Dietary Fiber Reduces Peripheral Arterial Disease Risk in Men[1]

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ABSTRACT We prospectively evaluated the relationship between dietary fiber and peripheral arterial disease risk (PAD) among 46,032 men, aged 40 to 75 y, in 1986. Subjects answered a vascular disease questionnaire and completed a validated 131-item food frequency questionnaire, and were free of PAD, cardiovascular disease and diabetes. During 12 y of follow-up 308 incident PAD cases were documented. After adjusting for age, smoking, hypertension, hypercholesterolemia, family history of early coronary heart disease, alcohol consumption, BMI, physical activity and energy intake, PAD risk in each quintile of cereal fiber intake compared with the lowest quintile was 0.69, 95% CI 0.49–0.97 for quintile 2; 0.65, 95% CI 0.45–0.94 for quintile 3; 0.68, 95% CI 0.47–0.98 for quintile 4; and 0.67, 95% CI 0.47–0.97 for quintile 5. In a nonlinear model the overall inverse association ($P = 0.02$) and nonlinear components ($P = 0.03$) were significant. Fruit, vegetable and total fiber intakes were not associated with PAD risk. These results suggest an inverse association between cereal fiber intake and PAD risk in men. Increasing cereal fiber intake may prevent PAD. J. Nutr. 133: 3658–3663, 2003.

KEY WORDS: • *dietary fiber* • *peripheral arterial disease* • *cereal fiber* • *prospective study*

Peripheral arterial disease (PAD)[3] is a major cause of morbidity, and people with PAD are more than four times as likely to die of any cause over 2 y from diagnosis than those without (1). Severe disease often requires surgery, including limb amputation, and operative mortality is high (2). PAD results mainly from atherosclerotic narrowing of the blood vessel lumen and shares some risk factors with coronary heart disease (CHD) and stroke, including diabetes (3), hypertension (4) and cigarette smoking (5). There is little direct evidence, however, for the role of diet. An inverse association between fiber and PAD has been suggested in a cross-sectional study (6), a case-control study (7) and a cohort study conducted among Finnish smokers (8). This is biologically plausible because soluble fiber reduces LDL (9). Cereal fiber intake specifically has been inversely associated with the risk of CHD (10) and diabetes (11), and has been shown to favorably impact total cholesterol, LDL and fasting serum insulin (12). Therefore, we prospectively examined the association of dietary fiber intake with incident PAD in a large cohort of men followed for 12 y.

MATERIALS AND METHODS

Study population. The Health Professionals Follow-up Study began in 1986 when 51,529 U.S. male health professionals, aged 40 to 75 y, volunteered to participate in the study (29,683 dentists, 4185 pharmacists, 3745 optometrists, 1600 podiatrists and 10,098 veterinarians; 531 African-American and 877 Asian-American) (13). The participants received questionnaires at baseline and biennially to determine lifestyle and medical conditions, and validated food frequency questionnaires (FFQ) every 4 y to determine diet.

We excluded men with a history of PAD, CHD, stroke and diabetes, because they may have changed their diets following disease, and men with inadequate dietary data (reported energy intake <3352 or >17598 kJ, or >70 unanswered of 131 items in the FFQ) (14) resulting in 46,032 men in this analysis. The study was approved by the Human Subjects Committee of the Harvard School of Public Health.

Case ascertainment. If a participant reported intermittent claudication or surgery for PAD during follow-up, we requested permission to review his medical record to confirm the diagnosis and the date of occurrence of the disease. Cases of PAD were considered definite if the medical record contained either a report of surgery for PAD, ankle systolic blood pressure index (ABPI) < 0.80, a physician diagnosis, or an angiogram or Doppler ultrasound reporting 50% or more obstruction of at least one artery plus symptoms in the ipsilateral limb. Participants who confirmed the diagnosis of PAD by letter or over the telephone, but without available medical records, were considered probable PAD cases.

Diet and exposure information. Diet was assessed by a validated FFQ every 4 y starting in 1986 (14). For each food the FFQ contains a commonly used unit or portion, e.g., one apple or one cup of cooked spinach. The respondent was requested to estimate how often on average he consumed a unit or portion during the previous year.

