Lipid, protein and carbohydrate intake in relation to body mass index: an Italian study

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Abstract

Objective: To analyse the association between macronutrient intake and body mass index (BMI).
Design: A series of hospital-based case–control studies.
Settings: Selected teaching and general hospitals in several Italian regions.
Subjects: A total of 6619 subjects from the comparison groups of the case–control studies were included in the analysis.
Methods: We obtained data from a validated 78-item food-frequency questionnaire submitted between 1991 and 2002. For various macronutrients, the partial regression coefficient (variation of BMI ($kg\,m^{-2}$) per 100 kcal increment of energy intake) was derived from multiple linear regression models, after allowance for age, study centre, education, smoking habits, number of eating episodes and mutual adjustment for macronutrients.
Results: BMI was directly associated with protein intake among women only ($\beta = 0.68$) and with unsaturated fats in both genders (for monounsaturated fats $\beta = 0.27$ for men and 0.26 for women; for polyunsaturated fats $\beta = 0.27$ for men and 0.54 for women), and inversely related to carbohydrates ($\beta = -0.05$ for men and -0.21 for women) and number of eating episodes in both genders ($\beta = -0.42$ for men and -0.61 for women) and to saturated fats among women only ($\beta = -0.57$).
Conclusions: These results confirm and provide convincing evidence that, after allowance for selected covariates including total energy intake, a protein-rich diet is not inversely related to BMI, and a carbohydrate-rich diet is not directly related to BMI.

Overweight and obesity are precursors of several diseases, including cardiovascular disorders, diabetes mellitus and also cancer at different sites[1]. The mechanism may be direct or through the pathways of the metabolic syndrome, a series of manifestations that often characterise obesity and include glucose intolerance, insulin resistance, dyslipidaemia and hypertension[2].

It is still unclear how to control energy intake in order to achieve and maintain a reduction of body mass index (BMI). In particular, the most appropriate combination of macronutrients in the diet has not yet been identified[3]. Low-carbohydrate diets (e.g. Atkins and Protein Power) propose a reduction of carbohydrate intake to 5–10% of total energy, and an increase of protein intake up to 30% and of fats up to 65%[4]. Such diets have been reported to achieve a

decrease of *ad libitum* caloric intake, possibly due to the anorexic effect of proteins[5], and a clinically significant weight loss which, however, is associated with the duration of the diet and the restriction of energy intake, not with carbohydrate restriction itself[6]. More important, subsequent long-term effects on nutritional status and body composition after such diets have not been documented[6].

A study by Trichopoulou *et al.*[7] conducted in Greece between 1994 and 1999 found a positive association between protein intake and BMI, in both men and women. That study also suggested that neither fats (saturated or monounsaturated) nor carbohydrates play a major role in BMI determination. Likewise, the findings from the US Prostate Cancer Prevention Trial showed that energy from fat but not from carbohydrates was associated with obesity

in a cohort of 15 266 middle-aged and elderly men[8]. Further, a randomised trial on 34 individuals followed for 12 weeks showed that a high-carbohydrate diet consumed *ad libitum*, with no attempt at energy restriction or change in energy intake, results in losses of body weight and body fat for both genders[9].

In order to analyse the relationship between BMI and macronutrient intake in another Mediterranean population, we repeated the analysis of Trichopoulou *et al.*[7] in a data set collected in Italy between 1991 and 2002.

Methods

Overall, 6619 subjects (3090 men and 3529 women; median age 58, range 17–82 years) were included in the present analysis. These were derived from the comparison groups of a series of case–control studies on cancer at several sites and recruited by trained interviewers from several teaching and general hospitals in four Italian areas: greater Milan and the provinces of Pordenone, Gorizia, Padua and Forlì (North-eastern Italy); the province of Genova (North-western Italy); the province of Latina (Central Italy); and the urban area of Naples (Southern Italy)[10].

