Associations of Dietary Fiber With Glucose Metabolism in Nondiabetic Relatives of Subjects With Type 2 Diabetes

The Botnia Dietary Study

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OBJECTIVE — To study cross-sectional associations of dietary fiber intake with insulin resistance, insulin secretion, and glucose tolerance in a population at high risk for type 2 diabetes.

RESEARCH DESIGN AND METHODS — The subjects consisted of 248 male and 304 female adult nondiabetic relatives of patients with type 2 diabetes. Dietary intake was measured by means of two 3-day food records. Associations of total, water-insoluble, and water-soluble fiber with measures of glucose metabolism based on an oral glucose tolerance test, were analyzed by multiple linear regression analysis adjusting for sex, age, length of education, physical activity, BMI, waist-to-hip ratio, systolic blood pressure, and serum triglyceride and HDL cholesterol concentrations. The homeostasis model assessment insulin resistance index, the incremental 30-min serum insulin concentration divided by the incremental 30-min glucose concentration, and fasting and 2-h glucose concentrations were the outcome variables.

RESULTS — The dietary intake of total as well as water-insoluble and water-soluble fiber was inversely associated with insulin resistance: −0.17 (0.07), $P = 0.012$; −0.15 (0.07), $P = 0.024$; and −0.14 (0.07), $P = 0.049$ [regression coefficients (SE)]. Fiber variables were unrelated to insulin secretion and plasma glucose concentrations.

CONCLUSIONS — The results support evidence that a high intake of dietary fiber is associated with enhanced insulin sensitivity and therefore may have a role in the prevention of type 2 diabetes.

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Diet is regarded as one of the environmental determinants of type 2 diabetes. A typical feature of the modern western lifestyle diet is a low fiber intake that has been implicated in several diseases of western civilization, including type 2 diabetes. Although experimental high-fiber diets have been associated with improved glucose metabolism (1,2), the results of epidemiological studies are inconsistent. Available data suggest a positive effect on insulin sensitivity (3–6), while association with glucose tolerance and diabetes risk has been more controversial (7–14).

The beneficial effect of dietary fiber has mainly been ascribed to the water-soluble fiber fraction, while the role of water-insoluble fiber has been regarded as less convincing (15,16). However, some recent prospective studies (13,14, 17) suggest a protective role specific to water-insoluble dietary fiber against type 2 diabetes.

In the present cross-sectional study, we sought to determine whether habitual dietary fiber intake (total, water-insoluble, and water-soluble fiber) was related to insulin resistance, insulin secretion, or glucose concentrations in a population at high risk for type 2 diabetes.

RESEARCH DESIGN AND METHODS

— The Botnia Dietary Study investigates relationships between diet and glucose metabolism in relatives of patients with type 2 diabetes. The study was conducted between October 1994 and June 1997 as part of the follow-up investigation of the Botnia Study, which is a prospective family study in western Finland aimed at the identification of genetic and metabolic defects in type 2 diabetes (18). The study was approved by the local ethics committees. The inclusion criteria for the dietary study were *1*) a first- or second-degree family history of type 2 diabetes, *2*) aged 20–70 years at the time of the baseline investigation, and *3*) normal or impaired glucose tolerance according to the 1985 World Health Organization criteria (19) at baseline investigation. A consecutive sample of 746 subjects fulfilling the inclusion criteria was invited to

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Abbreviations: HOMA, homeostasis model assessment; IAUC, incremental area under the curve; MET, metabolic unit value; NEFA, nonesterified fatty acid.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

participate. Accepted data on dietary intake were received from 590 (79%) of those invited. However, 17 subjects were excluded from the present analyses because of missing laboratory data, 14 subjects with newly diagnosed diabetes, and 7 subjects using fiber-containing laxatives. Among the remaining 552 subjects (comprising 74% of the invited subjects), the proportion of women willing to participate and included in the analyses (77%) was higher ($P = 0.037$) than that of men (71%). There was no difference in sex-adjusted mean age, BMI, waist-to-hip ratio, physical activity, or length of education between those who did and did not participate. However, in participants, a lower fasting plasma glucose concentration (5.4 vs. 5.6 mmol/l, $P = 0.017$), a lower 2-h plasma glucose concentration (5.8 vs. 6.5 mmol/l, $P = 0.001$), and a lower fasting serum insulin concentration (48 vs. 54 pmol/l, $P = 0.016$) were observed. Of the participants, 539 (98%) were first- and 13 (2%) were second-degree relatives of subjects with type 2 diabetes.

