Dietary Fat Is Associated With Metabolic Syndrome in Japanese Brazilians

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OBJECTIVE — The aim of this study was to examine the association of nutrient intakes with metabolic syndrome in a Japanese descendant population at high risk for metabolic abnormalities.

RESEARCH DESIGN AND METHODS — In a population-based study of Japanese Brazilians aged ≥30 years, 412 men and 465 women were studied. The diagnosis of metabolic syndrome was based on the National Cholesterol Education Program criteria modified for Asians. Food intake was assessed by a validated food frequency questionnaire.

RESULTS — Men and women showed similar mean ages (55.7 ± 12.7 and 54.4 ± 11.9 years) and 49% (95% CI 44.8–54.6) and 43% (38.4–47.6) had metabolic syndrome, respectively. As expected, clinical parameters were less favorable in the subset of subjects with metabolic syndrome. Men with metabolic syndrome showed higher cholesterol (233.2 ± 116.3 vs. 211.7 ± 58 g/day, P < 0.05) and lower carbohydrate (288.5 ± 45.8 vs. 300.1 ± 39.8 g/day, P < 0.001) intakes than those without metabolic syndrome, but no difference was observed among the women. After adjusting for sex, age, smoking, education level, generation, physical activity, total energy, and dietary fiber intake, a positive association between metabolic syndrome and total fat intake was detected. Comparing people in the highest quintile of total fat consumption with those in the lowest quintile, odds ratio (OR) of metabolic syndrome was 5.0 (95% CI 1.38–16.00). In contrast, linoleic acid intake was inversely associated with metabolic syndrome (OR 0.50 [95% CI 0.26–0.98]; P < 0.05). Considering food groups, after adjustments only fried food intake was shown to be associated with increased risk of metabolic syndrome.

CONCLUSIONS — Despite the limitation of such a study design in investigating cause-effect relationships, our findings favor the hypothesis that dietary total fat may increase whereas linoleic acid intake may reduce the risk of metabolic syndrome in Japanese descendants living in Brazil.

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Metabolic syndrome is highly prevalent in the U.S. with an estimated 24% of the adult population affected (4). The National Cholesterol Education Program (5) defined metabolic syndrome based on several parameters including anthropometric measurements. However, anthropometric cutoffs to identify high-risk subjects may be influenced by ethnicity (6,7). Based on the fact that in Asian populations morbidity and mortality are occurring in people with lower BMI values and waist circumferences, the World Health Organization recently proposed different cutoff values to define increased morbidity in Asians (7).

Migration studies indicate that adoption of the Western lifestyle is strongly associated with type 2 diabetes. Our group conducted a population-based study in Japanese migrants and their descendants in Brazil who have one of the highest prevalences of glucose metabolism disturbances worldwide (8). High prevalence rates of type 2 diabetes and associated diseases in Japanese migrants living in the Americas (8–11) suggest that the exposure to a different lifestyle exacerbated an inherent tendency to accumulate fat and develop diabetes (12). Our group and others reported that dietary changes, such as an increase in animal fat intake and reduction in complex carbohydrates, were imposed by immigration (12–15).

Animal studies suggested that the type of fat in diet may affect insulin sensitivity by changing the fatty acid composition of membrane lipids (16). In humans, a detrimental effect of saturated fat or a benefit of polyunsaturated fat is controversial (3,17–19). Few data are available regarding the association of dietary factors with clusters of diseases that have a common nutritional basis, such as the metabolic syndrome (20). Considering the complexity of establishing relationships between diet and disease, the focus of this study was on a population in which several diseases cluster together. Therefore, we examined the association of nutrient intakes with metabolic syndrome in a Japanese-Brazilian population at high risk for metabolic abnormalities.
**RESEARCH DESIGN AND METHODS** — A survey was designed to estimate the prevalence and incidence of diabetes and associated diseases in a Japanese-Brazilian population living in Bauru, São Paulo, Brazil (8). This was approved by the Institutional Ethics Committee and written informed consent was obtained from all participants. The entire Japanese-Brazilian population ≥30 years of age (n = 1,651) was invited, and 1,330 first-generation (Japan-born) and second-generation (Brazil-born) subjects participated in all phases of the survey. Self-reported diabetes, hypertension, dyslipidemia, and other diseases whose treatment could interfere in the dietary plan were excluded. Thus, results refer to 877 eligible subjects. They were interviewed at home by trained interviewers using standardized questionnaires and scheduled for physical examination and laboratory procedures after overnight fasting. The protocol has been described in detail elsewhere (8).

