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Associations Between Dietary Fiber and Inflammation, Hepatic Function, and Risk of Type 2 Diabetes in Older Men

Potential mechanisms for the benefits of fiber on diabetes risk

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OBJECTIVE — To examine the relationship between dietary fiber and the risk of type 2 diabetes in older men and the role of hepatic and inflammatory markers.

RESEARCH DESIGN AND METHODS — The study was performed prospectively and included 3,428 nondiabetic men (age 60–79 years) followed up for 7 years, during which there were 162 incident cases of type 2 diabetes.

RESULTS — Low total dietary fiber (lowest quartile ≤20 g/day) was associated with increased risk of diabetes after adjustment for total calorie intake and potential confounders (relative risk −1.47 [95% CI 1.03–2.11]). This increased risk was seen separately for both low cereal and low vegetable fiber intake. Dietary fiber was inversely associated with inflammatory markers (C-reactive protein, interleukin-6) and with tissue plasminogen activator and γ-glutamyl transferase. Adjustment for these markers attenuated the increased risk (1.28 [0.88–1.86]).

CONCLUSIONS — Dietary fiber is associated with reduced diabetes risk, which may be partly explained by inflammatory markers and hepatic fat deposition.

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Several prospective cohort studies have observed a protective effect of dietary fiber on the risk of type 2 diabetes (1–4). However, this has not been observed in all studies (4), and the biological mechanisms by which dietary fiber may be beneficial for diabetes are unclear. Several studies have shown inverse associations between dietary fiber and markers of inflammation, insulin sensitivity, and hepatic function (5–8), factors that have been linked to the development of diabetes in other studies (9). It has been suggested that dietary fiber may reduce diabetes risk through its effect on hepatic function and insulin sensitivity or by mediating the proinflammatory process (5,6). However, these possibilities have not been examined in detail. We assessed the prospective relationship between dietary fiber and the risk of type 2 diabetes in older men and evaluated whether this relationship is associated with serum inflammatory marker (interleukin-6 [IL-6] and C-reactive protein [CRP]) levels and hepatic function (γ-glutamyl transferase [GGT]).

RESEARCH DESIGN AND METHODS

— The British Regional Heart Study is a prospective study of cardiovascular disease involving 7,735 men (age 40–59 years), drawn from general practices in each of 24 British towns, who were screened between 1978 and 1980 (10). In 1998–2000, 4,252 men (77% of survivors now age 60–79 years) attended a 20th-year follow-up examination. All relevant local research ethics committees provided approval. All men have been followed up for all-cause mortality, cardiovascular morbidity, and development of type 2 diabetes from initial examination to July 2006 (11); follow-up has been achieved for 99% of the cohort. This analysis is based on follow-up from rescreening in 1998–2000, a mean follow-up period of 7 years (range 6–8). At rescreening the men completed a questionnaire that included questions on their medical history and lifestyle behavior and provided a fasting blood sample. Anthropometric measurements including body weight, height, and waist circumference were carried out. Details of measurement and classification methods for smoking status, physical activity, social class, blood pressure, HDL cholesterol, triglycerides and blood glucose, and hemostatic and inflammatory markers in this cohort have been described (12–13). Insulin resistance was estimated according to the homeostasis model assessment (HOMA) (14).

Dietary assessment

Dietary intake was assessed using a detailed validated 7-day recall food frequency questionnaire, developed for use in the World Health Organization MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease) surveys and later used in the Scottish Heart Health Study (15). Nutrient intakes were calculated using a validated program that multiplied the food frequency by the standard portion sizes for each food and by the nutrient composition of the foods obtained from the U.K. food composition tables.