Food consumption in the Botnia Dietary Study was measured by means of two 3-day estimated food records kept ~6 months (range 5–11) apart. Trained study nurses instructed the participants to record every item of food or drink consumed, in as much detail as possible, immediately after each eating episode. It was emphasized that it was very important not to change food habits, i.e., the amount or quality of the food or drink consumed during the study period, because of the record keeping. The record form also included detailed written instructions for record keeping. Each 3-day recording period mainly included 2 weekdays and 1 weekend day. Participants estimated portion sizes using a food picture booklet. Participants returned the food record to the nurse, who reviewed it with the participant and completed missing or incomplete information. The study nurses who took care of the field work completed an intensive training program arranged by one of the authors (K.Y., MSc in nutrition, authorized nutritionist), and the quality in which the food records were checked was monitored continuously. Food intake data were entered into the computer by two of the authors (C.K-K., majoring in nutrition at the time of the field study, and K.Y.) and processed by the Nutnet software developed at the National Public Health Institute, Helsinki, Finland (20). This software allowed us to input recipes and specific ingredients for analysis. The dietary intake was calculated as the mean of the 6 recording days. Fiber variables included total dietary fiber, analyzed by the enzymatic gravimetric method of Asp et al. (21), water-insoluble dietary fiber (including cellulose, lignin, and water-insoluble noncellulosic polysaccharides), and water-soluble dietary fiber (water-soluble noncellulosic polysaccharides), both of which were analyzed by the method of Englyst (22). The intake of energy and energy-adjusted intake of saturated fatty acids, thiamin, vitamin C, and β-carotene were also calculated (amounts from supplements were included).

After an overnight fast, the subjects underwent a 75-g oral glucose tolerance test. Blood samples for the measurement of glucose and insulin were drawn at −5, 0, 30, and 120 min and, for nonesterified fatty acids (NEFAs), at 0 and 120 min. Plasma glucose was measured with a glucose oxidase method (Beckman Glucose Analyzer II; Beckman Instruments, Fullerton, CA). Serum insulin was measured by radioimmunoassay (Pharmacia, Uppsala, Sweden) with an interassay coefficient of variation <9%. Serum NEFAs were measured by an enzymatic colorimetric method using a commercially available kit (Wako Chemicals, Neuss, Germany). From fasting venous samples, serum triglyceride and total and HDL cholesterol concentrations were measured by enzymatic methods using the Cobas Mira autoanalyzer (Hoffman-La Roche, Basel, Switzerland). Serum HDL cholesterol concentration was measured enzymatically after precipitation of the apolipoprotein B–containing lipoproteins with heparin and manganese chloride. Serum LDL cholesterol concentration was calculated by the Friedewald formula (23) if the serum triglyceride concentration did not exceed 5 mmol/l.

As a measure of insulin resistance we used the homeostasis model assessment (HOMA) insulin resistance index (24). The insulinogenic index, i.e., incremental serum insulin concentration at 30 min during the oral glucose tolerance test divided by the incremental glucose concentration at 30 min $[(Ins_{30} - Ins_0)/(Glu_{30} - Glu_0)]$, was used as the measure of insulin secretion (25). Twelve subjects with a 30-min glucose concentration less than or equal to the fasting glucose concentration were excluded. The insulinogenic index is a surrogate of first-phase insulin release during an intravenous glucose tolerance test (25). Glucose tolerance status at the time of this study was determined according to the 1998 World Health Organization criteria (26).

Body weight and height were measured with the subject in light indoor clothing without shoes. BMI (body weight in kilograms divided by the square of height in meters) was used as the measure of relative body weight. Waist circumference was measured midway between the lowest rib and the iliac crest, and hip circumference over the widest part of the gluteal region. The waist-to-hip ratio was used as the measure of central obesity. Two blood pressure recordings were obtained from the right arm with the subject seated after 30 min of rest. The mean value of the two readings was used.