**Dietary data**
Dietary data were obtained by a quantitative food frequency questionnaire, developed and validated for the Japanese-Brazilian population (21). Subjects were asked about their usual consumption of foods and food groups (122 items) during the last year. Participants reported their habitual frequency of consumption of each item, the respective unit of time (if daily, weekly, monthly, or annually), and size of the usual individual portion (if small, average, large, or extra-large in relation to the reference portion for each item of the food frequency questionnaire). Questions concerning use of sauce, frequency of intake of visible fat, and type of fat used in cooking procedures were also included. Complete re-checking of the coding as well as double keying were performed on every questionnaire. In addition to standard range edits, internal consistency edits and nutrient calculations for the diets were performed using Dietsys 4.01 software (22). The nutrient database used was based primarily on U.S. Department of Agriculture publications supplied by Dietsys, supplemented by the most recent edition of Standard Food Composition Tables of Brazil (23) and Japan (24). The variables selected for this study were total calories, carbohydrate, protein, total fat, saturated fatty acid, oleic acid, linoleic acid, cholesterol, total fiber, and alcohol. Macronutrients were also considered as percentages of total calories.

Physical activity was assessed by a questionnaire including items regarding the types of physical activities performed during work and leisure periods. A score was attributed to each subject, and three categories were created: light, moderate, or heavy. Smoking habit was classified into two categories: current smoker or not. Education level was classified into three categories (<1, 1–8, and >8 years) and generation as Japan-born or Brazil-born subjects. Body weight and height were measured while subjects wore light clothing and no shoes using calibrated electronic scales and a fixed stadiometer. Waist circumference was measured at the umbilicus. BMI was calculated as weight (kilograms) divided by height (meters) squared. Blood pressure was taken three times by automatic device (Omron model HEM-712C; Omron Health Care) and the mean value of the two last measurements was used to express systolic and diastolic blood pressure.

**Laboratory methods**
Total cholesterol, its fractions, triglyceride, and uric acid were measured enzymatically by automatic analyzer. Samples for insulin determination were stored at −80°C until assay; this was determined by monoclonal antibody-based immunofluorimetric assay (AutoDelfia; Perkin Elmer Life Sciences, Norton, OH). Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated according to Matthews et al. (25).

Diagnosis of metabolic syndrome was based on the Third Report of the National Cholesterol Education Program—Adult Treatment Panel III (5), replacing the anthropometric cutoffs by those previously proposed by the World Health Organization for Asians (7). The presence of three or more of the following components defined metabolic syndrome: fasting plasma glucose ≥110 mg/dl (6.1 mmol/l); systolic or diastolic blood pressure ≥130 or ≥85 mmHg; HDL cholesterol <50 mg/dl (1.29 mmol/l) for women or <40 mg/dl (1.04 mmol/l) for men; triglyceride ≥150 mg/dl (1.79 mmol/l); and waist circumference ≥80 for women or ≥90 cm for men.