Study subjects

Dietary intake and blood measurements were available for 3,891 men studied in 1998–2000. Men with prevalent diabetes (those with a doctor's diagnosis of diabetes, those diagnosed with diabetes in the

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Table 1—*Dietary total fiber and mean levels of biological risk markers and adjusted relative risk of type 2 diabetes by quartiles of total, cereal, and vegetable/fruit fiber intake*

	Quartiles of total fiber (g/day)					*P* for trend
	1 (≤20)	2 (20.1–24.9)	3 (25.0–30.9)	4 (31.0+)		
n	864	854	841	869		
Systolic blood pressure (mmHg)	148.4	148.0	148.9	148.3		0.96
Triglycerides (mmol/l)*	1.63	1.58	1.57	1.57		0.04
HDL cholesterol (mmol/l)	1.34	1.32	1.34	1.34		0.79
Glucose (mmol/l)*	5.53	5.53	5.53	5.53		0.94
HOMA	0.68	0.72	0.69	0.63		0.05
GGT (IU/dl)*	30.6	28.2	26.0	25.8		<0.0001
ALT (IU/dl)	15.3	15.3	15.6	15.6		0.40
CRP (mg/l)*	2.14	1.70	1.60	1.35		<0.0001
IL-6 (pg/ml)*	2.80	2.36	2.34	2.16		<0.0001
t-PA (ng/ml)	11.7	11.1	10.4	10.1		<0.0001
Total fiber (quarters)					Low (≤20 g/day) vs. rest	
Diabetes rate/1,000 person-years (*n*)	9.5 (54)	7.7 (41)	5.4 (30)	6.5 (37)		
Relative risk (95% CI)						
Age adjusted	1.00	0.72 (0.48–1.17)	0.53 (0.34–0.83)	0.63 (0.42–0.96)	1.60 (1.15–2.21)	
A	1.00	0.68 (0.44–1.04)	0.59 (0.37–0.95)	0.82 (0.51–1.32)	1.47 (1.03–2.11)	
B	1.00	0.70 (0.45–1.07)	0.61 (0.38–0.98)	0.83 (0.52–1.13)	1.43 (1.00–2.02)	
C	1.00	0.70 (0.46–1.03)	0.64 (0.40–0.97)	0.86 (0.50–1.20)	1.39 (0.97–1.99)	
D	1.00	0.76 (0.49–1.18)	0.69 (0.43–1.13)	0.95 (0.59–1.53)	1.28 (0.88–1.86)	
Cereal fiber (quarters)					Low (<6.9 g/day) vs. rest	
Diabetes rate/1,000 person-years (*n*)	10.0 (55)	6.9 (38)	6.1 (35)	6.1 (34)		
Relative risk (95% CI)						
Age adjusted	1.00	0.69 (0.46–1.05)	0.61 (0.40–0.94)	0.56 (0.37–0.86)	1.61 (1.16–2.23)	
A	1.00	0.75 (0.48–1.17)	0.64 (0.41–1.02)	0.70 (0.44–1.12)	1.43 (1.00–2.06)	
B	1.00	0.76 (0.50–1.19)	0.65 (0.41–1.03)	0.71 (0.44–1.14)	1.42 (0.98–2.04)	
C	1.00	0.77 (0.49–1.20)	0.66 (0.42–1.05)	0.72 (0.45–1.16)	1.39 (0.97–2.04)	
D	1.00	0.79 (0.51–1.24)	0.71 (0.45–1.13)	0.76 (0.47–1.22)	1.32 (0.91–1.91)	
Vegetable fiber (quarters)					Low (<11.3 g/day) vs. rest	
Diabetes rate/1,000 person-years (*n*)	10.3 (61)	7.2 (42)	5.7 (32)	5.9 (34)		
Relative risk (95% CI)						
Age adjusted	1.00	0.71 (0.47–1.06)	0.55 (0.36–0.85)	0.57 (0.37–0.88)	1.64 (1.18–2.29)	
A	1.00	0.83 (0.55–1.27)	0.59 (0.37–0.93)	0.74 (0.46–1.19)	1.40 (0.98–1.98)	
B	1.00	0.84 (0.55–1.29)	0.60 (0.38–0.94)	0.76 (0.49–1.22)	1.38 (0.97–1.95)	
C	1.00	0.87 (0.57–1.32)	0.60 (0.38–0.95)	0.75 (0.51–1.21)	1.36 (0.96–1.94)	
D	1.00	0.93 (0.61–1.42)	0.63 (0.39–0.99)	0.83 (0.50–1.31)	1.28 (0.89–1.82)	

