Dietary inflammatory index and anthropometric measures of obesity in a population sample at high cardiovascular risk from the PREDIMED trial

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Abstract

BACKGROUND: The Dietary Inflammatory Index (DII) is applied to measure the inflammatory potential related to the intakes of nutrients and food groups. A higher score in the DII represents a higher pro-inflammatory potential of the diet.

OBJECTIVES: To determine the association between the DII and body mass index (BMI), waist circumference and waist-to-height ratio (WHtR).

DESIGN: Baseline cross-sectional assessment of all participants of the "PREvención con DIeta MEDiterránea" (PREDIMED) trial.

METHODS: Diet was assessed with a validated 137-item food frequency questionnaire. Trained nurses/dietitians measured weight, height and waist circumference. Sex-specific multivariable linear regression models were fitted to estimate differences (and 95% confidence intervals) in the anthropometric adiposity measures across quintiles of the DII.

RESULTS: We included 7236 participants (mean age=67 yrs, 57% women) at high-risk of cardiovascular disease. All macro- and micronutrient intakes were higher in the quintile with lowest DII score (more *anti*-inflammatory values) except for the intake of animal protein, saturated and monounsaturated fat. Higher consumption of healthy foods and adherence to the Mediterranean diet (MeDiet) were also associated with a lower DII score. Though an inverse association between DII and total energy was apparent, the DII was associated with higher average BMI, higher waist circumference and higher WHtR after adjusting for known risk factors of obesity, including age, smoking, type 2 diabetes, hypertension, physical activity, educational level and marital status. BMI, waist circumference and WHtR increased progressively across quintiles compared with the first quintile of DII. The multivariable-adjusted difference in WHtR for women and men between the highest and the lowest quintile of DII was 1.60% (95% CI 0.87 to 2.33) and 1.04% (95% CI 0.35 to 1.74), respectively. Pro-inflammatory scores remained associated with indexes of general obesity and abdominal obesity after controlling for the effect that adherence to a MeDiet had on inflammation.

CONCLUSION: This study has shown an inverse association between the DII and indices of general and abdominal obesity. This finding supports the hypothesis that diet may have a role in the development of obesity through inflammatory modulation mechanisms.

Trial Registration International Standard Randomised Controlled Trial Number Registry ISRCTN35739639

Introduction

The obesity pandemic constitutes a major public health problem in most high-income countries and it is emerging as a threat in more affluent sectors of developing countries.[1] In 2008 more than 10% of the World's adult population, i.e. around 500 million people, were obese according to the WHO.[2] It is estimated that each year, 2.8 million adult deaths are attributable to obesity or overweight. This is a global crisis since 65% of the world's population live in countries where overweight and obesity kill more people than underweight.

Obesity is the result of the accumulation of excess body fat and it is often characterized as a state of low-grade chronic inflammation.[3] This obesity-induced inflammation has multi-organ metabolic effects affecting adipose tissue, liver, muscle, pancreas and brain.[4] Metabolic differences exist according to the location of the fat cells. For example, excessive deposition of fat in visceral adipose tissue (i.e., intra-abdominal fat) is associated with higher health risks than subcutaneous fat accumulation in the extremities.[5] For this reason, different anthropometric adiposity measures including waist circumference or WHtR are used to assess the role of adiposity in cardiovascular disease risk.[6-7]

A number of studies have shown an association between diet and inflammatory biomarkers and how this translates into increased or decreased risk of chronic metabolic diseases[8-15]. For this reason, part of the preventive role of healthy dietary patterns, such as the Mediterranean diet, could be attributed to the anti-inflammatory properties of some of their main components.[14-19] This anti-inflammatory effect may decrease the low-grade inflammation found in obese patients[20,21] but it may also reduce inflammation in the absence of weight loss.[22] Thus, a bidirectional association between inflammation and obesity can be hypothesized.[23]

Consequently, it can be useful to characterize an individual's diet according to its inflammatory properties in order to investigate the inflammatory links between obesity and diet.[24] The dietary inflammatory index (DII) is a new tool to assess this inflammatory potential of the diet.[22] In this article we examine the relationships between nutrient intake or food group consumption and the DII as well as the association between the DII and indices of both general and abdominal obesity in the PREDIMED trial.

