MACRONUTRIENT INTAKE AND METABOLIC SYNDROME AMONG HIGH CARDIOVASCULAR RISK SUBJECTS

Running title: Macronutrient intake and risk of metabolic syndrome

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Background: The role of macronutrient intake on metabolic syndrome is controversial. Our aim was to assess the relationships between macronutrient intake and the risk of the metabolic syndrome (MS), among patients at high cardiovascular risk.

Methods: In this cross-sectional study, 967 high-risk men and women (55-80 years) were assessed. Two definitions for MS: the National Cholesterol Education Program Adult Treatment Panel III (ATP3) and the International Diabetes Federation (IDF) were applied. A 137-item validated food frequency questionnaire was used. We adjusted the estimates for potential confounders, using logistic regression.

Results: Using ATP3 criteria, an inverse association was found for fibre and PUFA (polyunsaturated fatty acids) intake with Odds Ratios (OR) of 0.55 (95% CI: 0.35-0.86) and 0.60 (95% CI: 0.39-0.94) respectively, for the fifth versus the first quintile.

Using IDF criteria the inverse association between fibre intake and MS was maintained, and a direct association between carbohydrate intake and MS was found OR=1.71 (95% CI: 1.05-2.79) for the highest versus the lowest quintile.

Conclusions: A diet rich in fibre and PUFA is associated with reduced risk of metabolic syndrome among high cardiovascular risk subjects.

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1 Introduction:

2 The metabolic syndrome (MS) is a cluster of interrelated risk factors that increased risk

3 of cardiovascular disease and diabetes. that includes central obesity,

4 hypertriglyceridemia, reduced HDL-cholesterol, high blood pressure, and raised fasting

5 plasma glucose [1, 2]

6 The prevalence of MS differs depending on the criteria used [3, 4]. Male gender,

7 obesity, diabetes mellitus (DM), a lower educational level and high blood pressure are

8 all well established determinants for MS [5, 6]. However, the role of the dietary

9 composition has been less studied. In particular, the information regarding the role of

10 macronutrient intake has shown conflicting results [5, 7]. In a large cross-sectional

11 study in British civil servants, a higher intake of carbohydrate and polyunsaturated fatty

12 acids (PUFA) was linked to benefits with regard to central obesity, fasting triglycerides

13 and LDL cholesterol. In contrast, higher carbohydrate intake was linked with lower

14 HDL cholesterol, increase postprandial glucose and insulin levels in normoglycaemics

15 subjects [8]. Another cross-sectional study evaluated the association between

16 macronutrient intake and the prevalence of MS in a sample of 1626 subjects (mean age

17 52 y) with at least one cardiovascular risk factor, and reported an inverse relationship

18 between carbohydrate intake and the prevalence of the MS [9].

19 Taking into account these controversial results, the aim of our study was to evaluate the

20 role of macronutrients in the risk of the MS in a population of subjects at high risk of

21 cardiovascular disease (CVD).

22 Subjects and Methods:

23 The study design is a cross-sectional study. Nine hundred sixty seven at high

24 cardiovascular risk and community-dwelling subjects were selected (343 men and 533

women); mean age 67.6 years, who were attending seven primary health care centres of Pamplona (city in a North region of Spain). The selection was made from March 2004 to April 2005 using computerized data store of the clinical records of these patients. The main inclusion criteria were: type 2 diabetes mellitus (DM) or three or more cardiovascular risk factors: current smoking, hypertension (blood pressure ≥ 140/90 mm Hg or treatment with antihypertensive drugs), high LDL-cholesterol level ≥160mg/dL or low HDL-cholesterol (< 40 mg/dl), or treatment with hipolipidemic drugs, body mass index (BMI) ≥ 25 kg/m^2. Exclusion criteria were previous history of cardiovascular disease, severe chronic illness, and drug or alcohol addiction. All pre-selected subjects were contacted by their physicians who informed them about nature and purpose of the study. The patients who agreed to participate gave their written consent; the proportion of selected candidates who entered the study was 54.9% (Figure 1). The protocol was approved by the ethics committee of the Clinica Universitaria of Navarra.