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[3] Abbreviations used: ABPI, ankle brachial blood pressure index; CHD, coronary heart disease; FFQ, food frequency questionnaire; MET, metabolic equivalents; PAD, peripheral arterial disease; RR, relative risk.

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There were nine possible responses, ranging from never or less than once a month up to six or more times per day. Nutrient (including fiber) intake was estimated by multiplying the mean nutrient content of the specified unit or portion by the number of times it was consumed (14). The nutrient content of foods was estimated from the Harvard University Food Composition Database that is derived from USDA sources, manufacturers' information and data from peer-reviewed literature. Whole grain foods classified as described by Jacobs et al. (15) and Liu et al. (16), included brown rice, dark breads, whole grain breakfast cereal, cooked cereal, popcorn, wheat germ, bran and other grains. The validity of the FFQ has been described elsewhere (14). When compared with diet records the FFQ was found to be a good measure of breakfast cereal intakes ($r = 0.86$), dark bread ($r = 0.77$) (17) and dietary fiber ($r = 0.68$) (14). Fiber intakes for total energy were adjusted by regression analysis as described elsewhere (18). Briefly, we calculated a residual from a linear regression model with fiber as the dependent variable and total energy as the independent variable. The residual was added to the mean fiber intake for that population. Energy-adjusted intake of cereal fiber, for example, was interpreted as the composition of cereal fiber in the diet independent of the total quantity of food eaten.

The enrollment and follow-up questionnaires requested information on age, smoking, diagnosed or treated hypertension, hypercholesterolemia, angina, supplement use, weight and physical activity. Subjects were asked the average amount of time they spent per week on various physical activities including walking, jogging, running, bicycling, calisthenics, aerobics, machine rowing, swimming, squash, racquetball and tennis. From this information weekly energy expenditure in metabolic equivalent task-hours (MET) were calculated. BMI was computed by dividing weight (kg) by the squared height (m^2) for every 2-y follow-up period.

Statistical analysis. We considered mean intakes of fiber from all dietary assessments before the date of first report of PAD. PAD incidence between each questionnaire cycle was related to the mean dietary intake before that period (19). For example, disease incidence from 1986 to 1988 was related to the intake measured in 1986, and disease incidence from 1990 to 1992 was related to the mean intake from 1986 to 1990. Using this approach long-term diet was assessed and within person error was reduced. Diet update was stopped during follow-up if a person developed heart disease, stroke or had coronary artery by-pass surgery because the diet would change as a result of the condition or procedure. If dietary data were missing for one questionnaire we used the value derived from the preceding questionnaire. Fiber intake was evaluated as a continuous variable and in quintiles. The distribution of potential confounders across categories of fiber intakes was compared.

Person time was calculated for each participant from the return date of the questionnaire in 1986 to the date of report of PAD, death or the end of follow-up, whichever came first. Deaths were reported by family members, the Postal Service or ascertained through state registries or the National Death Index. The ascertainment of death was >98% complete (20). We measured incidence rates of PAD by quintiles of nutrient intakes stratifying by age and smoking using the Mantel-Haenszel method (21). The Cox proportional hazard model with failure time measured in age (mo) in the multivariate analysis was used to estimate the relative risks (RR) and 95% CI of PAD. In the multivariate analysis age was controlled for in months, smoking (never smokers, past smokers who had smoked for <20, 20–30 and >30 y, and current smokers who smoked 1–14, 15–24 or ≥25 cigarettes per day), BMI (<21, 21–22.9, 23–24.9, 25–29.9 and 30+ kg/m^2), alcohol use (never, 0.1–4.9, 5.0–14.9 15.0–29.9 and 30+ g/d), and physical activity (quintiles of MET), hypertension, hypercholesterolemia, family history of heart disease (dichotomous variables) and total energy (continuous). Diabetics were excluded. The analyses excluding probable cases were repeated. Tests for trend were completed with the Mantel extension test using the median value of the quintiles.