Methods

Ethics statement

The protocol was approved by the Research Ethics Committees at all recruiting centers: University of Navarra, University of Valencia, University Rovira i Virgili, IMIM-Hospital del Mar Medical Research Institute, University of Barcelona, University Hospital of Alava, University of Malaga, University of Balearic Islands, University of Las Palmas de Gran Canaria, University Hospital of Bellvitge, Hospital Clinic.

Participants signed a written informed consent.

Study design and participants

The PREDIMED study is a parallel group, multicenter, clinical trial that aims to assess the effects of the traditional MedDiet on the primary prevention of cardiovascular disease (protocol available at www.predimed.es). A detailed description of methods and patients has been published elsewhere.[26,27] The study was conducted between October 2003 and December 2010 by 11 recruiting centers at Spain.

Eligible participants were men 55 to 80 years of age and women 60 to 80 years of age with no previous cardiovascular disease. At baseline the study participants should have had a diagnosis of type 2 diabetes mellitus or at least three of the following major cardiovascular risk factors: smoking (more than 1 cig/day during the last month), hypertension (systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg or antihypertensive medication), elevated low-density lipoprotein cholesterol levels (≥ 160 mg/dl), low high-density lipoprotein cholesterol levels (≤ 40 mg/dl in men or ≤ 50 mg/dl in women, independently of lipid-lowering therapy), BMI ≥ 25 kg/m^2, or a family history of premature coronary heart disease.

Participants were randomly assigned to one of three diet interventions following a stratified random sequence of allocation according to the recruitment order in blocks of 50 participants, balanced by sex and age group (< 70 years and > 70 years). The randomization process was elaborated by the Coordinating Unit which provided a stratified random sequence of allocation for each center using closed envelopes. A total of 7447 participants were randomized in a 1:1:1 ratio to a parallel-design intervention trial of dietary advice: a) a MedDiet supplemented with extra-virgin olive oil, b) a MedDiet supplemented with nuts, or c) advice to follow a low-fat diet (control group).

Medical conditions and risks factors related to eligibility were collected with a questionnaire during the first screening visit. Participants, with the assistance of trained dietitians, completed a food frequency questionnaire (FFQ). This FFQ was adapted from the Willett questionnaire and validated in Spain.[28] It includes 137 items plus vitamin/minerals supplements and with specific questions for patterns of alcohol consumption. Participants also completed the Spanish validated version of the Minnesota physical activity questionnaire,[29] and a 14-item dietary screener to assess adherence to the MedDiet.[30] PREDIMED dietitians were responsible for the accurate completion of the questionnaires.

For the present study, participants who reported extremely low or high values for total energy intake (<800 or >4200 kcal/d for men and <600 or >3500 kcal/d for women) and those with missing values from the FFQ were excluded from the analyses, which left data from 7194 participants.

The Dietary Inflammatory Index (DII)

The design and development of the DII has been described elsewhere.[22] Briefly, the DII is a scoring algorithm based on an extensive review of the literature published from 1950 to 2010 linking 1943 articles to a total of forty-five food parameters including various macronutrients, micronutrients, flavonoids and food items. These dietary parameters were scored according to whether they increased (+1), decreased (-1) or had no effect (0) on six inflammatory biomarkers (IL-1β, IL-4, IL-6, IL-10, TNF-α and C-reactive protein). An overall food parameter-specific inflammatory effect score was calculated and multiplied by a centered percentile value for each food. This percentile was calculated by first linking the dietary data from a study to the regionally representative world database intake which is based on actual human consumption in 11 populations from different parts of the world that provided a robust estimate of a mean and standard deviation for each parameter. These then become the multipliers to express an individual's exposure relative to the "standard global mean" as a z-score. This is achieved by subtracting the “standard global mean” from the amount reported and dividing this value by the standard deviation. To minimize the effect of “right skewing”, this value is then converted to a centered percentile score. The centered percentile score for each food parameter for each individual was then multiplied by the respective food parameter effect score, which is derived from the literature review, in order to obtain a food parameter-specific DII score for an individual. All of the food parameter-specific DII scores are then summed to create the overall DII score for every participant in the study. The DII score could take on values ranging from 7.98 (maximally pro-inflammatory) to -8.87 (maximally anti-inflammatory).[25]

Construct validation of the DII has been performed using data derived from two different sources of dietary intake information and serum high-sensitivity C-reactive protein as the construct validator.[31]

Outcome

Trained and certified PREDIMED nurses performed all baseline anthropometric adiposity measures including weight and height [from which BMI (kg/m^2) was computed], waist circumference (cm) and WHtR (%) following validated procedures. Baseline weight was measured using a calibrated balance beam scale with the subject barefoot and wearing light clothes. The nurse measured height using a wall-mounted calibrated stadiometer. Waist circumference was measured using an anthropometric measuring tape, at a horizontal plane midway between the lowest rib and the iliac crest.

