

## Dietary inflammatory index and anthropometric measures of obesity in a population sample at high cardiovascular risk from the PREDIMED (PREvención con Dieta MEDiterránea) trial

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### Abstract

The dietary inflammatory index (DII) is a new tool to assess the inflammatory potential of the diet. In the present study, we aimed to determine the association between the DII and BMI, waist circumference and waist:height ratio (WHtR). We conducted a cross-sectional study of 7236 participants recruited into the PREvención con DIeta MEDiterránea trial. Information from a validated 137-item FFQ was used to calculate energy, food and nutrient intakes. A fourteen-item dietary screener was used to assess adherence to the Mediterranean diet (MeDiet). Sex-specific multivariable linear regression models were fitted to estimate differences (and 95% CI) in BMI, waist circumference and WHtR across the quintiles of the DII. All nutrient intakes, healthy foods and adherence to the MeDiet were higher in the quintile with the lowest DII score (more anti-inflammatory values) except for intakes of animal protein, saturated fat and monounsaturated fat. Although an inverse association between the DII and total energy was apparent, the DII was associated with higher average BMI, waist circumference and WHtR after adjusting for known risk factors. The adjusted difference in the WHtR for women and men between the highest and

**Abbreviations:** CRP, C-reactive protein; DII, dietary inflammatory index; MeDiet, Mediterranean diet; PREDIMED, PREvención con DIeta MEDiterránea; WHtR, waist:height ratio.

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lowest quintiles of the DII was 1.60% (95% CI 0.87, 2.33) and 1.04% (95% CI 0.35, 1.74), respectively. Pro-inflammatory scores remained associated with obesity after controlling for the effect that adherence to a MeDiet had on inflammation. In conclusion, the present study shows a direct association between the DII and indices of obesity, and supports the hypothesis that diet may have a role in the development of obesity through inflammatory modulation mechanisms.

**Key words: Inflammation: Diet: Obesity: BMI: Waist circumference: Waist:height ratio**

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<sup>(1)</sup>. In 2008, more than 10% of the World's adult population, i.e. about 500 million people, were obese according to the WHO<sup>(2)</sup>. It was estimated that 3.4 million adult deaths worldwide were, in 2010, attributable to obesity or overweight<sup>(1)</sup>. This is a global crisis because 65% of the world's population live in countries where overweight and obesity kill more people than being underweight<sup>(2)</sup>.

Obesity usually is the result of the accumulation of excess body fat, and it is often characterised as a state of low-grade chronic inflammation<sup>(3)</sup>. This obesity-induced inflammation has multi-organ metabolic effects affecting the adipose tissue, liver, muscle, pancreas and brain<sup>(4)</sup>. Metabolic differences exist according to the location of 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<sup>(5)</sup>. In fact, different anthropometric adiposity measures including waist circumference or waist:height ratio (WHtR) are used to assess the role of adiposity in CVD risk<sup>(6,7)</sup>.

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<sup>(8–15)</sup>. Part of the preventive role of healthy dietary patterns, such as the Mediterranean diet (MeDiet), could be attributed to the anti-inflammatory properties of some of their main components<sup>(15–19)</sup>. This anti-inflammatory effect may decrease the low-grade inflammation usually found in obese patients<sup>(20,21)</sup>. However, a MeDiet may also attenuate inflammation in the absence of weight loss<sup>(22)</sup>. A recent hypothesis is that obesity could also be partly the consequence of a previous chronic low-grade inflammation; therefore, a bidirectional association between inflammation and obesity may exist<sup>(23)</sup>.

Consequently, it can be useful to characterise an individual's diet according to its inflammatory properties in order to investigate the inflammatory links between obesity and diet<sup>(24)</sup>. The dietary inflammatory index (DII) is a new tool to assess this inflammatory potential of the diet<sup>(25)</sup>. In the present study, 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 PREención con DIeta MEDiterránea (PREDIMED) trial.

## Methods

### Ethics statement

The protocol was approved by the Research Ethics Committees at all recruiting centres: 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 the Balearic Islands; University of Las Palmas de Gran Canaria; University Hospital of Bellvitge; Hospital Clinic. Participants signed a written informed consent form.

### Study design and participants

The 'PREDIMED' study was a parallel-group, multi-centre, clinical trial that aimed to assess the effects of the traditional MeDiet on the primary prevention of CVD (protocol available at <http://www.predimed.es>). A detailed description of methods and patients has been published elsewhere<sup>(26,27)</sup>. The study was conducted between October 2003 and December 2010 by eleven recruiting centres in Spain.