MS diagnosis was based on the ATP3 criteria (National Cholesterol Education Program Adult Treatment Panel III) and the IDF criteria (International Diabetes Federation).The ATP3 definition included: waist circumference (men >102 cm women >88 cm), triglycerides (TAG) ≥150 mg/dL, low HDL-cholesterol (<40 mg/dL men; <50 mg/dL women), blood pressure ≥130/≥85 mmHg, fasting glucose ≥110 mg/dL. Diagnosis of the MS is made when 3 or more of the risk determinants shown above are present. [10]. The IDF criteria consist in abdominal obesity (waist circumference ≥94 cm for men and ≥80 cm for women or BMI ≥30 kg/m^2) and two or more of the following requirements: TAG ≥150 mg/dl; HDL-cholesterol <40 mg/dL in men; <50 mg/dL in women; blood pressure ≥ 130 mmHg/≥ 85 mmHg, fasting glucose ≥100 mg/dl. Subjects receiving pharmacological treatment for high blood pressure, hypertriglyceridemia, low HDL-cholesterol or diabetes are considered as positive for the respective components [1].

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2 Dietary assessment

3 Food intake was assessed by a trained dietician, using a 137-item semi-quantitative food

4 frequency questionnaire, previously validated in Spain [11]. Nutrient intake was

5 calculated as frequency of consumption multiplied by nutrient composition of specified

6 portion size. Nutrient composition was estimated from Spanish food composition tables

7 [12, 13].

8 Measurements

9 Weight and height were measured using calibrated scales and a wall-mounted

10 stadiometer, respectively; waist circumference was measured at the midline

11 between the last rib and the iliac crest. Blood pressure (average of three

12 measurements) was recorded using a validated semiautomatic oscillometer (Omron

13 HEM-705CP, Hoofddorp, Netherlands). A fasting venous blood sample was drawn by

14 a trained nurse. Blood plasma glucose was determined by the glucose– oxidase method;

15 cholesterol and triglyceride

16 levels by enzymatic procedures; HDL cholesterol level was measured after precipitation with

17 phosphotungstic acid and magnesium chloride.

18 Covariates

19 Smoking status was categorized into never, current or past smoking. Educational

20 status was categorized into illiterate, primary, secondary or higher. Physical activity

21 was assessed using the validated Spanish version of the Minnesota questionnaire

22 [14, 15]. The metabolic rate was derived from the information on sixty-seven different

23 activities and their energy expenditure, and expressed in kJ/day.

24 Statistical analysis.

25 Nutrient intakes (g/day) were examined as individual variables adjusted for total energy

intake. Energy-adjusted nutrients intakes were calculated as the residuals from regression models with total intake of each nutrient as the dependent variable and total caloric intake as the independent variable [16].

We run several logistic regression models using the MS as the outcome, and four dummy variables corresponding to the four upper quintiles of intake of each nutrient (the lowest quintile was the reference category) as independent variables. We did the same procedure to analyze quintiles of different ratios of fat (%CHO/fat; MUFA/SFA, MUFA/PUFA and MUFA+PUFA/SFA) and risk of MS.

We adjusted for potential confounders: age, sex, total energy intake, DM, smoking, alcohol intake, educational level, marital status, and physical activity. We have not adjusted for BMI or waist circumference because BMI is not a reliable measure of obesity in the elderly, due to changes in height with age and to the different ratio of lean to fat mass compared to younger adults [17]. Since waist circumference is included in the definition of the outcome, adjusting for it would be redundant.

We calculated the "p for linear trend," taking the median of each quintile of intake, this new variable was modelled as a continuous variable. All presented "p" values are two tailed. A "p" value <0.05 was considered "statistically significant". All tests were performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA).

Results

The clinical, laboratory and nutrient intake characteristics of participants are presented in table 1, according to presence of MS for each definition used. 55.1% were female, mean age of the group was 67.6 ±6.2 years (mean ±SD). As expected, participants with the MS showed higher values for waist circumference, weight, BMI, triglyceride levels, fasting plasma glucose, blood pressure, but also (and unexpectedly) for physical activity

with respect to those not meeting the criteria for the MS, however this difference was not significant. Additionally, the percentage of former smokers and the percentage of DM were also higher in the MS group (Table 1).