Data are means or *geometric means, as shown, unless otherwise indicated. A, adjusted for age, waist circumference, cigarette smoking, physical activity, social class, alcohol intake, preexisting myocardial infarction, stroke, use of statins, and total calorie intake; B, adjusted for A and IL-6; C, adjusted for A and IL-6 and t-PA; D, adjusted for A and IL-6, t-PA antigen, and GGT. Low = bottom quartile of the fiber distribution, rest = 2nd–4th quartile.

year of reexamination, and those with a fasting glucose of ≥7 mmol/l) were excluded (n = 463), leaving 3,428 men for analysis.

Mortality and incident diabetes cases

Information on deaths was collected through the established "tagging" procedures provided by the National Health Service registers. Evidence regarding diabetes was obtained from reports by general practitioners through biennial reviews of the patients' notes (including hospital and clinic correspondence) through to the end of the study period. Cases are based on self-reported diagnoses confirmed by primary care records, an approach that has been validated in the present study.

Statistical methods

The men were divided by quartiles of total, cereal, and fruit/vegetable fiber intake. The Cox's proportional hazards model was used to assess the multivariate-adjusted relative risk for each quartile compared with the reference group (lowest quartile). In the adjustment, waist circumference, total calorie intake, GGT, IL-6, and tissue plasminogen activator (t-

PA) were fitted as continuous variables; all other confounders were fitted as categorical variables.

RESULTS — During the mean 7-year follow-up, there were 162 incident type 2 diabetes cases in the 3,428 men with no prevalent diabetes. The mean ± SD intake of total fiber by these men was 25.9 ± 8.6 g/day.

Total fiber intake was significantly and inversely associated with markers of inflammation (CRP, IL-6, t-PA) and GGT (but not alanine aminotransferase), and these relationships persisted after adjustment for age, waist circumference, and possible confounders. Weak associations were seen with triglyceride and HOMA of insulin resistance, which was attenuated after adjustment for waist circumference. No associations were seen with blood pressure, HDL cholesterol, or blood glucose (Table 1).

Low total fiber and cereal fiber intake were associated with significantly increased risk of diabetes after adjustments for demographic factors and total calorie intake; the increased risk associated with low fruit/vegetable fiber intake was of marginal significance ($P = 0.06$) (Table 1). Further adjustments for IL-6 and t-PA attenuated the associations, and the increased risk was of marginal significance ($P = 0.07$, $P = 0.08$, and $P = 0.08$ for total, cereal, and fruit/vegetable fiber, respectively). Simultaneous adjustments for IL-6, t-PA, and GGT attenuated the associations further, and the increased risks were no longer significant.

CONCLUSIONS — In this study of older men (age 60–79 years), low dietary fiber intake (≤20 g/day) was associated with significantly increased risk of diabetes. Our findings support the presence of an inverse association between dietary fiber (including both cereal and vegetable/fruit fiber) and risk of diabetes as observed in previous studies (1–3) and add insights into the potential mechanisms by which fiber intake may lessen diabetes risk. We have observed that a diet high in fiber is associated with reduced inflammation (IL-6 and CRP) and decreased GGT (a marker of hepatic fat deposition) as well as t-PA; all these factors have been shown to be strong predictors of diabetes (9). Adjustments for these factors attenuated the increased risk associated with low dietary fiber intake. We cannot establish the nature of the association between fiber intake and hepatic function and the inflammatory process. The data suggest that a high-fiber diet (at least 20 g fiber/day) in older men may reduce the risk of diabetes, and this appears to be partly explained by its favorable association with hepatic (fat) function and inflammatory processes. This study was carried out in a predominantly white European male population, and further studies are required in women and other ethnic groups.

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