Eligible participants were men aged 55–80 years and women aged 60–80 years with no previous CVD. At baseline, participants should have a diagnosis of type 2 diabetes mellitus or at least three of the following major cardiovascular risk factors: smoking (more than one cigarette per d during the last month); hypertension (systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg or antihypertensive medication); elevated LDL-cholesterol levels ( $\geq 1600$  mg/l); low HDL-cholesterol levels ( $\leq 400$  mg/l in men or  $\leq 500$  mg/l in women, independently of lipid-lowering therapy); BMI  $\geq 25$  kg/m<sup>2</sup>; family history of premature CHD.

A total of 7447 participants were randomised in a 1:1:1 ratio to a parallel-design intervention trial of dietary advice: (1) a MeDiet supplemented with extra-virgin olive oil; (2) a MeDiet supplemented with nuts; (3) a low-fat diet (control group). Medical conditions and risk factors related to eligibility were collected using a questionnaire during the first screening visit. Participants, with the assistance of trained dietitians, completed an FFQ. This FFQ was adapted from the Willett questionnaire and validated in Spain<sup>(28)</sup>. It includes 137 items plus vitamin/mineral supplements, and specific questions for patterns of alcohol consumption. Energy and nutrient intakes were calculated from Spanish food composition tables<sup>(29)</sup>. Participants also completed the Spanish validated version of the Minnesota physical activity questionnaire<sup>(30)</sup>, and a fourteen-item dietary screener to assess the adherence to the MeDiet<sup>(31)</sup>. PREDIMED dietitians were responsible for the accurate completion of the questionnaires.

For the present study, 133 participants were excluded from the analyses because they reported values for total energy intake outside of the predefined limits ( $< 3347$  kJ ( $< 800$  kcal)/d or  $> 17\,573$  kJ ( $> 4200$  kcal)/d for men;  $< 2510$  kJ ( $< 600$  kcal)/d or  $> 14\,644$  kJ ( $> 3500$  kcal)/d for women). These limits were set in accordance with those recommended by Willett in Nutritional Epidemiology<sup>(32)</sup>. Another seventy-eight participants were excluded

because of lack of information on the FFQ needed to calculate the DII. This study was registered as an International Standard Randomised Controlled Trial, number ISRCTN35739639.

### Dietary inflammatory index

The design and development of the DII has been described elsewhere<sup>(25)</sup>. 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 and including various macronutrients, micronutrients, flavonoids and food items (Fig. 1). These dietary parameters were scored according to whether they increased (+1), decreased (-1) or had no effect (0) on six inflammatory biomarkers (IL-1 $\beta$ , IL-4, IL-6, IL-10, TNF- $\alpha$  and C-reactive protein (CRP)). An overall food parameter-specific inflammatory effect score was calculated and multiplied by a centred 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 was based on actual human consumption in eleven populations from different parts of the world that provided a robust estimate of a mean and standard deviation for each parameter. These values then become the multipliers to express an individual's exposure, relative to the 'standard global mean' as a *z*-score. This was achieved by subtracting the 'standard global mean' from the amount reported, and dividing this value by the standard deviation. To minimise the effect of 'right skewing', this value was then converted to a centred percentile score. The centred percentile score for each food parameter for each individual was multiplied by the respective food parameter effect score that was 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 were then summed to create the overall DII score for every participant in the study. The greater the DII score, the more pro-inflammatory the diet, and more negative values represent more anti-inflammatory diets. The DII score could take on values ranging from 7.98 (maximally pro-inflammatory) to -8.87 (maximally anti-inflammatory)<sup>(25)</sup>.

Construct validation of the DII was performed using data derived from two different sources of dietary intake information, and serum high-sensitivity CRP as the construct validator<sup>(33)</sup>.

### Outcome

Trained and certified PREDIMED nurses performed all baseline anthropometric adiposity measures including weight and height (from which BMI (kg/m<sup>2</sup>) was computed), waist circumference (cm) and WHtR (%) following validated procedures. A waist:height ratio equal to 1 was taken as 100%. Baseline weight was measured using a calibrated balance beam scale with the subjects 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 analyses

Statistical analyses were stratified by sex. Comparisons of quantitative variables across the quintiles of the DII were made using a one-way ANOVA. The compared variables included total energy intake, physical activity and nutrient and food consumption. Intakes of carbohydrate, protein and fat (and fat subtypes) are expressed as a percentage of total energy intake (Table 1). Categorical variables were compared using the Pearson  $\chi^2$  test.