A structured questionnaire was used to obtain data on length of education and physical activity during the last 12 months (27). Activity levels were changed to metabolic unit values (METs). METs represent an estimate of the relative intensity of activity by describing the amount of energy needed during exercise compared with resting energy expenditure (1 MET is approximately equal to an energy expenditure of 1 kcal [4.2 kJ] · kg body $wt^{-1} \cdot h^{-1}$). Physical activity at work was reported according to a seven-point scale ranging from no work and no activity (MET = 1.5) to very heavy manual work (MET = 10.0). Exercise while going to work was classified by tertiles: first tertile represented travel by motor vehicle (MET = 1.5), second by walking (MET = 3.5), and third by bicycle (MET = 5.0). Leisure time exercise received MET values from 2.0 to 12.5 depending on the type and intensity of the activity. The sum of MET values from work, the work trip, and leisure time described the total physical activity of the subject.

Statistical analyses were performed with the software programs BMDP (version 7.1; BMDP Statistical Software, Los Angeles, CA) and SAS (version 8.1; SAS Institute, Cary, NC). A two-sided $P < 0.05$ was considered statistically significant. Before analyses, variables with skewed distributions were transformed (logarithmic or reciprocal transformation). The intake of dietary fiber and other nutrients

was adjusted for total energy according to the residual adjustment method (28). Residual values were used in analyses.

The significance of difference in continuous variables between groups was tested by ANCOVA, and that in categorical variables by χ^2 test. Pearson's partial correlation coefficients were used to test relationships between dietary fiber and other variables after controlling for the effect of age. The associations between fiber variables and measures of glucose metabolism were studied by multiple linear regression analysis. The selection of variables included in the models was based on both correlation analysis and a priori knowledge about factors associated with the outcome variables. As the participants could be relatives, the analyses were performed with the PROC MIXED procedure (SAS/STAT software; SAS Institute, Cary, NC), where the family connection was considered. Dietary, clinical, anthropometric, and demographic variables, except sex, were included in the models as continuous variables.

Table 1—*Characteristics and intake of dietary fiber in 552 male and female nondiabetic relatives of subjects with type 2 diabetes*

	Men	Women
n	248	304
Age (years)	50.1 (10.2)	51.4 (10.4)
Length of education (years)		
6–9 (basic)	142 (57)	151 (50)
>9 (secondary or higher)	106 (43)	153 (50)
Physical activity (MET/day)	10.3 (3.8)	8.8 (3.2)
BMI (kg/m^2)	26.5 (3.0)	26.3 (4.0)
Waist-to-hip ratio	0.95 (0.06)	0.83 (0.06)
Systolic blood pressure (mmHg)	129 (15)	129 (17)
Diastolic blood pressure (mmHg)	80 (10)	80 (9)
Fasting plasma glucose (mmol/l)	5.5 (0.6)	5.4 (0.6)
Fasting serum insulin (pmol/l)	48 (27)	47 (25)
Serum triglycerides (mmol/l)	1.42 (0.78)*	1.24 (0.61)†
Serum total cholesterol (mmol/l)	5.63 (0.93)*	5.67 (1.07)†
Serum LDL cholesterol (mmol/l)	3.78 (0.86)‡	3.71 (0.98)§
Serum HDL cholesterol (mmol/l)	1.21 (0.27)‖	1.40 (0.32)†
Fasting serum NEFAs (μmol/l)	451 (168)¶	533 (182)#
2-h serum NEFAs (μmol/l)	167 (57)¶	149 (50)#
Glucose tolerance status**		
Normal glucose tolerance	191 (77)	241 (79)
Impaired fasting glucose	33 (13)	33 (11)
Impaired glucose tolerance	24 (10)	30 (10)
Energy intake (kcal)	2,249 (1,883–2,721)	1,604 (1,377–1,856)
Dietary intake (g)		
Total dietary fiber††	21.6 (17.6–25.7)	17.1 (14.2–20.6)
Water-insoluble dietary fiber‡‡	15.3 (12.4–18.5)	11.8 (9.8–14.1)
Water-soluble dietary fiber§§	4.7 (3.9–5.6)	4.0 (3.3–4.8)

Data are *n* (%) for categorical variables, median (25th–75th percentile) for dietary variables, and otherwise mean (SD). *n = 246; †n = 302; ‡n = 244; §n = 301; ‖n = 245; ¶n = 238; #n = 286; **glucose tolerance status according to 1998 WHO criteria (26); ††because different methods were used to analyze total fiber and fiber fractions, the sum of the fractions is not the same as the amount of total fiber; ‡‡water-insoluble dietary fiber consists of cellulose, lignin, and water-insoluble noncellulosic polysaccharides; §§water-soluble noncellulosic polysaccharides.

