scale (i.e. 5 when someone reported no consumption to 0 when they reported almost daily consumption). For olive oil we evaluated its weekly use for cooking and we assigned 0 when no consumption was reported, 1 for rare consumption, 2 for less than 1 times a week, 3 for 1-3 times a week, 4 for 3-5 times a week and 5 for daily use. For alcohol we did not use a monotonic function, but we assigned score 5 for consumption of less than 300 ml of alcohol/day, score 0 for consumption of more than 700 (or 0) ml/day and scores from 4 to 1 for daily consumption of 300, 400, 500 and 600 ml (100 ml has 12 g ethanol concentration), respectively (Panagiotakos et al., 2006).

Supplemental Table 2: List of food to minimize or avoid in the evening.

Cereals grains	Corn, Cornmeal, Couscous, Whole wheat, White rice, Semolina.
Breads	Wheat Breads, White wheat flour bread, Fiber-enriched, White bread, Specialty wheat breads (pita bread), Rice bread, Grissini, Taralli, Crackers.
Pasta/Noodles	White-flour Pasta, Rice noodles.
Breakfast cereals and related	All-Bran, Cornflakes, Oat bran, Muesli, Refined breakfast
Products	Cereals, Wheat biscuits, Breakfast cereal bar.
Bakery products	Cake, Muffin, Donut, Cupcake, Pancake, Croissant, Desserts.
Dairy products and alternatives	Cow and rice milk, Yoghurt, Ice cream, Soy-based product alternatives.
Fruit and fruit products	Apricot, Peach, Banana, Orange, Mango, Pineapple, Strawberry, Watermelon, Fig, Grape, Pear, Plum, Apple, Mango, Fruit jams and preserves.
Fruit juice	100% fruit juices like Apple juice, Orange juice, Grapefruit juice, Pineapple juice, Cranberry juice, Sugar sweetened juices.
Vegetables	Sweetcorn, Potato, Carrot, Pumpkin, Peas.
Snack products and confectionery	Milk chocolate, White chocolate, Chocolate hazelnut spread, Candy bars, Fruits bar, Snack bar, Hard and gummy candies, Brownies, Cookies, Popcorn, Potato crisps, Potato tortilla chips, Corn chips.
Sauce/Condiments	Salad dressing, Dressing sauce for pasta other than tomato sauce, Barbeque sauce, Ketchup, Mustard.
Sugars/Syrups	Fructose, Glucose, Sucrose, Honey, Syrup.
Combination foods	Pizza, Focaccia, Panzerotto, White bread with accompaniments, Quiche.
Beverage	Sugar-sweetened beverages, sport drinks.

Supplemental Table 3. Baseline comparison of the two groups of the study population

VARIABLES	EXCELLENT (N:44)	POOR (N:63)	P
M/F	22/22	29/34	NS
AGE	54	52	NS
MS+ (T0)	33/44 (75%)	42/63 (67%)	NS
MS+ (T1)	26/44 (59%)	36/63 (57%)	NS
CONTINUOUS VARIABLES (BASELINE)	EXCELLENT	POOR	P
BW, kg	94.5±2.8	92.3±2.5	NS
BMI, kg/m ²	34.0±0.9	34.2±0.7	NS
WC, cm	113.5±2.0	112.6±1.8	NS
SBP, mmHg	135.7±2.4	133.0±1.7	NS
DBP, mmHg	84.8±1.7	83.6±1.2	NS
TOT CHOL, mg/dl	209.5±7.0	197.7±4.7	NS
HDL CHOL, mg/dl	45.2±1.7	46.9±1.3	NS
LDL CHOL, mg/dl	132.0±5.6	120.5±4.2	NS
TG, mg/dl	171.6±13.7	162.8±12.0	NS
GLC, mg/dl	113.6±6.7	112.6±5.0	NS
HbA1c, %	6.3±0.3	6.4±0.3	NS
INSULIN, UI/ml	24.1±5.2	15.4±1.6	NS
HOMA-IR	7.8±2.2	4.2±0.5	NS
AST,U/L	28.8±3.2	25.7±2.5	NS
ALT, U/L	48.5±6.4	46.4±4.3	NS
CVR, %	7.4±1.4	6.1±0.8	NS
TREATMENTS	EXCELLENT	POOR	P
Antidiabetics	11 (25%)	18 (29%)	NS
Antihypertensive	23 (52%)	35 (56%)	NS
Statins	8 (18%)	15 (24%)	NS
Fibrates / PUFA Ω 3	0 (0%)	5 (8%)	0.05
Physical exercise	6 (14%)	12 (19%)	NS