Sex-specific least-squared means of BMI, waist circumference and WHtR were estimated across the quintiles of the DII. Pearson's correlation coefficients (95% CI) between these anthropometric adipose measures and the DII were also calculated.

Sex-specific multiple linear regression models were used to estimate the differences (and 95% CI) in the indices of general obesity and abdominal obesity according to the quintiles of the DII. 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 (metabolic equivalents-min/d), educational level (illiterate/elementary education, secondary education or university), marital status (married, widowed, single or other), total energy intake (kJ/d) and study centre. In addition, tests of linear trend across the successive quintiles of the DII were conducted using the median value for each quintile category as a continuous variable, and after adjusting for the aforementioned confounding variables.

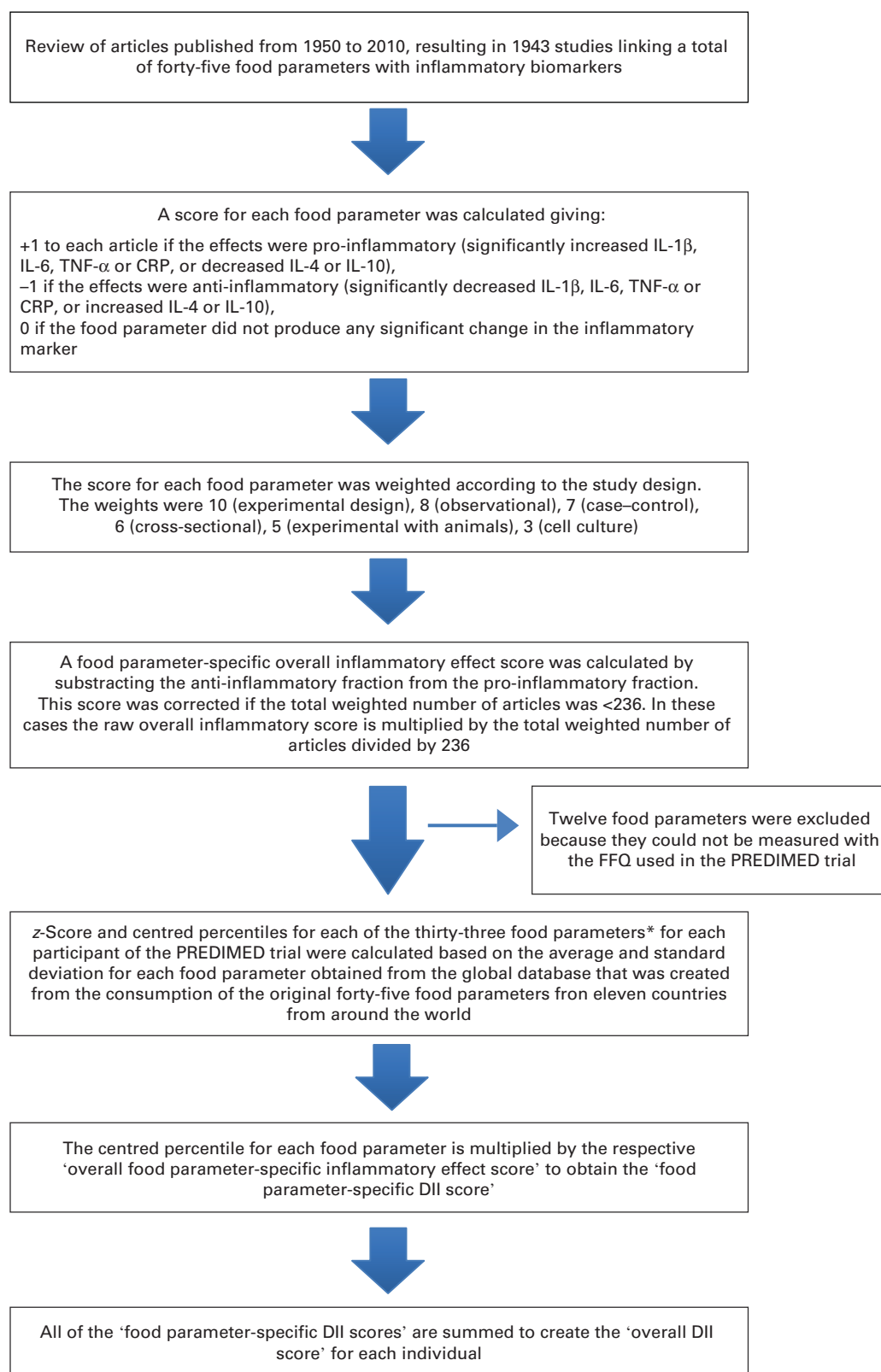
Residuals of the DII were obtained in a linear regression analysis of the association between the DII and a previously validated fourteen-item PREDIMED screener of adherence to the MeDiet<sup>(31)</sup>. These residuals represent the information provided by the DII, which is not explained at all by adherence 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 listed previously (residual model).