These subjects were admitted to hospitals for a wide spectrum of acute non-neoplastic conditions, unrelated to known or potential risk factors for cancers: 23% had traumatic conditions (mostly fractures and sprains), 31% non-traumatic orthopaedic disorders (mostly lower back pain and disc disorders), 18% acute surgical conditions (mostly abdominal, such as acute appendicitis or strangulated hernia) and 28% other miscellaneous illnesses such as eye, ear, nose, throat and dental disorders. Fewer than 4% of subjects approached refused to be interviewed, and response rates did not vary across hospitals and geographical areas.

In the hospital setting, trained interviewers administered to the patients a structured questionnaire which included information on age, education and other socio-economic factors, occupational and leisure-time physical activity, smoking habits, alcohol intake and coffee consumption. The subjects' diet during the 2 years before hospital admission was investigated through a validated and reproducible 78-item food-frequency section of the questionnaire[11–13]. We used an Italian food composition database to estimate energy and nutrient intake[14]. A detailed section of the questionnaire was prepared to collect information on self-reported height and weight measures 1 year prior to the interview. BMI was computed as weight divided by the square of height (Kg m^{-2}).

Data analysis

Multiple linear regression was applied to assess the effects of macronutrients and ethanol on BMI. We considered two models separately for men and women. The first model included adjustments for age, study centre, education, smoking habits, total energy intake and number of eating episodes per day, and the second one further mutual adjustments for the other macronutrients, including alcohol. Both analyses were performed for all the subjects and for the subset of subjects who had never been on a weight reduction diet.

Results

Almost 20% of men reported frequent or irregular dieting, while the percentage among women was 31%. Median values of BMI (kg m^{-2}) were 26.0 for men and 24.8 for women, and were 25.7 and 24.0, respectively, after exclusion of subjects who had been dieting.

Table 1 shows the cut-off points of quartiles of total energy intake (kJ) and of percentage of energy intake from specific macronutrients, including alcohol, among men and women. On average, carbohydrates accounted for ~47% of energy intake (median value: 46.5% for men and 48.3% for women), lipids for 30% (29.4 and 32.3%), proteins for 15% (14.5 and 16.4%), and alcohol varied greatly between genders (8.9% in men and 0.8% in women). After exclusion of subjects who had been dieting, the dietary nutrient composition was similar, but the cut-offs for energy intake were higher.

Table 2 shows the partial regression coefficients and the corresponding 95% confidence intervals giving a change of BMI for a 418.4 kJ (100 kcal) increment of energy intake for each macronutrient according to the two models applied to all subjects (upper part of the table) and then to subjects who had never been dieting (lower part of the table), separately among men and among women. Proteins were not associated with BMI among men: the estimates were −0.06 among all men and −0.01 for men with no restricted dietary habits, after mutual adjustment for other macronutrients. A positive association was shown between proteins and BMI among women in all models. The estimates varied from 0.68 among all women to 0.58 among women with no restricted dietary habits, after mutual adjustments for other macronutrients. Carbohydrates were moderately and inversely associated with BMI in all models for both genders. The coefficients in the second model were −0.05 and −0.06 among men and −0.21 and −0.16 among women. Saturated fats were inversely associated with BMI among women only, after mutual adjustment for other macronutrients. The estimates were −0.57 for all women and −0.54 for women with no restricted dietary habits. No association was found among men. Unsaturated fats were positively associated with BMI in all models for both genders. Estimates for mono-unsaturated fats were 0.27 both among all men and after exclusion of men who have been on a diet; corresponding values for women were 0.26 and 0.36. Similarly, for polyunsaturated fats, the corresponding estimates were 0.27 and 0.20 among men and 0.54 and 0.38 among women. Alcohol consumption was moderately associated with BMI among men ($\beta = 0.09$) and among women who

Table 1 Cut-off points of quartiles of total energy intake (in kJ) and of percentage of energy intake (macronutrient/total energy intake %) from specific macronutrients by gender*