Fiber intake at baseline, mean whole grain intake (main source of cereal fiber in the diet) and soluble and insoluble fiber in relation to PAD risk were also evaluated. To assess possible confounding by other factors in the diet, the associations between cereal fiber and PAD risk for intakes of fruits and vegetables, types of fats, magnesium, vitamins E and C and folic acid (including supplements) were adjusted. Cereal fiber contains magnesium, the intake of which is associated with improved insulin action (22). Men eating more fiber were also more likely to consume more micronutrients associated with PAD risk (23). To detect possible interactions, analyses were conducted stratified by age (<65 and ≥65 y), supplemental vitamin E use, smoking (never smokers and ever smokers), BMI (<25 and ≥25 kg/m^2), hypertension, hypercholesterolemia, a family history of early myocardial infarction and physical activity. Tests for interaction were conducted by the likelihood ratio method, comparing models with and without the interaction terms. The possibility of a nonlinear association between cumulatively averaged cereal fiber intake and PAD risk, adjusted for confounders, was evaluated using restricted cubic splines (24,25). Splines are regression models evaluating nonlinear associations between exposure and outcome adjusting for confounders and allowing for graphic representation of the results (24).

RESULTS

There were 308 incident cases of PAD in 12 y of follow-up. Of the 223 definite cases 113 (51%) had surgery, 58 (26%) had ABPI < 0.80, 47 (21%) had a physician's diagnosis and 7 (3%) had abnormal Doppler ultrasound results. In 73 of the 85 probable cases we received a note confirming the diagnosis; the remaining 12 were confirmed over the telephone. Because the results were consistent after excluding the probable cases, they were included in all analyses.

The median baseline intakes in the lowest and highest quintiles ranged from 13.4 to 29.6 g/d for total fiber and 2.5 to 10.2 g/d for cereal fiber. A bran muffin, for example, contains ~2.8 g of fiber (26). Men in the top quintile of total fiber intake were less likely to smoke, more likely to be nondrinkers, slightly leaner and exercised more than those in the bottom quintile. They were more likely to take vitamin C, E and vitamin supplements, and to eat less monounsaturated, saturated and *trans* fat. The trends were similar for cereal fiber (**Table 1**).

The age-adjusted rate of PAD declined with increasing cumulatively averaged total fiber intake, but this association was attenuated and no longer significant after adjustment for smoking (**Table 2**). Further adjustment for hypertension, hypercholesterolemia, family history of early cardiovascular disease, BMI, physical activity, alcohol intake, total energy and length of smoking did not change the results substantially (Table 2). Similar results were obtained using total fiber intake measured at baseline, and for fruit and vegetable fiber.

Cereal fiber intake was inversely associated with the risk of PAD when adjusted for age (Table 2). The association attenuated with further adjustment for smoking, but strengthened with multivariate adjustment. Men in the top quintile of cumulatively averaged cereal fiber intake had a 33% lower rate of PAD (RR = 0.67, 95% CI, 0.47–0.97, $P = 0.07$) compared with men in the bottom quintile in the multivariate model (Table 2). The multivariate model with cereal fiber measured at baseline was similar. The association between cereal fiber intake and PAD risk was nonlinear in the multivariate cubic spline model ($P = 0.02$) and significant ($P = 0.03$) (**Fig. 1**). The maximum risk reduction was at ~5 g/d intake of cereal fiber and higher intakes did not appear to further reduce risk.

Further adjustment for dietary intakes of vitamins E and C, folate, vitamin supplements, total magnesium, dietary lipids, fruits and vegetables did not change the results. Whole grain intake, the main source of cereal fiber in the diet, was inversely associated with the risk of PAD (RR = 0.67, 95% CI 0.47–1.06 comparing the top with the bottom quintiles, $P = 0.05$). Insoluble fiber was inversely associated with PAD risk (RR = 0.53, 95% CI 0.35–0.79 comparing extreme quintiles, P

TABLE 1

Baseline characteristics of men in the highest and lowest quintile categories of energy-adjusted total and cereal fiber intakes in a prospectively evaluated study of the relationship between dietary fiber and peripheral arterial disease