All *P* values presented are two-tailed, and differences were considered statistically significant at  $P \leq 0.05$ . All statistical analyses were performed using STATA<sup>®</sup> version 12.0 (Stata Corp).

### Results

Of the 7447 initially randomised subjects in the PREDIMED trial, 7236 were included in the present study. The remaining participants ( $n$  211, 2.8%) were excluded because of incomplete data on their FFQ ( $n$  78) or baseline energy intake outside of the predefined values ( $n$  133). Among the 7236 participants, 57% were women. The mean age of the participants was 68 (SD 5.8) years for women and 66 (SD 6.6) years for men. The median DII score for women was -0.78 (-4.90 to 3.68) and -0.91 (-5.23 to 3.69) for men.

Table 1 shows the main characteristics of the participants according to the categories of the DII score by sex. All differences between the quintiles of this index were statistically



**Fig. 1.** Sequence of steps in creating the dietary inflammatory index in the PREvención con Dieta MEDiterránea (PREDIMED) trial. \*Alcohol,  $\beta$ -carotene, caffeine, carbohydrate, cholesterol, energy, iron, fibre, folic acid, garlic, green/black tea, magnesium, MUFA, *n*-3 fatty acids, *n*-6 fatty acids, niacin, onion, pepper, protein, PUFA, riboflavin, saturated fat, Se, thiamin, total fat, *trans*-fat, vitamin A, vitamin B<sub>12</sub>, vitamin B<sub>6</sub>, vitamin C, vitamin D, vitamin E and Zn. CRP, C-reactive protein; DII, dietary inflammatory index. (A colour version of this figure can be found online at <http://www.journals.cambridge.org/bjn>).



**Table 1.** Description of the main characteristics of the participants according to quintiles (Q) of the dietary inflammatory index (DII) score in the PREvención con Dieta MEDiterránea (PREDIMED) Trial, 2003–9

(Mean values and standard deviations; median values, minimum and maximum values, and percentages)

	Quintiles of the DII											
	Women						Men					
	Q1*	Q2	Q3	Q4	Q5†	P	Q1*	Q2	Q3	Q4	Q5†	P
DII												
Median	-2.6	-1.6	-0.8	0.1	1.5		-2.7	-1.7	-0.9	-0.07	1.3	
Minimum, maximum	-4.9, -2	-2, -1.2	-1.2, -0.3	-0.3, 0.7	0.7, 3.7		-5.2, -2.2	-2.2, -1.4	-1.4, -0.5	-0.5, 0.5	0.5, 3.7	
n	829	829	829	829	829		619	618	618	618	618	
Age (years)						<0.001						0.180
Mean	67	67	68	68	69		66	66	66	66	66	
SD	6	6	6	6	6		6	6	7	7	7	
Family history of early CHD (%)	27	28	27	26	24	0.362	21	18	17	16	15	0.039
Hypertension (%)	84	86	87	87	87	0.359	76	78	79	79	77	0.436
Dyslipidaemia (%)	79	79	76	75	74	0.016	71	66	66	65	63	0.033
Diabetes (%)	44	40	44	44	49	0.011	53	53	53	56	56	0.625
Smoking (%)						0.250						0.176
Current smoker	4	5	6	6	6		24	24	25	28	27	
Former smoker	7	8	8	8	6		48	52	46	46	49	
Total energy intake (kcal/d)						<0.001						<0.001
Mean	2442	2281	2136	1990	1767		2769	2577	2412	2252	2038	
SD	478	449	435	414	400		585	558	511	459	463	
Total energy intake (kJ/d)						<0.001						<0.001
Mean	10 217	9544	8937	8326	7393		11 586	10 782	10 092	9422	8527	
SD	2000	1879	1820	1732	1674		2448	2335	2138	1920	1937	
Physical activity (MET-h/d)						<0.001						<0.001
Mean	3.4	2.9	3.0	2.8	2.4		6.1	5.3	5.1	4.8	4.3	
SD	3.2	2.8	2.8	2.7	2.4		6.0	4.7	4.9	4.4	3.9	
Alcohol intake (g/d)						0.001						<0.001
Mean	3.8	3.2	2.7	3.3	2.7		18.4	15.2	15.5	14.5	13.3	
SD	7.6	6.1	5.1	6.1	5.7		18.1	17.5	19.0	18.2	17.9	
Marital status (%)						0.004						0.043
Married	72	66	66	67	62		92	91	89	89	86	
Widowed	20	27	27	26	30		3	3	3	3	6	
Single/other	8	7	7	7	8		5	6	8	8	8	
Educational level (%)						<0.001						0.066
Primary education or less	80	86	87	86	88		64	66	71	69	67	
Secondary education	13	11	9	11	9		21	23	19	22	22	
Any college	7	3	4	3	3		15	12	11	10	11	