	Men			Women		
	Quartile cut-off points			Quartile cut-off points		
	1st	2nd	3rd	1st	2nd	3rd
All subjects (*n* = 6619)						
Energy (kJ)	8930.1	10 934.2	12661.9	7001.6	8719.3	10 163.6
Protein (%)	13.1	14.5	15.7	14.8	16.4	17.6
Animal (%)	7.8	9.1	10.6	9.4	10.9	12.5
Vegetable (%)	4.7	5.3	6.0	4.8	5.4	6.0
Carbohydrates (%)	41.2	46.5	50.7	43.9	48.3	51.7
Sugars (%)	11.8	14.7	17.8	14.5	17.7	21.3
Starch (%)	26.7	31.0	35.8	25.7	30.0	34.3
Lipids (%)	25.6	29.4	32.5	28.6	32.3	35.2
Saturated (%)	8.5	9.8	11.1	9.8	11.3	12.4
Monounsaturated (%)	11.8	14.5	16.7	13.0	15.5	17.7
Polyunsaturated (%)	3.6	4.3	5.0	3.8	4.5	5.3
Alcohol (%)	3.1	8.9	13.7	0.0	0.8	4.8
subjects on diet excluded (*n* = 4907)						
Energy (kJ)	9129.9	11 068.9	12 822.1	7193.7	8910.4	10 414.4
Protein (%)	13.1	14.5	15.6	14.7	16.2	17.3
Animal (%)	7.7	9.1	10.2	9.2	10.7	11.9
Vegetable (%)	4.7	5.3	5.8	4.8	5.4	5.8
Carbohydrates (%)	41.5	46.7	50.9	44.1	48.4	51.8
Sugars (%)	11.7	14.6	17.2	14.5	17.5	20.2
Starch (%)	26.8	31.2	35.0	26.0	30.2	33.7
Lipids (%)	25.6	29.2	32.3	28.6	32.3	35.0
Saturated (%)	8.4	9.8	11.0	9.9	11.4	12.5
Monounsaturated (%)	11.7	14.3	16.5	12.9	15.4	17.6
Polyunsaturated (%)	3.6	4.3	5.0	3.8	4.5	5.3
Alcohol (%)	3.4	8.9	13.7	0.0	1.5	5.1

* Note that the values denote the cut-off points of quartiles of energy intake from the different nutrients. Therefore, the figures in the columns do not add up to 100% and the sums increase, as they should, from the first to the third cut-off of quartiles.

had not been dieting ($\beta = 0.13$). The number of eating episodes per day was inversely related to BMI for both genders. The estimates varied between -0.42 and -0.40 for men, and -0.61 and -0.14 for women, respectively among all subjects and after exclusion of subjects who had been dieting.

Discussion

Our study showed that a protein-rich diet was associated with BMI only among women, in broad agreement with some studies from Greece[7] and the USA[8,9]. When we separated animal and vegetal proteins, vegetable proteins were inversely associated with BMI among men only. Although vegetable proteins may offer metabolic advantages over animal proteins[15], there is as yet no evidence suggesting that vegetable proteins *per se* may affect body weight differently from animal protein.

Inverse associations were found between BMI and carbohydrates, but our results do not show a different effect according to the type of carbohydrates, as suggested by a recent study where a positive association was found between BMI and the glycaemic index (GI), but not with total carbohydrate intake[16].

The inverse association between the number of eating episodes per day and BMI is in agreement with previous results by Ma *et al.*[17], supporting the hypothesis that increasing the number of eating episodes per day is inversely related to obesity, independently from energy intake and nutrient composition. Increasing the frequency of meals mimics a low GI diet and has been shown to produce similar metabolic effects to those of low GI diets[18].