RESULTS — The median intake of dietary fiber was 21.6 g in men and 17.1 g in women (Table 1). The intake of total fiber, as well as water-insoluble and water-soluble fiber fractions, inversely correlated with BMI and measures of insulin resistance in both sexes (Table 2). An inverse association between fiber variables and waist-to-hip ratio was observed in men, while in women, fiber variables were inversely related to serum triglycerides and 2-h serum NEFAs. Fiber intake was unrelated to insulin secretion and 2-h plasma glucose concentrations. However, in men, total and water-insoluble fiber intake showed a weak inverse association with the fasting plasma glucose concentration.

Table 3 presents multiple linear regression models with the HOMA insulin resistance index as the dependent variable. Of the demographic, clinical, and dietary variables, sex and those that showed a significant association with the dependent variable in the univariate model (model 1) were included in the multivariate model (model 2). When analyzing men and women together, all fiber variables remained inversely related to insulin resistance (Table 3). When the analyses were performed separately for men and women, fiber variables were not significantly related to insulin resistance (regression coefficients between −0.09 and −0.14, P between 0.14 and 0.46).

Elevated NEFA concentrations have been associated with insulin resistance and deterioration of glucose tolerance (29). We had data on serum NEFA concentrations for 524 subjects. In the univariate model (adjusted for sex and age), both fasting and 2-h serum NEFAs were directly associated with HOMA insulin resistance: 0.22 (0.06) and 0.40 (0.06) [regression coefficients (SE)], $P = 0.0002$ and $P < 0.0001$, respectively. Therefore, we reran the multivariate models in Table 3 and included, as an additional independent variable, either fasting or 2-h serum NEFA concentration. In these models, neither fasting nor 2-h serum NEFA was a significant contributor ($P > 0.14$) and the inverse association of fiber variables with insulin resistance remained unchanged. However, as 2-h serum NEFA and triglyceride concentrations were highly correlated with each other ($r = 0.54$, $P < 0.001$) and should therefore not be included simultaneously in a model, we also performed the multivariate models of Table 3 to exclude serum triglycerides but include 2-h serum NEFA as an independent variable. In these models, 2-h serum NEFA turned out to be a significant independent contributor: 0.13 (0.06), $P < 0.02$ [regression coefficient (SE)], but still had no effect on the inverse association between fiber variables and insulin resistance.

Although in the correlation analysis (Table 2) total and water-insoluble fiber were inversely associated with the fasting plasma glucose concentration in male subjects, in the linear regression models, fiber variables were unrelated to this outcome variable (data not shown).

Table 2—*Pearson's partial correlation coefficients (adjusted for age) between energy-adjusted dietary fiber intake and demographic and clinical characteristics in 248 male and 304 female nondiabetic relatives of subjects with type 2 diabetes*