MET, metabolic equivalents.

\* Highest anti-inflammatory values of the DII.

† Highest pro-inflammatory values of the DII.

**Table 2.** Nutrient and food consumption according to quintiles (Q) of the dietary inflammatory index (DII) in the PREvención con Dieta MEDiterránea (PREDIMED) trial, 2003–9 (Mean values and standard deviations)

	Quintiles of the DII													
	Women							Men						
	Q1*		Q2–Q4		Q5†		P	Q1*		Q2–Q4		Q5†		P
	Mean	SD	Mean	SD	Mean	SD		Mean	SD	Mean	SD	Mean	SD	
Carbohydrate intake (%E)	43.4	7.0	42.6	6.7	40.8	6.8	<0.001	41.2	7.0	41.5	7.3	39.2	7.8	<0.001
Protein intake (%E)	17.2	2.6	17.1	2.7	17.2	3.1	0.452	16.0	2.6	15.9	2.7	16.0	2.8	0.542
Vegetal protein intake (%E)	6.1	1.1	5.4	1.0	4.9	1.0	<0.001	5.8	1.1	5.4	1.0	4.9	1.0	<0.001
Animal protein intake (%E)	11.1	2.7	11.6	2.8	12.3	3.2	<0.001	10.2	2.7	10.5	2.8	11.1	2.9	<0.001
Total fat intake (%E)	38.4	6.8	39.4	6.6	40.9	6.9	<0.001	38.2	6.5	38.5	6.7	40.4	7.2	<0.001
Saturated fat (%E)	9.2	2.0	10.0	2.1	10.8	2.4	<0.001	9.3	2.1	9.9	2.2	10.8	2.4	<0.001
Monounsaturated fat (%E)	18.2	4.5	19.7	4.5	21.0	4.8	<0.001	18.3	4.2	19.2	4.4	20.9	4.6	<0.001
Polyunsaturated fat (%E)	7.2	2.2	6.2	2.1	5.6	1.7	<0.001	7.1	2.2	6.2	2.0	5.6	1.6	<0.001
Alcohol consumption (g/d)	3.8	7.4	3.0	5.8	2.8	5.8	0.002	18.5	18.1	15.0	18.2	13.4	17.8	<0.001
Fibre (g/d)	34.6	9.3	24.7	6.1	16.1	3.6	<0.001	34.4	8.8	25.8	6.5	17.1	3.8	<0.001
Vitamin E (mg/d)	12.5	3.7	9.7	3.7	7.0	2.6	<0.001	13.4	4.8	10.5	4.0	7.5	2.5	<0.001
Vitamin C (mg/d)	289	99	201	70	123	42	<0.001	271	98	195	72	122	44	<0.001
Vitamin A (µg/d)	1757	784	1235	640	847	485	<0.001	1870	907	1325	1095	849	500	<0.001
Vegetables (g/d)	483	168	327	107	213	78	<0.001	482	179	324	111	212	80	<0.001
Fruits (g/d)	487	214	379	186	231	118	<0.001	462	231	377	195	237	138	<0.001
Cereals (g/d)	143	78	132	76	111	63	<0.001	175	96	165	95	138	86	<0.001
Potatoes (g/d)	96	58	80	48	62	39	<0.001	102	58	86	46	70	40	<0.001
Legumes (g/d)	25.8	16.8	19.7	12.9	14.8	7.8	<0.001	26.2	15.1	21.5	14.0	16.3	8.4	<0.001
Nuts (g/d)	18.6	18.4	8.2	10.8	3.3	5.6	<0.001	20.6	19.6	10.3	12.9	4.9	8.1	<0.001
Fish and seafoods (g/d)	123.9	60.6	95.2	41.7	74.8	36.5	<0.001	130.7	56.2	101.0	53.8	79.7	39.3	<0.001
Meat and meat products (g/d)	125.0	57.3	127.2	50.9	114.5	49.1	<0.001	144.7	68.8	141.1	58.3	136.0	61.9	0.044
Dairy products (g/d)	435.5	238.4	408.1	221.0	381.4	218.9	<0.001	369.1	222.4	342.4	204.7	319	205.9	<0.001
Mediterranean diet score (0–14)	9.5	1.9	8.6	1.8	7.7	1.7	<0.001	9.8	1.9	8.7	1.9	8.0	1.7	<0.001