Statistical analysis

Baseline means were compared using one-way ANOVA, and categorical variables were compared using the Chi-squared Pearson test.

Least-squared means of BMI, waist circumference and WHtR were estimated across quintiles of DII, and linear trends were tested. Pearson correlation coefficients between these anthropometric adipose measures and the DII index were also calculated.

Sex-specific linear regression models were constructed to estimate the change (and 95% confidence interval) in each of the anthropometric adiposity measures according to quintiles of the DII index. Covariates included in these models were age (years), smoking status (never, current or former smoker), diabetes (yes or no), hypertension (yes or no), leisure-time physical activity (MET-min/d), educational level (illiterate/elementary education, secondary education or university), marital status (single, married, divorced or other) and research center. In addition, tests of linear trend across successive quintiles of DII index were conducted using the median value for each quintile category as a continuous variable and after adjusting for the confounding variables mentioned above. This was additionally adjusted for total energy intake in a second regression model.

Residuals of the DII were obtained in a linear regression analysis of the association between the DII and a previously validated 14-item PREDIMED screener of adherence to the MeDiet.[30] These residuals represent the information provided by the DII that is not explained at all by adherence to the MeDiet (i.e. they exhibit zero correlation with the MeDiet score). They were included as an independent variable after transformation into quintiles in a multivariable regression model with the same covariates previously listed.

All P values presented are 2-tailed and differences were considered statistically significant at $p \leq 0.05$. All statistical analyses were carried using the STATA® software for Windows version 12.0.

Results

A total number of 7236 participants out of the 7447 initially randomized subjects in the PREDIMED trial were included in this study (figure 1). The mean age of participants was 67 (±6.2) years and 57% were women. The median DII score was -0.83, ranging from a maximum anti-inflammatory value of -5.24 to a maximum pro-inflammatory value of +3.69.

Table 1 shows the main characteristics of participants according to caegories of the DII score. All differences between quintiles of this index were statistically significant except for the percentage of subjects with a family history of early CHD and the presence of hypertension. The level of physical activity was inversely associated with the DII as was total energy intake and alcohol intake.

All macro- and micronutrient intakes were higher in the quintile with *lowest* DII score (anti-inflammatory dietary pattern) except for intakes of animal protein, saturated fat and monounsaturated fat (Table 2). Better adherence to a MeDiet also was associated with *lower* DII scores.

Table 3 shows the adjusted indices of obesity based on BMI, waist circumference and WHtR according to the DII score stratified by sex. The lower and upper limits of this score are shown for each quintile. Mean values of all three adiposity indices monotonically increased across successive quintiles of DII scores (from anti-inflammatory to pro-inflammatory levels). A significant positive correlation was observed between these obesity indexes and the DII score.

Among women, the DII was directly associated with BMI after adjusting for multiple factors related to obesity (table 4). Being in the highest quintile of the DII was associated with an increase of 0.79 kg/m^2 in the BMI (95%CI, 0.35-1.23) compared with the lowest quintile (p for trend = 0.001). This association was not statistically significant for men.

Waist circumference and WHtR increased progressively across quintiles 2 to 4 and 5 compared with the lowest quintile of DII, both in women and men (p for trend statistically significant in all comparisons).

Table 5 shows the association of the DII with the anthropometric indices independently of the adherence to the MeDiet. This analysis was conducted using as independent variable the quintiles of the residuals of DII (after the DII was regressed on the MeDiet). A higher pro-inflammatory level of diet (beyond the effect of lower adherence to the MeDiet) was associated with higher adjusted means of BMI, waist circumference and WHtR (p for trend < 0.05 in all comparisons except for BMI among men). The predicted increase in anthropometric measures was statistically significant in women except for the increase in BMI and in WHtR when the intermediate DII quintiles (2 to 4) were compared with the lowest category. On the contrary, results were not statistically significant among men except for the waist circumference and the WHtR when comparing the highest *versus* the lowest quintile of the residuals of DII.