Statistically significant differences were observed for total energy intake, simple sugar intake, dietary glicemic load and percentage of dietary protein, between subjects with and without MS, regardless of the criteria used to define it. In addition we observed differences in PUFA and fibre intake for subjects with SM according ATP3 criteria.

According to the ATP3 criteria, MS prevalence was 42.4% for men and 47.5% for women.. On the other hand, using the IDF definition we found that the MS prevalence was 63.6%, without differences between men and women. The most prevalent components of MS over total sample were hypertension, central obesity and elevated fasting glucose for both definitions. These findings are presented as percentages of total sample in table 2.

Tables 3 show the adjusted-OR by metabolic syndrome according to quintiles of macronutrient intake and total-fat, and table 4 show adjusted- OR for quintiles of fatty acids for each definition.

According to ATP3 criteria, after adjusting for confounding we found a lower risk for MS in the highest quintile of fibre intake with OR= 0.55 (95% CI: 0.35-0.86) with respect to lowest quintile, (p for linear trend=0.016). We also found that PUFA intake was inversely associated with the prevalence of MS, with an adjusted OR = 0.60 (95% CI: 0.39-0.94) for the fifth vs. the first quintile (p for linear trend =0.012). Finally, when analyzed the different ratios of fat only ratio MUFA/PUFA showed a direct association with MS, with an adjusted OR of 1.99 (95% CI: 1.28-3.07) for the fifth vs. the first quintile (p for linear trend =0.006).

When we defined MS according to IDF criteria, we found that carbohydrate intake exhibited an adjusted OR=1.71 (95% CI: 1.05-2.79) for the highest vs. the lowest quintile of intake, (p for linear trend =0.038) whereas total fat intake was associated with a lower risk for MS; however the association was not statistically significant OR= 0.65 (95% CI: 0.04-1.02). When we study the OR for simple sugar, polysaccharides, glycemic load and glycemic index and MS, we only found high risk by polysaccharides intake OR=1.56 (95% CI:1.00-2.45) p for linear trend 0.038 for the highest vs lowest quintile of intake.

Dietary fibre maintained the inverse association with adjusted OR= 0.60 (95% CI: 0.38-0.95) for the fifth versus the first quintile, p for linear trend = 0.012 (Table 4). We did not observe any relationship, statistically significant, between the different ratios of fat and metabolic syndrome.

Discussion

There remains uncertainty about the aetiology and diagnostic criteria of MS. Many studies has been published comparing those criterias proposed by the IDF and ATPIII, among others. In this study, we have used both criteria in order to expand the scope of our findings.

According to the ATP3 definition, the prevalence of the MS in our study population was 45.2%, being slightly higher in women than in men. With the IDF criteria we found that the prevalence of the MS was 63.4%, without differences between men and women. The prevalence found according to IDF criteria was higher than that reported in series with similar demographical characteristics. The study PREVENCAT (Control of cardiovascular risk factors in primary care in Spain) in a sample of 2649 patients, average age 64 yr, with hypertension, DM or dyslipidemia found a 50.6% prevalence of

MS according to IDF criteria [18]. The prevalence of MS in the general Spanish population is uncertain. Small studies in Canarias and Segovia have shown prevalence estimates between 24.4% and 17% respectively [19, 20]. A recently published study with a random sample (n=1433) of the adult population of Madrid (mean age 53 y) found a prevalence of 24.6% and 30.9%, using the ATP3 or the IDF definitions, respectively [21]. Furthermore a study on the general population of Navarra has shown prevalence for MS of 22.1% for men and 17.2% for women using ATP3 criteria (22)

High blood pressure and obesity were the most common conditions found in our sample independently of the diagnostic criteria used. This finding is consistent with a previous meta-analysis of cardiovascular risk factors in Spain showing that hypertension was the most common risk factor [23] and PREVENCAT study where, hypertension was also the most prevalent risk factor followed by DM and obesity [18].