%E, percentage of energy.

\*Highest anti-inflammatory values of the DII.

†Highest pro-inflammatory values of the DII.



significant among women, except for the percentage of subjects with a family history of early CHD, the presence of hypertension and smoking status. Among men, differences between the quintiles of the DII according to age, hypertension, diabetes and smoking status were not statistically significant. In both sexes, 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 the lowest DII score (anti-inflammatory dietary pattern), except for intakes of animal protein, saturated fat and monounsaturated fat, both among women and men (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 increased linearly across the successive quintiles of DII scores (from anti-inflammatory to pro-inflammatory levels). A significant positive correlation was observed between these obesity indices 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 in BMI of 0.79 kg/m<sup>2</sup> (95% CI 0.35, 1.23) compared with the lowest quintile (*P* for trend=0.001). This association was not statistically significant for men.

Table 4 further shows that waist circumference and WHtR increased progressively across quintiles 2–4 and 5 compared with the lowest quintile of the DII, both in women and men (*P* for trend being statistically significant in all comparisons).

Table 5 shows the association of the DII with the anthropometric indices, after considering the possible contribution of the MeDiet elements to the anti- or pro-inflammatory capacity of the diet. A higher pro-inflammatory level of the 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 WHtR, when the intermediate DII quintiles (2–4) were compared with the lowest category. On the contrary, the results were not statistically significant among men, except for waist circumference and WHtR, when comparing the highest *v.* the lowest quintile of the residuals of the DII.

**Discussion**

In the present study, we used the dietary inflammatory index (DII) score to assess the capacity of the overall dietary pattern to promote inflammation. Higher values of the DII represent a higher inflammatory potential of the diet. As expected, we observed that the DII was inversely associated with the intake of healthy foods, nutrients and adherence to the MeDiet. A pro-inflammatory DII was directly associated with the indices of general and abdominal obesity, independent

**Table 3.** General obesity and abdominal obesity according to quintiles (Q) of the dietary inflammatory index in the PREvención con Dieta MEDiterránea (PREDIMED) trial, 2003–9 (Adjusted average indices and 95% confidence intervals)

	Quintiles of the dietary inflammatory index									
	Q1 (highest anti-inflammatory)		Q2		Q3		Q4		Q5 (highest pro-inflammatory)	
	Adjusted average indices	95% CI	Adjusted average indices	95% CI	Adjusted average indices	95% CI	Adjusted average indices	95% CI	Adjusted average indices	95% CI
<b>Women (n)</b>	829		829		829		829		829	
Range	-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	
BMI (kg/m <sup>2</sup> )*	29.9	29.6, 30.2	30.3	30.0, 30.5	30.5	30.3, 30.8	30.7	30.4, 31.0	30.8	30.5, 31.1
Waist circumference (cm)*	96.5	95.8, 97.3	97.9	97.2, 98.6	99.0	98.3, 99.7	99.1	98.4, 99.8	99.5	98.8, 100.3
Waist:height ratio (%)*†	62.7	62.2, 63.1	63.6	63.9, 64.8	64.0	63.5, 64.4	64.1	63.7, 64.6	64.3	63.9, 64.8
<b>Men (n)</b>	619		618		618		618		618	
Range	-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	
BMI (kg/m <sup>2</sup> )*	29.2	28.9, 29.5	29.1	28.8, 29.3	29.2	29.0, 29.5	29.5	29.3, 29.8	29.6	29.3, 29.9
Waist circumference (cm)*	102.2	101.4, 103.0	102.4	101.6, 103.2	103.0	102.3, 103.8	104.4	103.7, 105.2	104.2	103.4, 105.0
Waist:height ratio (%)*†	61.2	60.8, 61.7	61.2	60.8, 61.7	61.7	61.3, 62.1	62.3	61.9, 62.7	62.4	61.9, 62.9
										Pearson coefficient (r)
										0.06
										0.05
										0.06
										0.05
										0.08
										0.09
										0.01, 0.08
										0.05, 0.20
										0.06, 0.13

\*Adjusted for age, smoking status, diabetes, hypertension, marital status, educational level, physical activity, total energy intake and study centre.  
† A waist:height ratio equal to 1 was taken as 100%.