Discussion

In our study, we used a score (DII) to appraise the capacity of the overal dietary pattern to promote inflammation. Higher values of DII represent a higher inflammatory potential. As expected, we observed that DII was inversely associated with the intake of healthy foods, nutrients and adherence to MeDiet. A pro-inflammatory DII was directly associated with indices of general and abdominal obesity, independent of established risk factors for obesity including total energy intake, age, smoking, diabetes, hypertension, physical activity, educational level and marital status. These results were consistent for both sexes except for the BMI in men. In the residual model (after removing the variability explained by MeDiet), the association between the inflammatory potential of the diet and higher adiposity indices remained apparent, but there was a clearer association between the DII and the abdominal indices of obesity for women than for men.

The associations observed between nutrient intake or food consumption with the DII are consistent with previous research. Several studies have shown an inverse association between healthy diets and markers of inflammation as well as a direct association with “Western-like” dietary patterns.[8-15] Specifically, a lower C-reactive protein concentration has been associated with higher intake of fruits and vegetables,[32-34] legumes,[35] nuts,[36] and low-fat dairy consumption.[37] Previous studies also have observed associations of specific nutrients such as total dietary fiber intake,[38] moderate alcohol consumption,[39] vitamin E and vitamin C intake,[40] with lower levels of inflammation markers. On the contrary, animal protein seems to increase the inflammatory status of obese individuals.[41]

We also found that a higher consumption of dairy products and meat (or meat products) was more frequent in the highest DII quintile. A systematic review has found no impact of dairy products consumption on biomarkers of inflammation on overweight and obese adults.[42] Concerning the consumption of meat, a higher intake of meat protein has been found to be associated with higher plasma levels of inflammatory markers in obese adults.[43] However, a recent study has shown that the association between red meat intake and inflammatory markers was no longer observed after adjustment for BMI.[44] Therefore, it is suggested that the association between red meat intake and inflammation is probably mediated by obesity.

In our study, a higher pro-inflammatory diet was observed in participants with higher BMI, waist circumference and WHtR. This result suggest the hypothesis that a diet-induced inflammation might be contributing to increase or maintain obesity, specially abdominal obesity, in a population that is mostly overweight or obese. The origin of inflammation during obesity is not yet fully understood. It is acknowledged that inflammation is induced by adiposity[4,5], but this relationship can be bidirectional (i.e., a pro-inflammatory diet can increase or maintain adiposity), thus creating a vicious circle, because nutrient excess and some specific foods or nutrients also have been associated with inflammation.[45] The potential mechanisms underlying this association is the activation of pathogen-associated molecular patterns, such as toll-like receptors and nod-like receptors, which induce the activation of inflammatory markers in several tissues including the adipose tissue.[46] Moreover, dietary patterns and single specific nutrients appear to have important consequences in the gut microbiota which is also involved in the low-grade inflammation associated with obesity.[47,48]

The pro-inflammatory score (DII) was also associated with obesity indices after excluding the part of variability that adherence to a MeDiet was able to explain (residual model). This association was stronger between the DII and the obesity indices (waist circumference and WThR). These results are in close agreement with previous findings showing that central adiposity-related indices are more strongly correlated with plasma proinflammatory markers than indices assessing total adiposity in healthy young adults.[5] Moreover, abdominal adiposity has been associated with elevated CRP levels independent of BMI in older adults.[49] As a consequence, our results are important because they reinforce the usefulness of the DII to assess the inflammatory properties of a diet, and specifically in this case using a semi-quantitative FFQ to assess the dietary intake.

Our results are also consistent with those of studies reporting a stronger association of CRP and BMI in women than in men.[50,51] This between-sexes difference could be partially explained by a greater accumulation of subcutaneous fat in women than in men and higher lean mass in men.[52] Sex differences in the metabolic activity of adipose tissues as well as in the association between leptin and CRP may also explain these differences.[53]