The differences found in the prevalence according to the criteria used were explained because the definition of IDF for both abdominal obesity and fasting glucose has a lower threshold [1] therefore includes more subjects.

Remarkably in accordance to our results about a detrimental role of CHO intake, the NHANES III survey (Third National Health and Nutrition Examination Survey) using ATP3 criteria, reported that a lower and moderate consumption of CHO was associated with a lower prevalence of MS in men but not in women in [24]. Related to this finding, it had been shown that a high CHO intake was associated with lower HDL cholesterol levels and higher concentrations of triglycerides. Similar results were observed by Knopp in an intervention study with diets with different content in CHO and fat; those with the higher consumption of CHO exhibited a 39% increase in their triglyceride levels [25]. However, a recently published study based on a model of substitution of nutrients found controversial data compared with the previous results, those subjects

1   with higher CHO and lower fat intake would exhibit the lower risk for the onset of the

2   MS [9]. Nevertheless, methodological issues may confound these findings: total energy

3   intake was lower than expected for this population and there was no adjustment for

4   dietary fibre intake. In the OMNIHEART study, replacement of CHO by proteins or

5   MUFA led to further improvements in cardiovascular risk factors [26].

6   We only observed a significant inverse association between PUFA intake and the

7   prevalence of MS when using ATP3 criteria. Previous studies have found that dietary n-

8   3 PUFA may contribute to reduce insulin resistance in muscle, improve the plasma

9   lipoprotein profile decreasing triacylglycerol concentrations and increase anti-

10 inflammatory and antithrombotic responses [27, 28]; there is also evidence that they

11 could reduce plasma glucose and thereby improve insulin sensitivity [29]

12 Briefly, a higher intake of PUFA over SFA may improve the control of blood pressure,

13 endothelial dysfunction, coagulation factors and insulin resistance and could also reduce

14 the risk of the MS [30].

15 A review about effects of MUFA suggests that a MUFA-enriched diet reduces the need

16 for insulin, reduce glycaemia in diabetics and could also have an effect in reducing

17 blood pressure [27].The insulin secretion is directly related with the MUFA intake,

18 independently of the level of insulin resistance (IR) [31]; there is also laboratory and

19 epidemiological evidence to suggest that MUFA, and particularly olive oil, could be

20 components of a diet with some potential effect for the prevention of hypertension [32].

21 In our study we observed no relationship between MUFA intake and risk of MS.

22 However, we noted that a larger MUFA/PUFA ratio increased the risk of MS. These

23 observations could be explained by the different consumed sources of MUFA in our

24 participants. The main source of MUFA was olive oil, although MUFA from meat was

25 also important, on average 23 percent of MUFA intake in our sample came from

1   meat/meat products. Therefore, the beneficial effects that could be ascribed to MUFA

2   consumption may be offset by the increase in the consumption of meat. In this sense,

3   the type of fat, rather than total fat intake is an emerging determinant associated with the

4   development of MS [30].

5   Respect to fibre, in our study was associated with lower risk of MS. Available evidence

6   supports the notion that diets supplemented with fibre may improve lipid profiles,

7   glucose tolerance and the intestinal function [33]. Dietary fibre exerts clinical benefits

8   on all abnormalities of the MS. It has been shown that a fibre-rich diet reduces body

9   weight gain [34], dyslipidemia and blood pressure and improves insulin sensitivity [35].

10 A pooled analysis from several large cohort studies showed that dietary fibre from fruits

11 and cereals was inversely associated with the risk of coronary disease [34, 36].

12 The mechanisms involved in the beneficial effect of fibre intake remain largely

13 unexplained. It has been proposed that it accounts for a reduction in glucose absorption

14 inducing a reduction in the inflammatory mediators associated with the hyperglycaemia.