Data are reported as mean $\pm$ standard error (SEM) or frequencies (percentages) for continuous and categorical variables, respectively. Comparisons of clinical and biochemical parameters among groups (“excellent” vs. “poor” adherence) are performed for baseline values with the Pearson χ^2 test and the Mann Whitney U test. Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; BW, body weight; CVR, cardiovascular risk; DBP, diastolic blood pressure; GLC, fasting glucose; HbA1c, glycosylated hemoglobin; HDL CHOL, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LDL CHOL, low-density lipoprotein cholesterol; PUFA, polyunsaturated fatty acids; SBP, systolic blood pressure; TG, triglyceride; TOT CHOL, total cholesterol; WC, waist circumference.

Supplemental Table 4. Characteristics of the study population in the two groups before and after the MedLowC protocol in the “excellent” and “poor” adherence group.

	Excellent adherence (N:44)			Poor adherence (N:63)		
	Baseline	6 months	P	Baseline	6 months	P
BW, kg	94.5±2.5	85.5±2.5	<0.001	92.3±2.5	90.7±2.5	0.01
BMI, Kg/m ²	34.0±0.9	30.7±0.8	<0.001	34.2±0.7	33.6±0.7	0.01
WC, cm	113.5±2	105.7±1.8	<0.001	112.6±1.8	111.0±1.8	NS (0.07)
SBP, mmHg	135.7±2.4	131.7±2.0	NS	133.0±1.7	130.5±1.7	NS
DBP, mmHg	84.8±1.7	81.4±1.5	NS (0.07)	83.6±1.2	82.6±1.3	NS
TOT CHOL, mg/dl	209.5±7.0	179.8±4.4	<0.001	197.7±4.7	197.7±4.8	NS
HDL CHOL, mg/dl	45.2±1.7	47.7±1.6	NS (0.06)	46.9±1.3	48.1±1.2	NS (0.08)
LDL CHOL, mg/dl	132.0±5.6	111.8±4.6	<0.001	120.5±4.2	122.2±4.0	NS
TG, mg/dl	171.6±13.7	109.8±6.4	<0.001	162.8±12	148.2±13.7	NS
GLC, mg/dl	113.6±6.7	97.0±2.3	<0.001	112.6±5	107.0±4.0	0.02
HbA1c, %	6.3±0.3	5.6±0.1	0.003	6.4±0.3	6.1±0.1	NS
INSULIN, UI/ml	24.1±5.2	13.1±2.8	<0.001	15.4±1.6	13.1±1.5	NS
HOMA-IR	7.8±2.2	3.2±0.7	<0.001	4.2±0.5	3.2±0.4	0.04
AST, U/L	28.8±3.2	23.0±1.5	0.04	25.7±2.5	22.9±1.9	0.01
ALT, U/L	48.5±6.4	30.6±3.0	0.001	46.4±4.3	36.6±4.0	0.001
CVR, %	7.4±1.4	6.3±1.1	0.04	6.1±0.8	5.4±0.7	NS (0.07)

Data are reported as mean ± standard error (SEM) or frequencies (percentages) for continuous and categorical variables, respectively. Time dependent changes in continuous variables are assessed, separately in the two groups of adherence, with the non-parametric Wilcoxon Signed Rank Test. Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; BW, body weight; CVR, cardiovascular risk; DBP, diastolic blood pressure; GLC, fasting glucose; HbA1c, glycosylated hemoglobin; HDL CHOL, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LDL CHOL, low-density lipoprotein cholesterol; PUFA, polyunsaturated fatty acids; SBP, systolic blood pressure; TG, triglycerides; TOT CHOL, total cholesterol; WC, waist circumference.