**Statistical methods**
Statistical analysis was performed using SPSS version 10.0 (SPSS, Chicago, IL). Rates of metabolic syndrome were calculated by point and interval. Nutrient intake was expressed in grams and as percentages of total energy adjusted for total energy through the residual method. Energy-adjusted nutrient intakes were calculated as the residuals from the regression model, with absolute nutrient intake as the dependent variable and total energy intake as the independent variable (26). Nutritional, clinical, and laboratory data of the participants with and without metabolic syndrome were compared by Student’s t test; for categorical variables, the Mantel-Haenszel χ² test for trend was applied. Logistic regression was used to calculate the odds ratios (ORs) and their 95% CIs for metabolic syndrome, with individuals in the lowest quintile category of macronutrients as the reference category. ORs were adjusted for sex, age, smoking, generation, leisure physical activity, level of education, total energy, dietary fiber, and alcohol intake and for a number of possible sex interactions. To assess trends across quintile categories, we assigned the median intake of each nutrient category to individuals with intakes in the category and then included this quintile median variable as a continuous factor in logistic regression models. The P for trend was the resulting P value for the associated logistic regression coefficient (27). Statistical significance was defined as a two-tailed P value <0.05.

**RESULTS** — Similar proportions of men (47%, n = 412) and women (53%, n = 465) were included, and their mean ages were 55.7 ± 12.7 and 54.4 ± 11.9 years, respectively. Slightly higher prevalence of metabolic syndrome was found in women (49.8% [95% CI 44.8–54.6]) than in men (43.0% [38.4–47.6]). As expected, clinical and biochemical parameters were less favorable, and HOMA-IR values were higher in the subsets of Japanese-Brazilian men and women with metabolic syndrome (Table 1). Proportions of generations, current smokers, and physical activity levels did not differ between subjects with or without metabolic syndrome.

Nutrient intakes according to sex and the presence of metabolic syndrome are shown in Table 2. Men with metabolic syndrome had significantly higher total

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fat (in grams and percentage of total energy), oleic acid, and cholesterol intakes than those without metabolic syndrome \((P < 0.05)\). In women, significantly lower protein intake adjusted for total energy was observed when comparing subsets with and without the syndrome.

ORs of metabolic syndrome across quintiles of dietary nutrients showed that the highest quintile of total fat was associated with a fivefold increase in risk of having the syndrome, after adjustment for sex, age, smoking, education level, generation, physical activity, total energy intake, dietary fiber, alcohol, and sex times years of education interaction (Table 3). Conversely, the highest consumption of linoleic acid was associated with a protection against metabolic syndrome (OR 0.50 [95% CI 0.26–0.98]).

Nutrients were also considered in food groups such as quintiles of fruits, bread/cereals/rice, red meat, fish, eggs, and oils/fried food. After adjustment for sex, age, smoking, education, generation, physical activity, total energy, total fat, and linoleic acid, only fried food intake was shown to be associated with increased risk of metabolic syndrome (OR \(2.61 [95\% \text{ CI} 1.27–5.39]\), \(2.19 [0.92–4.37]\), \(1.31 [0.85–2.04]\), and 1.69 [1.10–2.16]) for the second, third, fourth, and fifth quintiles, respectively; \(P = 0.02\).

**CONCLUSIONS**—Although aspects of diet have been linked to individual metabolic features of the metabolic syndrome (2, 3, 17, 18), the role of dietary factors in the etiopathogenesis of this syndrome has been poorly investigated (20). As far as type 2 diabetes is concerned, conflicting relationships with carbohydrates and fat intake have been reported (28, 29). Grouping diseases that share a common etiopathogenetic basis was an attempt to clarify the relationships of the insulin resistance syndrome with dietary factors. We had an opportunity to study a population of Japanese ancestry that was shown to be highly susceptible to metabolic syndrome when exposed to the Western world (30). Since 1993, our group has followed a cohort of Japanese Brazilians with high prevalence of central obesity, diabetes, dyslipidemia, and hypertension (8, 9, 12).