**Table 4.** Multivariable-adjusted\* differences in the indices of general obesity and abdominal obesity according to quintiles (Q) of the dietary inflammatory index in the PREvención con Dieta MEDiterránea (PREDIMED) trial, 2003–9

(Adjusted differences and 95% confidence intervals)

	Quintiles of the dietary inflammatory index						
	Q1 (highest anti-inflammatory)		Q2–Q4		Q5 (highest pro-inflammatory)		P for trend
	Adjusted difference	95% CI	Adjusted difference	95% CI	Adjusted difference	95% CI	
<b>Women</b>							
BMI (kg/m <sup>2</sup> )*	0	Reference	0.56	0.23, 0.89	0.79	0.35, 1.23	0.001
Waist circumference (cm)*	0	Reference	2.03	1.17, 2.90	2.79	1.64, 3.93	< 0.001
Waist:height ratio (%)*†	0	Reference	1.19	0.64, 1.74	1.60	0.87, 2.33	< 0.001
<b>Men</b>							
BMI (kg/m <sup>2</sup> )*	0	Reference	0.05	−0.26, 0.37	0.33	−0.08, 0.74	0.100
Waist circumference (cm)*	0	Reference	0.98	0.07, 1.89	1.74	0.53, 2.94	0.005
Waist:height ratio (%)*†	0	Reference	0.44	−0.09, 0.97	1.04	0.35, 1.74	0.003

\* Adjusted for age, smoking status, diabetes, hypertensive, physical activity, total energy intake, educational level, marital status and study centre.

† A waist:height ratio equal to 1 was taken as 100%.

of established risk factors for obesity including total energy intake, age, smoking status, diabetes, hypertension, physical activity, educational level and marital status. These results were consistent for both sexes except for BMI in men. In the residual model (after removing the variability explained by the MeDiet), the association between the inflammatory potential of the diet and higher adiposity indices remained apparent; however, there was a clear association between the DII and the abdominal indices of obesity for women compared with men.

The associations observed between nutrient intake or food consumption and 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<sup>(8–14)</sup>. Specifically, a lower CRP concentration has been associated with a higher intake of fruits and vegetables<sup>(34–36)</sup>, legumes<sup>(37)</sup>, nuts<sup>(38)</sup>, and low-fat dairy consumption<sup>(39)</sup>. Previous studies have also observed associations of specific

nutrients such as total dietary fibre intake<sup>(40)</sup>, moderate alcohol consumption<sup>(41)</sup>, and vitamin E and vitamin C intake<sup>(42)</sup> with lower levels of inflammation markers. On the contrary, animal protein seems to increase the inflammatory status of obese individuals<sup>(43)</sup>.

We also found that a higher consumption of dairy products and meat (or meat products) was less frequent in the highest DII quintile. A systematic review has found no impact of dairy product consumption on biomarkers of inflammation in overweight and obese adults<sup>(44)</sup>. However, only one out of eight trials included in this review defined inflammation as its primary outcome, and there were some methodological limitations in them such as insufficient statistical power<sup>(44)</sup>. Concerning the consumption of meat, a cross-sectional analysis of data from 3690 diabetes-free female participants found that a higher intake of meat protein was associated with higher plasma levels of inflammatory markers<sup>(45)</sup>. However, a cross-sectional study has shown that the association between red meat intake and inflammatory markers was no

**Table 5.** Multivariable-adjusted\* differences in the indices of general obesity and abdominal obesity according to adherence to the residuals of the dietary inflammatory index on the fourteen-item PREvención con Dieta MEDiterránea (PREDIMED) score of adherence to the Mediterranean diet in the PREDIMED trial 2003–9

(Adjusted differences and 95% confidence intervals)