	Men (n = 248)			Women (n = 304)		
	Total fiber	Water-insoluble fiber	Water-soluble fiber	Total fiber	Water-insoluble fiber	Water-soluble fiber
Length of education	0.04 (0.52)	0.03 (0.62)	0.03 (0.61)	0.11 (0.056)	0.10 (0.096)	0.16 (0.005)
Physical activity	0.10 (0.12)	0.09 (0.15)	0.13 (0.043)	0.06 (0.31)	0.04 (0.44)	0.05 (0.41)
BMI	−0.15 (0.019)	−0.14 (0.033)	−0.14 (0.033)	−0.14 (0.012)	−0.15 (0.009)	−0.11 (0.058)
Waist-to-hip ratio	−0.18 (0.004)	−0.15 (0.017)	−0.21 (0.001)	−0.06 (0.30)	−0.05 (0.36)	−0.06 (0.30)
Systolic blood pressure	−0.05 (0.47)	−0.06 (0.38)	−0.07 (0.26)	−0.08 (0.18)	−0.07 (0.23)	−0.03 (0.55)
Diastolic blood pressure	−0.06 (0.32)	−0.06 (0.33)	−0.08 (0.21)	−0.08 (0.19)	−0.08 (0.14)	−0.02 (0.70)
Serum triglycerides	−0.10 (0.11)*	−0.10 (0.10)*	−0.07 (0.31)*	−0.16 (0.005)†	−0.15 (0.009)†	−0.16 (0.006)†
Serum total cholesterol	−0.01 (0.93)*	0.01 (0.91)*	0.01 (0.83)*	−0.06 (0.29)†	−0.04 (0.52)†	−0.10 (0.075)†
Serum LDL cholesterol	0.01 (0.94)‡	0.02 (0.80)‡	0.02 (0.76)‡	−0.06 (0.33)§	−0.04 (0.52)§	−0.10 (0.078)§
Serum HDL cholesterol	0.09 (0.18)‖	0.09 (0.14)‖	0.05 (0.41)‖	0.09 (0.13)†	0.09 (0.12)†	0.08 (0.15)†
Fasting serum NEFAs	−0.03 (0.70)¶	−0.04 (0.54)¶	−0.06 (0.37)¶	−0.12 (0.050)#	−0.10 (0.10)#	−0.07 (0.24)#
2-h serum NEFAs	−0.10 (0.11)¶	−0.11 (0.086)¶	−0.09 (0.19)¶	−0.18 (0.002)#	−0.18 (0.003)#	−0.13 (0.028)#
Fasting plasma glucose	−0.13 (0.037)	−0.13 (0.034)	−0.10 (0.10)	0.02 (0.70)	0.03 (0.63)	0.03 (0.62)
2-h plasma glucose	0.01 (0.84)	0.004 (0.95)	0.02 (0.75)	0.01 (0.93)	0.003 (0.96)	−0.005 (0.93)
Fasting serum insulin	−0.22 (0.0004)	−0.21 (0.001)	−0.20 (0.001)	−0.18 (0.002)	−0.17 (0.003)	−0.15 (0.009)
HOMA isulin resistance index	−0.24 (0.0002)	−0.22 (0.0004)	−0.21 (0.001)	−0.16 (0.006)	−0.15 (0.010)	−0.13 (0.025)
Insulin secretion during OGTT $(Ins_{30} - Ins_0) / (Glu_{30} - Glu_0)$	−0.09 (0.19)**	−0.08 (0.21)**	−0.06 (0.33)**	−0.05 (0.36)††	−0.05 (0.38)††	−0.07 (0.23)††

Data are r (P); *n = 246; †n = 302; ‡n = 244; §n = 301; ‖n = 245; ¶n = 238; #n = 286; **n = 243; ††n = 297; OGTT, oral glucose tolerance test.

CONCLUSIONS — The present results show that the dietary intake of total fiber as well as water-insoluble and water-soluble fiber was inversely related to insulin resistance, as estimated by HOMA and reflected in fasting serum insulin levels in this high-risk population. The associations were independent of sex, age, physical activity, BMI, waist-to-hip ratio, systolic blood pressure, and serum triglyceride, HDL cholesterol, and NEFA concentrations. On the other hand, the

Table 3—*Multiple linear regression models with the HOMA insulin resistance index as dependent variable and fiber and other dietary and clinical variables as independent variables in nondiabetic relatives of subjects with type 2 diabetes*