BMI was directly associated with mono- and polyunsaturated fats in both genders, but inversely with saturated fat among women only, in agreement with the report by Trichopoulou *et al.*[7] Monounsaturated fats (such as olive oil) are the main type of fats consumed in Italy, and it is possible that an overconsumption of these fats could result in weight gain.

Alcohol intake was directly associated with BMI in this study, but inversely in the Greek study[7]. This apparent discrepancy may be due to higher alcohol consumption in Italy, especially among men (median values of percentage of energy from alcohol was 8.9% for Italian and 3.2% for Greek men).

Physical activity is inversely related to overweight[2]. In order to consider its potential effect, we repeated the analysis adjusting for occupational and leisure-time physical activity, but estimates were not materially different.

The strengths and weaknesses of the present study include those typical of a cross-sectional design, which

Table 2 Partial regression coefficients (β) and 95% confidence intervals (95% CI) of variation of body mass index by an increase of 418.4 kJ (100 kcal) of energy intake from selected macronutrients (bold font is used for statistically significant estimates)

| | Without mutual adjustment among nutrients | | | | With mutual adjustment among nutrients | | | |
| | Men | | Women | | Men | | Women | |
Macronutrients	β*	95% CI	β*	95% CI	β†	95% CI	β†	95% CI
All subjects								
Protein	**− 0.31**	**− 0.53, − 0.09**	**0.54**	**0.24, 0.83**	− 0.06	− 0.31, 0.19	**0.68**	**0.40, 0.96**
Vegetable‡	**− 1.32**	**− 1.82, − 0.82**	**− 0.72**	**− 1.41, − 0.04**	− 1.10	− 2.09, − 0.11	1.03	− 0.14, 2.19
Animal‡	− 0.05	− 0.28, 0.17	**0.56**	**0.30, 0.83**	0.04	− 0.23, 0.32	0.67	0.36, 0.97
Carbohydrates	**− 0.18**	**− 0.24, − 0.13**	**− 0.27**	**− 0.35, − 0.18**	**− 0.05**	**− 0.10, − 0.01**	**− 0.21**	**− 0.26, − 0.14**
Sugars‡	**− 0.16**	**− 0.25, − 0.06**	**− 0.16**	**− 0.28, − 0.05**	− 0.04	− 0.13, 0.06	**− 0.17**	**− 0.28, − 0.06**
Starch‡	**− 0.17**	**− 0.23, − 0.10**	**− 0.19**	**− 0.27, − 0.10**	0.07	− 0.06, 0.20	− 0.26	− 0.42, − 0.10
Saturated lipids	0.06	− 0.14, 0.26	0.11	− 0.16, 0.38	− 0.05	− 0.30, 0.19	**− 0.57**	**− 0.87, − 0.28**
Monounsaturated lipids	**0.24**	**0.14, 0.34**	**0.29**	**0.15, 0.43**	**0.27**	**0.17, 0.37**	**0.26**	**0.13, 0.40**
Polyunsaturated lipids	**0.25**	**0.04, 0.46**	**0.66**	**0.39, 0.93**	**0.27**	**0.06, 0.47**	**0.54**	**0.29, 0.80**
Alcohol	**0.08**	**0.03, 0.14**	0.04	− 0.09, 0.17	**0.09**	**0.05, 0.14**	− 0.03	− 0.16, 0.10
Number of eating episodes	**− 0.53**	**− 0.86, − 0.20**	**− 0.73**	**− 1.14, − 0.32**	**− 0.42**	**− 0.76, − 0.09**	**− 0.61**	**− 1.02, − 0.20**
Subjects on diet excluded								
Protein	**− 0.26**	**− 0.51, − 0.02**	**0.35**	**0.01, 0.69**	− 0.01	− 0.29, 0.27	**0.58**	**0.24, 0.93**
Vegetable‡	**− 1.17**	**− 1.73, − 0.61**	**− 0.81**	**− 1.58, − 0.03**	− 0.98	− 2.06, 0.11	1.39	0.05, 2.72
Animal‡	− 0.04	− 0.28, 0.21	**0.42**	**0.11, 0.73**	0.06	− 0.25, 0.37	0.54	0.18, 0.90
Carbohydrates	**− 0.18**	**− 0.24, − 0.12**	**− 0.30**	**− 0.40, − 0.21**	**− 0.06**	**− 0.11, 0.00**	**− 0.16**	**− 0.23, − 0.09**
Sugars‡	**− 0.18**	**− 0.28, − 0.07**	**− 0.18**	**− 0.31, − 0.05**	− 0.07	− 0.17, 0.04	**− 0.16**	**− 0.29, − 0.03**
Starch‡	**− 0.15**	**− 0.22, − 0.07**	**− 0.22**	**− 0.32, − 0.12**	0.07	− 0.07, 0.21	**− 0.31**	**− 0.48, − 0.13**
Saturated lipids	0.04	− 0.19, 0.26	0.09	− 0.22, 0.39	− 0.07	− 0.35, 0.20	**− 0.54**	**− 0.89, − 0.19**
Monounsaturated lipids	**0.23**	**0.11, 0.34**	**0.37**	**0.21, 0.52**	**0.27**	**0.15, 0.39**	**0.36**	**0.20, 0.52**
Polyunsaturated lipids	0.17	− 0.06, 0.40	**0.59**	**0.28, 0.90**	0.20	− 0.03, 0.42	**0.38**	**0.08, 0.69**
Alcohol	**0.09**	**0.03, 0.14**	0.13	− 0.02, 0.29	**0.10**	**0.04, 0.15**	0.13	− 0.02, 0.29
Number of eating episodes	**− 0.53**	**− 0.90, − 0.17**	**− 0.53**	**− 1.01, − 0.06**	**− 0.40**	**− 0.77, − 0.02**	− 0.14	− 0.64, 0.36

