Potential mechanisms for the benefits of fiber on diabetes risk

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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Dietary fiber and type 2 diabetes

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) | 1 (≤20) | 2 (20.1–24.9) | 3 (25.0–30.9) | 4 (31.0+) | P for trend
|-----------------|--------|--------------|--------------|-----------|------------|
| n               | 864    | 854          | 841          | 869       | 0.96       |
| Systolic blood pressure (mmHg) | 148.4  | 148.0        | 148.9        | 148.3     | 0.04       |
| Triglycerides (mmol/l)* | 1.63   | 1.58         | 1.57         | 1.57      | 0.79       |
| HDL cholesterol (mmol/l) | 1.34   | 1.32         | 1.34         | 1.34      | 0.05       |
| Glucose (mmol/l)* | 5.53   | 5.53         | 5.53         | 5.53      | 0.94       |
| HOMA             | 0.68   | 0.72         | 0.69         | 0.63      | <0.0001    |
| 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) | 864    | 854          | 841          | 869       |            |
| Diabetes rate/1,000 person-years (n) | 9.5 (54) | 7.7 (41) | 5.4 (30) | 6.5 (37) |
| Relative risk (95% CI) | 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) |
| Age adjusted     | 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) |
| A                | 1.00   | 0.70 (0.45–1.07) | 0.61 (0.38–0.98) | 0.83 (0.52–1.33) | 1.43 (1.00–2.02) |
| B                | 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) |
| C                | 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) |
| D                | 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) |
| Cereal fiber (quarters) | 10.0 (55) | 6.9 (38) | 6.1 (35) | 6.1 (34) |            |
| Diabetes rate/1,000 person-years (n) | 10.0 (55) | 6.9 (38) | 6.1 (35) | 6.1 (34) |            |
| Relative risk (95% CI) | 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) |
| Age adjusted     | 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) |
| A                | 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) |
| B                | 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) |
| C                | 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) |
| D                | 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) |
| Vegetable fiber (quarters) | 10.3 (61) | 7.2 (42) | 5.7 (32) | 5.9 (34) |            |
| Diabetes rate/1,000 person-years (n) | 10.3 (61) | 7.2 (42) | 5.7 (32) | 5.9 (34) |            |
| Relative risk (95% CI) | 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) |
| Age adjusted     | 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) |
| A                | 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) |
| B                | 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-
produced inflammation (IL-6 and CRP) and diet high in fiber is associated with risk of diabetes. We have observed that a fiber intake of 25.9 ± 8.6 g/day was inversely associated with risk of diabetes as observed in previous studies (1–3) and for IL-6, t-PA, and GGT attenuated the associations further, and the increased risk associated with marginal significance (P = 0.08) (Table 1). Further adjustments for IL-6, t-PA attenuated the associations, and the increased risk of diabetes after adjustments 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 = 0.07, 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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References

1. Schulze MB, Schulz M, Heidemann C, Schienkiewitz A, Hoffmann K, Boeig H. Fiber and magnesium intake and incidence of type 2 diabetes: a prospective study and meta-analysis. Arch Intern Med 2007;167:956–965
2. Meyer KA, Kushi LH, Jacobs DR Jr, Slavin J, Sellers TA, Folsom AR. Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. Am J Clin Nutr 2000;71:921–930
3. Barclay AW, Flood VM, Rochtchina E, Mitchell P, Brand-Miller J.C. Glycemic index, dietary fiber, and risk of type 2 diabetes in a cohort of older Australians. Diabetes Care 2007;30:2811–2813
4. Hodge AM, English DR, O’Dea K, Giles G. Glycemic index and dietary fiber and the risk of type 2 diabetes. Diabetes Care 2004;27:2701–2706
5. Weickert MO, Pfeiffer AF. Metabolic effects of dietary fiber consumption and prevention of diabetes. J Nutr 2008;138:439–442
6. Galisteo M, Duarte J, Zarzuelo A. Effects of dietary fibers on disturbances clustered in the metabolic syndrome. J Nutr Biochem 2008;19:71–84
7. Herder C, Peltonen M, Koening W, Sutels K, Lindstrom J, Martin S, Ilanne-Parikka P, Eriksson JG, Aurnola S, Keinanen-Kiukaanniemi S, Valle TT, Uusitupa M, Kolb H, Tuomilehto J. Finnish Diabetes Prevention Study Group. Anti-inflammatory effect of lifestyle changes in the Finnish Diabetes Prevention Study. Diabetologia. 2009;52:433–442
8. Bo S, Durazzo M, Guidi S, Carello M, Sacchidone C, Silli B, Rosato R, Cassader M, Gentile L, Pagano G. Dietary magnesium and fiber intake and inflammatory and metabolic indicators in middle-aged subjects from a population-based cohort. Am J Clin Nutr 2006;84:1062–1069
9. Sattar N, Wannamethee SG, Forouhi NG. Novel biochemical risk factors for type 2 diabetes: pathogenic insights or prediction possibilities? Diabetologia 2008;51:926–940
10. Shaper AG, Pocock SJ, Walker M, Cohen NM, Wale CJ, Thomas AG. British Regional Heart Study: Cardiovascular risk factors in middle-aged men in 24 towns. Br Med J (Clin Res Ed) 1981;283:179–186
11. Walker M, Shaper AG, Lennon L, Whincup PH. Twenty year follow-up of a cohort based in general practices in 24 British towns. J Public Health Med 2000;22:479–485
12. Wannamethee SG, Lowe GD, Whincup PH, Rumley A, Walker M, Lennon L. Physical activity and hemostatic and inflammatory variables in elderly men. Circulation 2002;105:1785–1790
13. Emberson JR, Whincup PH, Walker M, Thomas M, Alberti KG. Biochemical measures in a population-based study: effect of fasting duration and time of day. Ann Clin Biochem 2002;39:493–501
14. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412–419
15. Bolton-Smith C, Casey CE, Geg KF, Smith WC, Tuntiell-Pedoe H. Antioxidant vitamin intakes assessed using a food-frequency questionnaire: correlation with biochemical status in smokers and non-smokers. Br J Nutr 1991;65:337–346

Wannamethee and Associates