	Model 1 (n = 552)		Model 2a (n = 546)		Model 2b (n = 546)		Model 2c (n = 546)	
	Regression coefficient (SE)	P	Regression coefficient (SE)	P	Regression coefficient (SE)	P	Regression coefficient (SE)	P
Intercept	—	—	−5.27 (0.81)	<0.0001	−5.25 (0.81)	<0.0001	−5.30 (0.81)	<0.0001
Sex	−0.05 (0.04)*	0.20	0.20 (0.05)	<0.0001	0.20 (0.05)	<0.0001	0.21 (0.05)	<0.0001
Age	0.01 (0.002)†	<0.0001	−0.004 (0.002)	0.058	−0.004 (0.002)	0.053	−0.004 (0.002)	0.032
Length of education	−0.11 (0.09)	0.23	—	—	—	—	—	—
Physical activity	−0.26 (0.06)	<0.0001	−0.20 (0.05)	<0.0001	−0.20 (0.05)	<0.0001	−0.20 (0.05)	<0.0001
BMI	1.81 (0.14)	<0.0001	0.91 (0.15)	<0.0001	0.91 (0.15)	<0.0001	0.93 (0.15)	<0.0001
Waist-to-hip ratio	3.06 (0.28)	<0.0001	1.38 (0.28)	<0.0001	1.39 (0.28)	<0.0001	1.36 (0.28)	<0.0001
Systolic blood pressure	1.28 (0.19)	<0.0001	0.69 (0.16)	<0.0001	0.69 (0.16)	<0.0001	0.69 (0.16)	<0.0001
Serum triglycerides	0.49 (0.04)‡	<0.0001	0.23 (0.05)	<0.0001	0.23 (0.05)	<0.0001	0.23 (0.05)	<0.0001
Serum HDL cholesterol	−0.74 (0.09)§	<0.0001	−0.17 (0.09)	0.045	−0.17 (0.09)	0.047	−0.18 (0.09)	0.043
Saturated fatty acids	0.07 (0.11)	0.51	—	—	—	—	—	—
Thiamin	−0.002 (0.07)	0.97	—	—	—	—	—	—
Vitamin C	−0.05 (0.03)	0.10	—	—	—	—	—	—
β-Carotene	−0.04 (0.03)	0.13	—	—	—	—	—	—
Total fiber	−0.38 (0.08)	<0.0001	−0.17 (0.07)	0.012	—	—	—	—
Water-insoluble fiber	−0.35 (0.08)	<0.0001	—	—	−0.15 (0.07)	0.024	—	—
Water-soluble fiber	−0.33 (0.09)	0.0002	—	—	—	—	−0.14 (0.07)	0.049

Model 1: univariate models (adjusted for sex and age) for each independent variable; Model 2: all variables simultaneously in the model; *adjusted for age; †adjusted for sex (men = 1, women = 2); ‡n = 548; §n = 547.

fiber intake was unrelated to post–glucose load insulin secretion and glucose concentrations. The lack of an association between insulin secretion and fiber intake does not, however, indicate an inconsistency with the finding of a relation between insulin resistance and fiber intake since the insulinogenic index we used estimates only one aspect of insulin secretion (representing a surrogate of first-phase insulin release during an intravenous glucose tolerance test) and is not correlated with insulin resistance (25).

That dietary fiber and insulin resistance are related to each other has been observed earlier. The cross-sectional analysis in the CARDIA (Coronary Artery Risk Development in Young Adults) study among 18- to 30-year-old black and white subjects found an inverse age- and BMI-adjusted association between fiber and fasting serum insulin among white women (3), and, in the 10-year follow-up, fiber intake predicted insulin levels (30). Among normoglycemic lean and obese subjects, dietary fiber intake was positively associated with insulin sensitivity and inversely with fasting glucose concentrations (4); fiber intake accounted for 18% of the variance in insulin sensitivity, but the significance of the association was removed after adjustment for BMI. In a cross-sectional study of elderly nondiabetic men, the intake of total dietary fiber was inversely associated with insulin levels and fasting C-peptide (5). The effect of dietary fiber on insulin levels, when comparing lowest and highest quartiles, was assessed to be of similar magnitude as physical activity. In the ARIC (Atherosclerosis Risk in Communities) study (6) population of nondiabetic middle-aged subjects, an inverse association between dietary fiber and fasting serum insulin was observed among women. A 7-g/day higher intake of fiber was associated with a 2.9% lower fasting insulin level. Thus, both our study and earlier findings suggest that fiber intake and insulin resistance are inversely related.

In accordance with our data, previous cross-sectional studies (8,31,32) have not found an association between fiber intake and glucose tolerance. Among middle-aged and elderly nondiabetic men, total dietary fiber was not associated with fasting glucose or with the incremental area under the glucose curve (IAUC) (31). The intake of pectin, a water-soluble fraction of fiber, however, was inversely associated with the IAUC. The reduced pectin intake during a 10-year follow-up was also inversely associated with the IAUC (31). In a cross-sectional analysis in the San Luis Valley Diabetes Study population, dietary fiber did not have an effect on glucose tolerance independent of fat intake (8). The subsequent detailed analysis of dietary fiber and glucose metabolism in that population found that *1*) the recalled intake of dietary fiber before the diagnosis of type 2 diabetes was directly related to the disease, *2*) current fiber intake and fasting plasma insulin concentration were inversely associated among subjects without a history of diabetes (fiber explaining <1% of the variation in fasting insulin), and *3*) the intake of dietary fiber was not associated with newly diagnosed diabetes (32). The authors concluded that the weak and inconsistent findings did not support the hypothesis that increasing dietary fiber intake would reduce occurrence of diabetes. However, the inverse association between dietary fiber and fasting insulin concentration was confirmed in a longitudinal analysis of the population (33). The association was strongest in lean subjects.