15 It has also been suggested that dietary fibre could reduce oxidative stress and

16 inflammation mediators release when analyzed as a component of the Mediterranean

17 diet [37-42]. A study in the Framingham Offspring cohort found that after adjustment

18 for a wide array of confounding factors, the fibre from cereals was inversely related

19 with the prevalence of the MS. These data suggest a greater role for cereal fibre rather

20 than other fibre sources in the development of IR [40]. Considering the types and

21 numerous sources of dietary fibres, it is difficult to establish which mechanisms

22 predominate in the beneficial effects exerted by dietary fibre on MS. Both types of fibre,

23 regardless of its solubility, are beneficial and probably complementary to reduce the risk

24 of cardiovascular disease and DM [35]. Another limitation of the studies about fibre

25 intake is the difficulty to separate the effects of fibre respect to those derived from trace

elements such as magnesium, or from other dietary components such as PUFA which are highly correlated with fibre intake [43, 44]. This limitation may be also present in our analysis.

Our study has limitations because of its cross-sectional design, and this precludes establishing a cause-effect relationship (because inverse causality bias cannot be ruled out). The sample is not representative of the general population because it was selected on the basis of the existence of various risk factors for CVD, inducing low between-subjects variability. Perhaps our results are not valid for the general population, but described the effect of macronutrient intake at high cardiovascular risk patients with metabolic syndrome.. Our data about food intake were obtained using food frequency questionnaires with the limitations of these instruments, although they are the tool most used in nutritional epidemiology [16]. A trained dietician conducted interviews to collect the food frequency data; this approach (as compared with self-administration) could reduce the potential misclassification biases because this information is closer to the true consumption. In spite of multivariate adjustments we cannot exclude totally the possibility of residual confounding.

Based on available data about the influence of diet on inflammation, the best dietary approach for the prevention of metabolic disorders, associated with obesity and the MS, should include a high provision of whole-grain cereals, nuts, fruits, vegetables, fish, olive oil, moderate wine consumption and a low proportion of beef, sausage and trans fatty acids [38-41].

The association of macronutrient intake and MS is different depending of diagnosis criteria used, probably because some of the cut-off points are different between two definitions, IDF criteria could be allow an earlier detection of those subjects affected by MS and probably allows better approach to the impact of macronutrient intake on

metabolic syndrome.

The contribution of our study was to analyzed the effect of macronutrient intake on the cluster of risk factors (hypertension, hypertrigliceridemia, impaired glucose tolerance, low HDL, central obesity) called metabolic syndrome.

The MS is a major risk factor for CVD and diabetes, well-designed dietary recommendations are needed to reduce its prevalence in the population. Our results suggest the use of diet with a high provision of fibre and PUFA as potential strategies for the prevention of this disorder among high risk patients. However, larger prospective studies with better controlled diet are needed to establish nutritional recommendations in order to reduce the risk of MS.

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45. Figure 1: Flow diagram of subject selection process.

Table 1: Baseline characteristics of the sample categorized according to diagnostic criteria by ATP3 and IDF described in the text. The continuous variables are represented by mean ± (standard deviation) and the categorical variables are represented by the number of subjects (percentage).