Supplemental Table 5. Multiple regression analysis of continuous variables with confounding factors.

	Δ% POOR vs Δ% EXCELLENT			
	PHYSICAL	STATIN	ANTI-DIABETIC	FIBRATE/ PUFA Ω3
	ACTIVITY	THERAPY	THERAPY	THERAPY
BW, kg	NS (0.08)	NS	NS	NS
BMI, Kg/m ²	NS (0.08)	NS	NS	NS
WC, cm	NS	NS	NS	NS
SBP, mmHg	NS	NS	NS	NS
DBP, mmHg	NS	NS	NS	NS
TOT CHOL, mg/dl	NS	0.001	NS	NS
HDL CHOL, mg/dl	0.05	NS	NS	NS
LDL CHOL, mg/dl	NS	NS (0.07)	NS	NS
TG, mg/dl	NS	NS (0.09)	NS	NS
GLC, mg/dl	NS	NS	NS (0.07)	NS
HbA1c, %	NS	NS (0.08)	0.02	NS
INSULIN, UI/ml	NS	NS	NS	NS
HOMA-IR	NS	NS	NS	NS
AST, U/L	NS (0.09)	NS (0.08)	NS	NS
ALT, U/L	NS	NS	NS	NS
CVR, %	NS	0.05	NS	NS

In order to compare the time dependent changes of each continuous variable between the two groups of adherence to the MedLowC protocol, we used a multiple regression analysis. This method provides a way of accounting for potentially confounding factors. Abbreviations: ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; BW, body weight; CVR, cardiovascular risk; DBP, diastolic blood pressure; GLC, fasting glucose; HbA1c, glycosylated hemoglobin; HDL CHOL, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LDL CHOL, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TG, triglyceride; TOT CHOL, total cholesterol; WC, waist circumference.

Supplemental Table 6. Correlations between changes in WC ($\Delta\%$) and changes in patient biochemistry and clinical values ($\Delta\%$).

CONTINUOUS VARIABLE (overall)	R	P
Δ BW, kg	0.7	<0.001
Δ BMI, kg/m ²	0.7	<0.001
Δ HDL CHOL, mg/dl	-0.2	NS (0.07)
Δ GLC, mg/dl	0.2	0.03
Δ INSULIN, UI/ml	0.4	0.01
Δ HOMA-IR	0.4	0.005
Δ ALT, U/L	0.2	NS (0.09)

The strength of the linear relationship between continuous variables was calculated with the Pearson's correlation coefficient. Abbreviations: ALT, alanine transaminase; BMI, body mass index; BW, body weight; GLC, fasting glucose; HDL CHOL, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance.

Supplemental Figure 1. Characterization of the study population. The flow chart shows the study population divided by the adherence to the unrestricted calorie Mediterranean diet with low carbohydrate intake in the evening. In the table, we characterized the same population according to their treatment for diabetes, hypercholesterolemia, hypertension and hypertriglyceridemia.

Salvia et al., Supplemental Figure 2

Supplemental Figure 2. Absence of changes in systolic (SBP, A) and diastolic blood pressure (DBP, B) following nutritional intervention. Diet had no impact on SBP and DBP compared to baseline values. Means are represented as bars: (grey) "poor" adherence group; (white) "excellent" adherence group. Lines represent patients (before/after). Error bars represent SEM. Time dependent changes in continuous variables were assessed with the nonparametric Wilcoxon Signed Rank Test (P value in section 1 and 2 of each variable plot). In order to compare the time dependent changes of each continuous variable between the two groups we used a multiple regression analysis (adjusted P value in section 3 of each variable plot; P value of the confounding variables investigated in Table S5).

Supplemental Reference List

Reference List

Panagiotakos DB, Pitsavos C, Stefanadis C. 2006. Dietary patterns: a Mediterranean diet score and its relation to clinical and biological markers of cardiovascular disease risk. *Nutr Metab Cardiovasc Dis* 16:559-568.