Three studies have assessed associations between fiber intake and diabetes in high-risk populations: Among the Nauruan population, fiber intake was unrelated to the prevalence and incidence of type 2 diabetes, although the small number of subjects with newly diagnosed diabetes precluded firm conclusions on future diabetes risk (10). A study in Papua New Guinea (11) found a weak direct association between dietary fiber and newly diagnosed type 2 diabetes. In contrast, among a remote aboriginal community in Ontario, a high intake of dietary fiber was found to be associated with reduced risk of newly diagnosed diabetes (34).

Earlier prospective studies investigating a relationship between fiber and diabetes risk did not show a role for fiber. In normoglycemic elderly men and women, dietary fiber was not associated with the 4-year incidence of glucose intolerance (7). However, future cases of glucose intolerance had a lower intake of legumes, which have a high content of water-soluble fibers. In the 6-year follow-up of the U.S. Nurses' Health Study, the dietary fiber intake, whether evaluated as total intake or as contributions from fruits, vegetables, and cereals, was not related to the risk of type 2 diabetes (9). In the 20-year follow-up of the Finnish and Dutch cohorts of the Seven Countries Study in men, a borderline significant inverse association between past total fiber intake and 2-h glucose level was observed (12). However, later studies have yielded more promising results: in another 6-year follow-up in U.S. nurses (14), total dietary fiber intake and especially cereal fiber (mostly insoluble) were inversely related to the risk of type 2 diabetes, although fruit and vegetable fiber (mostly soluble) showed no association. In the 6-year follow-up of U.S. male health professionals (13), only cereal dietary fiber intake, but not total or fruit and vegetable fiber, was inversely associated with the risk of type 2 diabetes. In a cohort of older women in a 6-year follow-up, the intake of total and insoluble fiber, but not of soluble fiber, was inversely associated with the incidence of diabetes (17). Women in the highest quintile of fiber intake (median 27 g/day) had a 22% lower risk of developing diabetes than women in the lowest quintile (13 g/day). Thus, recent findings from prospective cohort studies suggest that a high intake of dietary fiber, and perhaps especially insoluble fiber, is associated with reduced diabetes risk.

Mechanisms linking dietary fiber with glucose metabolism are unclear but there are likely many. First, the effects of dietary fiber on insulin sensitivity might be mediated by obesity (4). Dietary fiber promotes food intake control (35). The physical and chemical properties of fiber aid in early signals of satiation and enhanced or prolonged signals of satiety, thus reducing total energy intake and adiposity (2,35). Second, the beneficial effects of fiber on glucose metabolism may be the result of delayed gastric emptying rate and slowed digestion and absorption of food, thereby reducing the rate of glucose absorption and plasma insulin levels (2,31). This effect has been attributed primarily to soluble fiber, which creates a gel-like substance in the stomach (15,16). Furthermore, fiber regulates several metabolic hormones that affect glucose metabolism (17,33). There is evidence that improvements in glucose homeostasis observed through the long-term high intake of dietary fiber may be explained by increased intestinal proglucagon gene expression (36,37). Proglucagon encodes several proglucagon-derived peptides known to modulate intestinal absorption capacity and pancreatic insulin secretion

(37). Finally, a concomitant intake of other dietary components that affect glucose metabolism and are highly correlated with fiber, e.g., chromium, magnesium, and manganese, may contribute to these beneficial effects. Bakker et al. (38) found that part of the association between fiber intake and glucose tolerance was attributable to concomitant thiamin intake.

To conclude, we observed an independent positive association between the dietary intake of total as well as water-insoluble and water-soluble fiber and enhanced insulin sensitivity in this population at high risk for type 2 diabetes. When gathering the data, special emphasis was placed to receive representative and accurate dietary data. In addition, we were able to adjust for relevant dietary and clinical factors in the analysis. The cross-sectional nature of the study, however, precludes interpreting the association as a causal one. Nevertheless, results support earlier evidence, suggesting a role for dietary fiber in insulin sensitivity and, therefore, in prevention of type 2 diabetes (39,40).

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