Baseline Characteristics	Total cohort	Metabolic Syndrome (ATP3 criteria)			Metabolic Syndrome (IDF criteria)		
		No	Yes	p value	No	Yes	p value
Subjects (%)	967	530 (54.8%)	437 (45.2%)	-	352 (36.4%)	615 (63.6%)	-
Women (%)	533 (55.1 %)	280 (52.5%)	253 (47.5%)	0.998	194 (36.4%)	339 (63.6%)	0.115
Diabetes Mellitus (%)	354 (36.6%)	127 (24%)	227 (51.9%)	<0.001	66 (18.1%)	288 (47.8%)	<0.001
Age (year)	67.6 (6.2)	67.5 (6.1)	67.7 (6.2)	0.506	67.5 (6.0)	67.7 (6.3)	0.664
Weight (kg)	75.7 (11.5)	73.1 (10.7)	78.8 (11.5)	<0.001	72.2 (10.7)	77.7 (11.4)	<0.001
Height (m)	1.6 (0.1)	1.6 (0.1)	1.6 (0.1)	0.157	1.6 (0.1)	1.6 (0.1)	0.632
Body mass index (kg/m^2)^a	29.5 (3.5)	28.3 (3.2)	30.9 (3.4)	<0.001	28.2 (3.3)	30.3 (3.4)	<0.001
Waist circumference (cm)	96.2 (10.2)	92.5 (9.5)	100.6 (9.3)	<0.001	91.5 (10.0)	98.9 (9.4)	<0.001
Total Cholesterol (mg/dl)	217.9 (36.9)	220.6 (36.1)	214.6 (37.8)	0.013	222.5 (35.6)	215.3 (37.5)	0.003
HDL_cholesterol (mg/dl)	55.1 (13.6)	59.8 (13.4)	49.4 (11.5)	<0.001	61.2 (13.3)	51.6 (12.5)	<0.001
Triglycerides (mg/dl)	139.1 (72.1)	108 (40.8)	176.8 (83.1)	<0.001	104.2 (38.9)	159.1 (78.8)	<0.001
Blood pressure:							
Systolic (mmHg)	155.7 (20.9)	152.4 (21.1)	159.7 (20.0)	<0.001	151.2 (21.3)	158.3 (20.3)	<0.001
Diastolic (mmHg)	86.5 (10.9)	85.2 (10.8)	88.0 (10.9)	<0.001	85.1 (11)	87.3 (10.8)	0.003
Fasting glucose (mg/dl)	117.5 (41)	103.5 (27.5)	134.8 (48.1)	<0.001	100.6 (31.5)	127.4 (43.0)	<0.001
Antihypertensive drugs:							
Beta blockers	113 (11.5%)	51 (9.6%)	62 (14.2%)	0.018	28 (8%)	85 (13.8%)	0.039
ACE inhibitors	264 (27.3%)	134 (25.3%)	129 (29.5%)	0.295	88 (25%)	176 (28.6%)	0.372
Diuretics	233 (24.1%)	123 (23.2%)	110 (25.2%)	0.401	79 (22.4%)	154 (25%)	0.250
Other (a)	354 (36.6%)	180 (34%)	174 (39.8%)	0.045	115 (32.7%)	249 (38.4%)	0.021
Lipid lowering drugs							
Statins	361 (37.3%)	200 (37.7%)	160 (36.6%)	0.459	124 (35.2%)	237 (38.6%)	0.615
Fibrates	25 (2.6%)	11 (2.1%)	14 (3.2%)	0.966	9 (2.6%)	16 (2.6%)	0.271
Other (b)	7 (0.7%)	5 (0.9%)	2 (0.5%)	0.053	5 (1.4%)	2 (0.3%)	0.467
Physical activity (kcal/day)	276 (207)	273 (195)	279 (221)	0.620	261 (189)	284 (216)	0.086
Smoking				0.445			0.842
Non-smoking	592 (61.2%)	322 (60.8%)	270 (61.8%)		218 (61.9%)	374 (60.8%)	
Smoker	167 (17.3%)	95 (17.9%)	72 (16.5%)		68 (19.3%)	99 (16.1%)	
Former smoker	208 (21.5%)	113 (21.3%)	95 (21.7%)		66 (18.8%)	142 (23.1%)	