	Quintiles of the dietary inflammatory index (adjusted for adherence to the Mediterranean diet)						
	Q1 (highest anti-inflammatory)		Q2–Q4		Q5 (highest pro-inflammatory)		P for trend*
	Adjusted difference	95% CI	Adjusted difference	95% CI	Adjusted difference	95% CI	
<b>Women</b>							
BMI (kg/m <sup>2</sup> )*	0	Reference	0.14	−0.19, 0.48	0.36	−0.08, 0.80	0.041
Waist circumference (cm)*	0	Reference	1.01	0.14, 2.81	1.67	0.52, 2.82	< 0.001
Waist:height ratio (%)*†	0	Reference	0.34	−0.20, 0.91	0.76	0.04, 1.49	0.007
<b>Men</b>							
BMI (kg/m <sup>2</sup> )*	0	Reference	0.06	−0.26, 0.36	0.31	−0.10, 0.73	0.057
Waist circumference (cm)*	0	Reference	0.77	−0.14, 1.69	1.46	0.24, 2.68	0.004
Waist:height ratio (%)*†	0	Reference	0.44	−0.09, 0.96	0.96	0.26, 1.67	0.005

\* Adjusted for age, smoking status, diabetes status, hypertensive status, physical activity, energy intake, educational level, marital status and study centre.

† A waist:height ratio equal to 1 was taken as 100%.



longer observed after adjustment for BMI<sup>(46)</sup>. Therefore, it is suggested that the association between red meat intake and inflammation is probably mediated by obesity.

In the present study, a higher pro-inflammatory diet was observed in participants with higher BMI, waist circumference and WHtR. This result suggests the hypothesis that a diet-induced inflammation might contribute to increasing or maintaining obesity, especially 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<sup>(4,5)</sup>, but this relationship can be bidirectional (i.e. a pro-inflammatory diet can increase or maintain adiposity), thus creating a vicious cycle, because nutrient excess and some specific foods or nutrients also have been associated with inflammation<sup>(47)</sup>. 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<sup>(48)</sup>. Moreover, dietary patterns (e.g. high-fat/low-fibre or low-fat/high-fibre diet) and single specific nutrients (e.g. dietary fibre) appear to have important consequences in the gut microbiota, which is also involved in low-grade inflammation associated with obesity<sup>(49–52)</sup>.

The residuals of the DII (from a regression model on adherence to the MeDiet) were also associated with obesity indices. These residuals represent the information provided by the DII about the anti- or pro-inflammatory capacity of a diet, which could not be explained by adherence to the MeDiet. The most pro-inflammatory diet showed a stronger association with waist circumference than with other anthropometric indices, both among women and men. These results are in close agreement with previous findings, which showed that central adiposity-related indices are more strongly correlated with plasma pro-inflammatory markers than indices assessing total adiposity in healthy young adults<sup>(5)</sup>. Moreover, abdominal adiposity has been associated with elevated CRP levels, independent of BMI in older adults<sup>(55)</sup>. As a consequence, the present results reinforce the usefulness of the DII to assess the inflammatory properties of a diet, and the association between inflammation and central obesity indices.

The present results are also consistent with those of studies reporting a stronger association between CRP and BMI in women than in men<sup>(54,55)</sup>. This between-sex difference could be partially explained by a greater accumulation of subcutaneous fat in women than in men, and higher lean mass in men<sup>(55)</sup>. Sex differences in the metabolic activity of adipose tissue, as well as in the association between leptin and CRP, may also explain these differences<sup>(56,57)</sup>.

The strengths of the present study include the following: large sample size; use of a validated instrument to measure the inflammatory potential of the diet; adjustment for a large number of factors associated with obesity; detailed measures of obesity indices; validation of all assessment instruments including the MeDiet screener, the FFQ and the physical activity questionnaire. The present study also has its limitations, the main one being the cross-sectional nature of our analyses. It is, therefore, unclear whether obese

individuals are more likely to choose pro-inflammatory diets, or if pro-inflammatory diets contribute to promoting or maintaining obesity. Both weight reduction and an overall 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<sup>(58)</sup>. 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 the existing knowledge of the inflammatory factors involved in obesity. However, the DII has been found to be associated with the following factors: inflammatory cytokines including CRP and IL-6<sup>(33,59,60)</sup>; glucose intolerance component of the metabolic syndrome<sup>(59)</sup>; odds of asthma and of reduced FEV<sub>1</sub> (forced expiratory volume in 1 s) in an Australian population<sup>(60)</sup>. It has also been reportedly associated with a higher risk of colorectal cancer<sup>(61)</sup>, prostate cancer<sup>(62)</sup> and pancreatic cancer<sup>(63)</sup>.

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

### Supplementary material

To view supplementary material for this article, please visit <http://dx.doi.org/10.1017/S0007114514004401>

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