* Adjusted for age, study centre, education, smoking habit, total energy intake and number of eating episodes per day.
† Adjusted for age, study centre, education, smoking habit, number of eating episodes per day and mutual adjustment for other macronutrients (proteins, carbohydrates, and saturated, monounsaturated and polyunsaturated lipids).
‡ Mutual adjustment model included vegetable and animal proteins, sugars and starch, and saturated, monounsaturated and polyunsaturated lipids.

discloses the degree of the association between BMI and macronutrients, but may leave open issues on causal interpretation. Furthermore, subjects admitted to hospital may not be representative of a healthy population with respect to BMI[19]. Our interviewers, however, specifically asked for average weight in the 2 years before admission to hospital and medical records could be checked to verify this. Moreover, great attention was paid in excluding subjects with chronic conditions leading to long-term modifications of diet. On the other hand, it is known that subjects tend to underestimate weight and overestimate height[20−22], but different self-reporting of weight and height across the strata of the various nutrients considered is unlikely. Moreover, distributions by height and weight in our subjects were similar to those from population surveys in Italy[23]. BMI is a measure of body mass uncorrelated to height[24] and is used to measure overweight (BMI ≥ 25 kg m^{-2}) and obesity (BMI ≥ 30 kg m^{-2}) according to standard criteria[25]. BMI does not, however, distinguish between body fat and lean body mass. The positive association between protein and BMI might therefore represent a direct association between protein intake and lean mass, since the same BMI could be shared by people with different body fat content and distribution. However, on a population level, other measurements of body fat, including waist circumference, percentage body fat mass, waist-to-height ratio and waist-to-hip ratio, had little advantage over BMI in the prediction of obesity-related metabolic risk[26,27].

Among other strengths of this study are the large number of subjects analysed and the collection of extensive dietary information using a validated food-frequency questionnaire[11−13].

In conclusion, the results found in this Italian population support those reported by a Greek study[7], and provide evidence that a diet rich in protein is not inversely related to BMI in Mediterranean populations.

Acknowledgements

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