The definition of metabolic syndrome used in the present study introduced a modification to the National Cholesterol Education Program criteria with respect to the waist circumference cutoffs (5), in accordance with recent World Health Organization recommendations for Asian populations (7). The same diagnostic approach was previously used in other Asian populations, namely the Omani from Saudi Arabia (31). A slightly higher proportion of Japanese-Brazilian men with metabolic syndrome are compatible with greater cardiovascular risk attributed to sex. Consistently higher HOMA-IR values in the subsets of Japanese-Brazilian men...
Dietary fat and metabolic syndrome

Table 2—Daily intake of energy and selected nutrients of the study participants

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<th>Men without metabolic syndrome</th>
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<th>Women without metabolic syndrome</th>
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<td>n</td>
<td>Energy (kcal)</td>
<td>Crude intake (g)</td>
<td>Total energy adjusted (g)</td>
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<td>207</td>
<td>2177 ± 615</td>
<td>293.0 ± 84.4</td>
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<td>2293 ± 670</td>
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<td>143.4 ± 264.7</td>
<td>188.5 ± 333.4</td>
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Data are means ± SD. *P < 0.001, †P < 0.05 vs. without metabolic syndrome. ‡Log-transformed values for statistical purposes.

and women classified with metabolic syndrome assured a reasonable identification of subjects with metabolic syndrome in whom associations with nutrient intake were investigated.

Although food frequency techniques have been largely used in cross-sectional surveys, they could be considered limited by their lack of quantitative accuracy. Underreporting of energy intake may be a problem when obese subjects are under investigation. The term “underreporting” applies to dietary assessment methods used to estimate total energy intake, such as the food frequency questionnaire. The small number of Japanese Brazilians with elevated BMI should minimize the possibility of systematic bias caused by underreporting in the present study. Additionally, as pointed out by Margenst and Nelson (32), differences in mean intake levels of macronutrients between underreporters and those who give valid records are reduced by energy adjustment.

In crude analysis, men with metabolic syndrome were shown to have higher total fat and cholesterol intake to the detriment of carbohydrate than those without the syndrome. However, no impact on the risk of metabolic syndrome was shown across quintiles of carbohydrate intake adjusted for a number of variables. The relationship between dietary carbohydrates and insulin sensitivity is a matter of controversy (28,33). Simple sugars may have a detrimental effect (33), whereas starches and polysacharides may have benefits for glucose metabolism (20,34,35). In a large sample of adult Swedish men and women, food patterns dominated by fiber bread provided favorable effects, whereas those high in refined bread or in cheese, cake, and alcoholic beverages increased the risk for several components of metabolic syndrome (36). Concordantly, recent data from the Framingham Offspring Study supported the fact that whole-grain intake is inversely associated with HOMA-IR and lower prevalence of metabolic syndrome (20). Our study and others provided conflict-
...ing results which could be attributed to the heterogeneity of study designs and/or source of dietary carbohydrates.

The lack of association of carbohydrate intake seen in the present study is somewhat in agreement with the study by Brunner et al. (37). However, these investigators did not detect considerable differences between types of dietary fat, which was the case in our study. Despite this, OR was seen as a measurement of risk for metabolic syndrome in the present study. Because OR may overestimate the risk of a common outcome such as metabolic syndrome, it is possible that an increase in risk attributed to fat intake by the OR is, in fact, less pronounced than a fivefold increase. Our findings of an adverse impact of total fat intake and protection of metabolic syndrome in a Japanese-Brazilian population. Our findings also corroborate a beneficial effect of polyunsaturated fatty acid such as linoleic acid to reduce risk for this clustering of diseases linked by insulin resistance. Prospective studies will help test the hypothesis in this population.

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APPENDIX

Members of Japanese-Brazilian Diabetes Study Group

Alcides Hirai, Amélia T. Hirai, Helena Harima, Magid Inunes (in memoriam), Mário Kikuchi, Katsumi Osiro, Sandra R. G. Ferreira, and Suely G. A. Gimeno (Department of Preventive Medicine, Federal University of São Paulo, Brazil); Lâercio J. Franco (Department of Social Medicine, Freire and Associates
Dietary fat and metabolic syndrome

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