	Total fiber		Cereal fiber	
	Quintile 1 13.4 g/d	Quintile 5 29.6 g/d	Quintile 1 2.5 g/d	Quintile 5 10.2 g/d
Subject characteristics				
Current smoker, %	19.6	3.8	18.1	4.4
Family history of myocardial infarction, %	12.0	12.1	11.9	12.2
Hypertension, %	20.0	21.8	23.8	20.0
Hypercholesterolemia, %	8.8	14.4	9.6	13.7
Vitamin E supplement, %	37.3	53.0	38.6	50.7
Vitamin C supplement, %	45.5	62.0	47.4	59.8
Multivitamin supplement, %	29.0	42.1	29.7	39.5
Median BMI, kg/m^2	25.2	24.4	25.5	24.4
Physical activity (MET)	7.8	17.7	9.1	15.1
Non-drinker, %	18.4	30.7	18.6	27.7
Median nutrient intake				
Vitamin C, *mg*	152	342	205	262
Vitamin B-6, *mg*	2.0	3.5	2.3	3.1
Folate, μg	290	510	331	460
Vitamin C from food, *mg*	107	208	144	160
Vitamin E, *mg*	9.4	15.5	11.0	12.8
Vitamin E from food, *mg*	8.3	11.3	9.5	10.0
Alpha carotene, μg	441	1270	585	685
Beta carotene, μg	2572	7259	3821	4558
Lycopene, μg	6079	11690	8548	8603
Lutein and zeaxanthine, μg	2044	4868	3035	3340
Total fiber, *g*	13.4	29.6	15.9	25.9
Cereal fiber, *g*	3.4	8.2	2.5	10.2
Fiber from fruit, *g*	1.7	6.9	2.9	4.5
Fiber from vegetables, *g*	4.2	9.8	5.9	6.6
Total saturated fat, *g*	27.9	19.4	27	21.2
Total monounsaturated fat, *g*	29.7	22.7	29.3	24.2
Total polyunsaturated fat, *g*	12.2	12.5	12.6	12.5
Trans-fat, *g*	3.1	2.0	2.7	2.4
Cholesterol, *mg*	321	242	322	249
Total energy intake, *kJ*	7879	7825	7724	7661

= 0.02), but not soluble fiber (RR = 0.77, 95% CI 0.53–1.12 comparing extreme quintiles, $P = 0.09$).

The test for interaction between cereal fiber intake and PAD was not significant among subgroups of age (<65 and ≥65 y, $P = 0.23$), smoking (never smokers and ever smokers, $P = 0.46$), and BMI (<25 and ≥25 kg/m^2, $P = 0.89$). The association between cereal fiber intake and PAD risk was stronger in men who took vitamin E supplements ($P = 0.02$) (**Table 3**). The relationship between cereal fiber intake and PAD risk did not change when the analysis was restricted to men who were physically inactive, and those without a history of hypertension, hypercholesterolemia or a family history of early myocardial infarction (data not shown).

DISCUSSION

In this large prospective investigation we found an inverse nonlinear relationship between cereal fiber intake and PAD risk. Recall bias would not explain these results because of the prospective study design, and selection bias is unlikely because the follow-up rate exceeded 90% (20). Dietary intake was estimated by a previously validated FFQ (14). To estimate fiber intake, the mean values assigned by the USDA or manufacturer for content in different types of foods were used. Therefore, there was some unavoidable misclassification of exposure, but being random would attenuate the effect on the results. We adjusted for a number of possible confounders in this study including dietary intakes of vitamins E and C, folate, vitamin supplements, total magnesium, dietary lipids, fruits and vegetables but the results did not materially change. Intakes of whole grain, the major dietary source of cereal and insoluble fiber, were also inversely associated with PAD risk. The inverse association with PAD was specific to cereal fiber and was not observe for fruit, vegetable or total fiber. Even though the numbers of cases were small in the stratified analyses, the inverse association persisted in men who were older and younger, lean and heavy. The association persisted when we excluded men with hypertension, hypercholesterolemia, family history of early heart disease, or restricted the analyses to physically inactive men. Because this was an observational study we cannot completely exclude the possibility of residual confounding, but for an unmeasured factor to explain these results it would have to be strongly associated with PAD, correlated with cereal fiber intake and prevalent in the source population. We cannot think of any such factor, so the chance that residual confounding explained these results is probably small. It is unlikely that the association between cereal fiber intake and PAD risk was due to residual confounding. Smoking is a strong risk factor for PAD but the relationship between cereal fiber intake and PAD risk was seen even in never-smokers (Table 3). Restricting the analyses to confirmed cases only did not materially change the conclusions.