The strengths of the current study include a large sample size, the use of a validated instrument to measure the inflammatory potential of the diet, the adjustment for a large number of factors associated with obesity, the detailed measures of obesity indexes and the validation of all assessment instruments including the MedDiet screener, the FFQ, and the physical activity questionnaire. This study also has some limitations the main of which is the cross-sectional nature of the present analyses. It is therefore unclear whether obese individuals are more likely to choose pro-inflammatory diets or if pro-inflammatory diets contribute to promote or maintain obesity. Both weight reduction and an overal healthy dietary pattern have the capacity to reduce inflammatory markers. Thus, the association between the DII and obesity indices remains to be confirmed in prospective analyses. Another limitation is that anthropometric measures are surrogate markers of abdominal obesity. Waist circumference and WHtR do not differentiate between visceral adipose tissue and subcutaneous abdominal adipose tissue.[54] Therefore, we cannot determine whether the DII is more strongly associated with visceral, subcutaneous or both types of abdominal fat mass. Finally, the DII is limited by current knowledge of the inflammatory factors involved in obesity; however, a comparison between results in our 2009 and later publications are broadly consistent with one another.[25,31,55,56]

In conclusion, the current findings indicate an association between anti-inflammatory values of the DII and healthy foods, nutrients and higher adherence to MeDiet. A pro-inflammatory diet was associated with elevated indices of central and abdominal obesity. This association suggest that the DII may have the capacity to help elucidate the role that diet plays in the development of obesity through inflammatory processes.

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Conflict of Interest Disclosures

Dr. Estruch reports serving on the board of and receiving lecture fees from the Research Foundation on Wine and Nutrition (FIVIN); serving on the boards of the Beer and Health Foundation and the European Foundation for Alcohol Research (ERAB); receiving lecture fees from Cerveceros de España and Sanofi-Aventis; and receiving grant support through his institution from Novartis. Dr. Ros reports serving on the board of and receiving travel support, as well as grant support through his institution, from the California Walnut Commission; serving on the board of the Flora Foundation (Unilever); serving on the board of and receiving lecture fees from Roche; serving on the board of and receiving grant support through his institution from Amgen; receiving consulting fees from Damm and Abbott Laboratories; receiving consulting fees and lecture fees, as well as grant support through his institution, from Merck; receiving lecture fees from Aegerion, AstraZeneca, Danone, Pace, and Rottapharm; receiving lecture fees and payment for the development of educational presentations, as well as grant support through his institution, from Ferrer; receiving payment for the development of educational presentations from Recordati; and receiving grant support through his institution from, Daiichi Sankyo, Feiraco, Karo Bio, Nutrexpa, Pfizer, Sanofi-Aventis, Synageva, Takeda, and, Unilever.

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Table 1. Description of main characteristics of participants according to quintiles of the Dietary Inflammatory index score.

	Quintiles of the Dietary Inflammatory index					
	Q1 (lowest)	**Q2**	**Q3**	**Q4**	**Q5 (highest)**	p
Median (min, max)	-2.63 (-5.24, -2.10)	-1.64 (-2.09, -1.24)	-0.83 (-1.23, -0.43)	0.04 (-0.42, 0.62)	1.36 (0.61, 3.69)	
N	1448	1447	1447	1447	1447	
Age, yr	66 (6)	67 (6)	67 (6)	67 (6)	68 (6)	<0.001
% Women	55	54	58	58	62	<0.001
% Family history of early CHD	24	23	22	22	20	0.062
% Hypertension	80	83	84	84	83	0.139
% Dislipidemia	76	73	72	71	70	0.007
% Diabetes	49	46	48	49	52	0.021
Smoking						0.027
% Current smokers	13	14	14	15	14	
% Former smokers	26	28	24	24	22	

Table 1 (CONTINUED). Description of main characteristics of participants according to quintiles of the Dietary Inflammatory index score.

	Quintiles of the Dietary Inflammatory index					
	Q1 (lowest)	**Q2**	**Q3**	**Q4**	**Q5 (highest)**	p
Total energy intake, kcal/d	2584 (552)	2414 (526)	2242 (454)	2098 (454)	1869 (443)	<0.001
Physical activity, METS-h/d	4.6 (4.8)	4.0 (4.0)	3.9 (4.0)	3.6 (3.7)	3.2 (3.2)	<0.001
Alcohol intake, g/d	10.4 (15.1)	8.7 (14.0)	8.1 (14.4)	8.0 (13.9)	6.8 (12.9)	<0.001
Marital status						<0.001
% Single	4	3	5	4	5	
% Married	81	78	76	76	72	
% Widow	13	16	16	17	20	
Low Educational level						<0.001
% Primary education or less	73	77	80	79	79	
% Secondary education	17	16	14	15	15	
% Any college	10	7	7	6	6	

Table 2. Nutrient and food consumption according to quintiles (Q) of the Dietary Inflammatory Index. The PREDIMED study 2003-2009.