Energy intake (Kcal/day)	2246 (539)	2302 (536)	2178 (536)	<0.001	2292 (525)	2219 (546)	0.042
Nutrients[b]						
Carbohydrate (g/day)	226 (40)	229 (40)	222 (40)	0.016	229 (40)	225 (40)	0.127
Simple sugar (g/day)	120 (27)	122 (27)	116 (25)	<0.001	123 (27)	118 (26)	0.003
Complex sugar (g/day)	106 (30)	106 (31)	106 (29)	0.971	105 (31)	106 (30)	0.311
Dietary glicemic load[c]	125 (46)	130 (46)	120 (43)	<0.001	130 (46)	122 (45)	0.012
Dietary glicemic index[d]	68 (6)	55 (6)	54 (6)	0.395	54 (5)	54 (6)	0.237
Protein (g/day)	87 (13)	87 (13)	88 (12)	0.130	86 (19)	88 (12)	0.014
Fat (g/day)	100 (16)	100 (17)	100 (15)	0.903	100 (17)	100 (163)	0.975
MUFA (g/day)	51 (10)	51 (10)	51 (9)	0.622	51 (10)	51 (10)	0.966
PUFA (g/day)	15 (5)	15 (5)	14 (5)	0.044	15 (5)	15 (5)	0.381
SFA (g/day)	24 (5)	24 (8)	24 (8)	0.280	24 (5)	24 (5)	0.174
Fibre (g/day)	22 (5)	23 (6)	21 (5)	0.027	23 (6)	22 (5)	0.060
Alcohol (g/day)	12 (18)	12 (17)	11 (19)	0.370	11 (17)	12 (19)	0.485
% Carbohydrate	40 (6)	40 (6)	39 (6)	0.052	40 (6)	39 (6)	0.057
% Protein	16 (3)	15 (2)	16 (2)	<0.001	15 (5)	16 (3)	<0.001
% Total fat	40 (6)	40 (6)	40 (5)	0.285	40 (6)	40 (6)	0.847

[a] Body mass index was calculated divided weight by height square.
[b] All dietary variables were adjusted for total energy intake by using the residual method.
[c] Dietary glicemic load is the amount of carbohydrate in a serving of food multiplied by that food's glycemic index (Using glucose as a reference).
[d] Dietary glicemic index is defined as glicemic load multiplied for 100 and divided by the total amount of carbohydrates.
MUFA: monounsaturated fatty acids; PUFA polyunsaturated fatty acids; SFA saturated fatty acids.

Table 2: Metabolic syndrome components, stratified by sex, according to IDF and ATP3 criteria.

Metabolic Syndrome Components	Total (n=967)		Men (n=434)		Women (n=533)	
	ATP3	IDF	ATP3	IDF	ATP3	IDF
Central Obesity[1] (%)	59.6	87.9	49.8	83.4	67.5	91.6
Hypertriglyceridaemia[2] (%)	33.6	33.6	34.3	34.3	33.0	33.0
Low HDL cholesterol[3] (%)	21.7	21.7	17.5	17.5	25.1	25.1
High blood pressure[4] (%)	92.0	95.9	91.0	94.2	92.9	97.2
High plasma glucose[5] (%)	41.3	57.0	44.5	63.1	49.8	52.0

[1] Waist circumference: $\geq$ 94 cm in men, $\geq$ 80 cm in women, or BMI $\geq$ 30 (IDF criteria); $\geq$ 102 cm in men, $\geq$ 88 cm in women (ATP3 criteria)

[2] Triglycerides: $\geq$ 150 mg/dL (IDF and ATP3 criteria)

[3] HDL-Cholesterol: < 40 mg/dL in men, < 50 mg/dL in women (IDF and ATP3 criteria).

[4] Systolic blood pressure $\geq$ 130 mmHg or diastolic blood pressure $\geq$ 85 mmHg or pharmacological treatment for high blood pressure (IDF criteria). Systolic blood pressure $\geq$ 130 and/or diastolic blood pressure $\geq$ 85 mmHg (ATP3 criteria).

[5] Plasma glucose: $\geq$ 100 mg/dL or pharmacological treatment for diabetes (IDF criteria). Plasma glucose $\geq$ 110 mg/dL (ATP3 criteria).

Table 3: Metabolic syndrome risk (Odds ratio and their 95% confidence intervals) across quintiles of macronutrient intake and fibre, according to ATP3 and IDF criteria.