	Quintiles of the Dietary Inflammatory index			
	Q1 lowest	**Q2-Q4 moderate**	**Q5 highest**	**P**
Median	-2.63	-0.83	1.36	
Total energy intake (Kcal/d)	2683 (669)	2273 (535)	1870 (449)	<0.001
Carbohydrate intake (% E)	42 (7)	42 (7)	40 (7)	<0.001
Protein intake (% E)	17 (3)	17 (3)	17 (3)	0.146
Vegetal protein intake (% E)	6 (1)	5 (1)	5 (1)	<0.001
Animal protein intake (%E)	11 (3)	11 (3)	12 (3)	<0.001
Total fat intake (% E)	38 (7)	39 (7)	41 (7)	<0.001
Saturated (% E)	9 (2)	10 (2)	11 (2)	<0.001
Monounsaturated (% E)	18 (4)	19 (4)	21 (5)	<0.001
Polyunsaturated (% E)	7 (2)	6 (2)	6 (2)	<0.001
Alcohol (g/d)	10 (15)	8 (14)	7 (13)	<0.001
Fiber (g/d)	35 (9)	25 (6)	17 (4)	<0.001
Vitamin E (mg/d)	13 (5)	10 (4)	7 (3)	<0.001

Table 2 (CONTINUED). Nutrient and food consumption according to quintiles (Q) of the Dietary Inflammatory Index. The PREDIMED study 2003-2009.

	Quintiles of the Dietary Inflammatory index			
	Q1 lowest	**Q2-Q4 moderate**	**Q5 highest**	**P**
Vitamin C (mg/d)	281 (100)	199 (71)	123 (43)	<0.001
Vitamin A (µg/d)	1801 (829)	1275 (870)	848 (489)	<0.001
Vegetables (g/d)	482 (173)	326 (109)	212 (78)	<0.001
Fruits (g/d)	476 (222)	378 (190)	234 (126)	<0.001
Cereals (g/d)	157 (88)	146 (68)	120 (73)	<0.001
Potatoes (g/d)	98 (58)	83 (47)	65 (39)	<0.001
Legumes (g/d)	26 (16)	21 (14)	15 (8)	<0.001
Nuts (g/d)	20 (19)	9 (12)	4 (7)	<0.001
Fish and seafood (g/d)	128 (59)	98 (47)	77 (38)	<0.001
Meat and meat products (g/d)	134 (64)	133 (55)	123 (55)	<0.001
Dairy products (g/d)	406 (233)	380 (217)	357 (215)	<0.001
Mediterranean diet score (0 to 14)	9.6 (1.9)	8.6 (1.9)	7.9 (1.7)	<0.001

[1] All values are means (standard deviations or percentages of total energy intake).

Table 3. Adjusted average indices (95% confidence intervals) of general obesity and abdominal obesity according to quintiles (Q) of the Dietary Inflammatory Index. The PREDIMED study, 2003-2009.

	Quintiles of the Dietary Inflammatory index						
	Q1 (lowest)	**Q2**	**Q3**	**Q4**	**Q5 (highest)**	**r (Pearson)**	**P**
Women (n)	(829)	(829)	(829)	(829)	(829)		
Limits	-4.9 to -2.0	-2.0 to -1.2	-1.2 to -0.3	-0.3 to +0.7	+0.7 to 3.7		
Body mass index (kg/m^2)[1]	29.6 (29.3-29.9)	30.0 (29.8-30.3)	30.3 (30.0-30. 5)	30.5 (30.2-30.7)	30.6 (30.3-30.9)	0.060	0.001
Waist circumference (cm)[1]	96.1 (95.3-96.8)	97.5 (96.8-98.2)	98.6 (97.9-99.3)	98.7 (97.9-99.4)	99.1 (98.3-99.8)	0.053	<0.001
Waist-to-height ratio (%)[1,2]	62.2 (61.8-62.7)	63.1 (62.7-63.6)	63.5 (63.0-63.9)	63.6 (63.2-64.1)	63.9 (63.4-64.4)	0.064	<0.001
Men (n)	(619)	(618)	(618)	(618)	(618)		
Limits	-5.2 to -2.2	-2.2 to -1.4	-1.4 to -0.5	-0.5 to +0.5	+0.5 to 3.7		
Body mass index (kg/m^2)[1]	29.5 (29.2-29.8)	29.4 (29.2-29.7)	29.5 (29.2-29.9)	29.9 (29.6-30.2)	29.9 (29.6-30.3)	0.048	0.007
Waist circumference (cm)[1]	102.5 (101.6-103.4)	102.9 (102.0-103.7)	103.6 (102.8-104.5)	104.3 (103.5-105.0)	105.0 (104.2-105.9)	0.082	<0.001
Waist-to-height ratio (%)[1,2]	61.7 (61.2-62.2)	61.7 (61.2-62.3)	62.3 (61.8-62.8)	63.0 (62.5-63.5)	63.2 (62.7-63.7)	0.093	<0.001

[1] Adjusted for age, smoking, diabetes, hypertension, marital status, educational level, physical activity, total energy intake and center.

[2] A waist-to-height ratio =1 is taken as 100%.

Table 4. Multivariable-adjusted[1] differences (95% confidence intervals) in indices of general obesity and abdominal obesity according to quintiles (Q) of the Dietary Inflammatory Index. The PREDIMED study 2003-2009.

	Quintiles of the Dietary Inflammatory index			
	Q1 lowest (ref)	**Q2-Q4 moderate**	**Q5 highest**	**P for trend**
Women				
Body mass index (kg/m^2) [1]	0 (ref.)	+0.56 (+0.23 to +0.89)	+0.79 (+0.35 to +1.23)	0.001
Waist circumference (cm) [1]	0 (ref.)	+2.03 (+1.17 to +2.90)	+2.79 (+1.64 to +3.93)	<0.001
Waist-to-height ratio (%)[1,3]	0 (ref.)	+1.19 (+0.64 to +1.74)	+1.60 (+0.87 to +2.33)	<0.001
Men				
Body mass index (kg/m^2) [1]	0 (ref.)	+0.05 (-0.26 to +0.37)	+0.33 (-0.08 to +0.74)	0.100
Waist circumference (cm) [1]	0 (ref.)	+0.98 (+0.07 to +1.89)	+1.74 (+0.53 to +2.94)	0.005
Waist-to-height ratio (%)[1,3]	0 (ref.)	+0.44 (-0.09 to +0.97)	+1.04 (+0.35 to +1.74)	0.003

[1] Adjusted for age, smoking, diabetes, hypertensive, physical activity, total energy intake, educational level, marital status, and centre.

[2] A waist-to-height ratio =1 is taken as 100%.

Table 5. Multivariable-adjusted[1] differences (95% confidence intervals) in indexes of general obesity and abdominal obesity according to adherence to the residuals of Dietary Inflammatory Index on the 14-item PREDIMED score of adherence to the Mediterranean diet.
The PREDIMED study 2003-2009.

	Quintiles of the Dietary Inflammatory index (*adjusted for Mediterranean diet adherence*)			
	Q1 lowest (ref)	**Q2-Q4 moderate**	**Q5 highest**	**P for trend[1]**
Women				
Body mass index (kg/m^2)[1]	0 (ref.)	+0.14 (-0.19 to +0.48)	+0.36 (-0.08 to +0.80)	0.041
Waist circumference (cm)[1]	0 (ref.)	+1.01 (+0.14 to +2.81)	+1.67 (+0.52 to +2.82)	<0.001
Waist-to-height ratio (%)[1,2]	0 (ref.)	+0.34 (-0.20 to +0.91)	+0.76 (+0.04 to +1.49)	0.007
Men				
Body mass index (kg/m^2)[1]	0 (ref.)	+0.06 (-0.26 to +0.36)	+0.31 (-0.10 to +0.73)	0.057
Waist circumference (cm)[1]	0 (ref.)	+0.77 (-0.14 to +1.69)	+1.46 (+0.24 to +2.68)	0.004
Waist-to-height ratio (%)[1,2]	0 (ref.)	+0.44 (-0.09 to +0.96)	+0.96 (+0.26 to +1.67)	0.005

[1] Adjusted for age, smoking, diabetes status, hypertensive status, physical activity, energy intake, educational level, marital status, and centre.

[2] A waist-to-height ratio =1 is taken as 100%.

Figure 1. Flow chart in the PREDIMED study

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