Quintiles of nutrient intake (g/day)	N	Cases MS ATP3/IDF	Adjusted[1] OR (95% CI) ATP3	Adjusted[1] OR (95% CI) IDF
Carbohydrates				
<192	193	86/126	1 (Reference)	1 (Reference)
192-214	194	99/130	1.39 (0.90-2.15)	1.23 (0.77-1.95)
214-233	194	90/122	1.32 (0.85-2.05)	1.21 (0.76-1.93)
233-259	194	80/115	1.11 (0.70-1.75)	1.17 (0.73-1.87)
>259	192	82/122	1.50 (0.94-2.38)	1.71 (1.05-2.79)
Linear trend			p=0.211	p=0.038
Proteins				
< 77.5	193	75/108	1 (Reference)	1 (Reference)
77.5– 84	194	85/124	1.24 (0.81-1.91)	1.44 (0.93-2.23)
84 – 90.5	194	89/128	1.14 (0.73-1.77)	1.33 (0.85-2.08)
90.5–97.5	194	90/121	1.38 (0.89-2.14)	1.28 (0.82-1.99)
> 97.5	192	98/134	1.37 (0.87-2.15)	1.51 (0.95-2.40)
Linear trend			p=0.152	p=0.161
Total fat				
< 87	193	85/122	1 (Reference)	1 (Reference)
87 - 96	194	87/127	0.91 (0.59-1.39)	1.02 (0.66-1.59)
96-103	194	87/122	0.80 (0.52-1.25)	0.81 (0.51-1.27)
103- 113	194	91/131	0.86 (0.56-1.34)	0.98 (0.62-1.55)
>113	192	87/113	0.80 (0.51-1.25)	0.63 (0.40-1.00)
Linear trend			p=0.363	p=0.071
Fibre				
< 18	193	95/127	1 (Reference)	1 (Reference)
18 - 20	194	93/135	0.85 (0.55-1.30)	1.09 (0.70-1.74)
20 - 23	194	82/115	0.64 (0.41-0.99)	0.63 (0.40-0.98)
23 - 26	194	89/124	0.83 (0.54-1.28)	0.90 (0.57-1.41)
> 26	192	78/114	0.55 (0.35-0.86)	0.60 (0.38-0.94)
Linear trend			p=0.016	p=0.018

[1] Adjusted for age, sex, total energy intake, type 2 diabetes mellitus, smoking, alcohol intake, education level, marital status and physical activity.

Table 4: Metabolic syndrome risk (Odds ratio and their 95% confidence intervals) across quintiles of fatty acids fraction and lipid ratio according to ATP3 and IDF criteria.

Fatty acids intake (g/day)	n	Cases MS ATP3/IDF	Adjusted OR (CI 95%)[1] ATP3	Adjusted OR (CI 95%)[1] IDF
MUFA				
≤43	193	88/130	1 (Reference)	1 (Reference)
43-49	194	77/114	0.75 (0.49-1.15)	0.65 (0.42-1.01)
49-54	194	87/119	0.89 (0.58-1.37)	0.72 (0.46-1.13)
54-59	194	88/127	0.84 (0.55-1.30)	0.79 (0.50-1.25)
>59	192	97/125	1.04 (0.67-1.60)	0.77 (0.49-1.22)
Linear trend			p=0.709	p=0.455
PUFA				
≤11	193	84/125	1 (Reference)	1 (Reference)
11-13	194	97/129	1.09 (0.70-1.67)	0.91 (0.58-1.44)
13-15	194	95/127	0.99 (0.63-1.54)	0.87 (0.54-1.38)
15-19	194	91/119	1.02 (0.66-1.58)	0.79 (0.50-1.23)
>19	192	70/115	0.60 (0.39-0.94)	0.71 (0.46-1.11)
Linear trend			p=0.012	p=0.114
SFA				
≤20	193	77/118	1 (Reference)	1 (Reference)
20-23	194	90/122	1.11 (0.72-1.72)	0.96 (0.63-1.50)
23-25	194	88/124	1.12 (0.73-1.73)	1.04 (0.67-1.62)
25-28	194	83/124	0.89 (0.57-1.38)	0.93 (0.59-1.45)
>28	192	99/127	1.36 (0.87-2.11)	1.06 (0.67-1.67)
Linear trend			p=0.291	p=0.823

[1] Adjusted for age, sex, total energy intake, type 2 diabetes mellitus, smoking, alcohol intake, education level, marital status and physical activity.

MUFA: monounsaturated fatty acids; PUFA polyunsaturated fatty acids; SFA saturated fatty acids