TABLE 2

Association of cumulatively averaged energy-adjusted fiber intake and incidence of peripheral arterial disease in men (relative risks and 95% CI)

	Quintiles of intake					
	1	2	3	4	5	*P* value
Total fiber						
Median intake cumulatively averaged, *g/d*	13.9	17.5	20.4	23.7	29.6	
Age-adjusted cumulatively averaged intake	1.00	0.73 (0.52–1.01)	0.53 (0.37–0.75)	0.51 (0.36–0.72)	0.54 (0.38–0.76)	<0.001
Age- and smoking-adjusted cumulatively averaged intake	1.00	1.05 (0.71–1.56)	0.87 (0.58–1.31)	0.84 (0.56–1.27)	1.01 (0.67–1.51)	0.58
Multivariate adjusted cumulatively averaged[1]	1.00	0.91 (0.64–1.29)	0.73 (0.50–1.06)	0.74 (0.51–1.08)	0.83 (0.57–1.21)	0.27
Cereal fiber						
Median intake cumulatively averaged, *g/d*	2.7	4.1	5.4	7.1	10.3	
Age-adjusted cumulatively averaged intake	1.00	0.59 (0.43–0.82)	0.50 (0.35–0.70)	0.49 (0.35–0.69)	0.49 (0.35–0.68)	<0.001
Age- and smoking-adjusted cumulatively averaged intake	1.00	0.65 (0.45–0.96)	0.64 (0.43–0.94)	0.72 (0.49–1.04)	0.77 (0.53–1.12)	0.20
Multivariate adjusted cumulatively averaged[1]	1.00	0.69 (0.49–0.97)	0.65 (0.45–0.94)	0.68 (0.47–0.98)	0.67 (0.47–0.97)	0.07
Fruit fiber						
Median intake cumulatively averaged, *g/d*	1.4	2.6	3.9	5.4	8.2	
Age-adjusted cumulatively averaged intake	1.00	1.04 (0.73–1.48)	0.79 (0.55–1.16)	0.64 (0.43–0.95)	0.67 (0.46–0.98)	0.001
Age- and smoking-adjusted cumulatively averaged intake	1.00	1.35 (0.88–2.06)	1.30 (0.84–2.01)	1.03 (0.64–1.65)	1.20 (0.75–1.91)	0.87
Multivariate adjusted cumulatively averaged[1]	1.00	1.24 (0.86–1.79)	1.10 (0.82–1.76)	0.95 (0.63–1.43)	0.91 (0.61–1.36)	0.24
Vegetable fiber						
Median intake cumulatively averaged, *g/d*	3.5	4.9	6.3	7.9	11.2	
Age-adjusted cumulatively averaged intake	1.00	1.02 (0.72–1.45)	1.07 (0.76–1.49)	0.76 (0.53–1.10)	0.75 (0.52–1.07)	0.04
Age- and smoking-adjusted cumulatively averaged intake	1.00	1.08 (0.73–1.60)	1.21 (0.83–1.76)	0.95 (0.64–1.41)	0.95 (0.64–1.41)	0.54
Multivariate adjusted cumulatively averaged[1]	1.00	1.16 (0.81–1.66)	1.21 (0.85–1.73)	0.95 (0.64–1.39)	0.98 (0.67–1.43)	0.54

[1] Adjusted for age in months, smoking (never smokers, past smokers who had smoked for <20 years, 20–30 years and >30 years, and current smokers who smoked 1–14, 15–24, or ≥25 cigarettes per day), BMI (<21, 21–22.9, 23–24.9, 25–29.9 and 30+ kg/m^2), alcohol (never users, 0.1–4.9, 5.0–14.9, 15.0–29.9 and 30+ g/d), energy, physical activity (quintiles of metabolic equivalents), hypertension, hypercholesterolemia and family history of early heart disease (dichotomous variables).

The associations found between total and cereal fiber and PAD are similar to those found in the same cohort for CHD (10). These results are also consistent with those of a few previous investigations. In a cross-sectional study, Donnan et al. found higher ABPI, indicating less evidence of PAD, in men with higher cereal fiber intake in a randomly selected population, aged 55–74 y, after adjustment for age, sex, height, smoking and total energy (6). Katsoyanni et al. also found an inverse association between dietary fiber and PAD in a case-control study (odds ratio = 0.33, 95% CI 0.17–0.64) after adjusting for age, sex, years of schooling, smoking, alcohol and coffee intake and total energy (7). Finally, Tornwall et al. found an inverse association with PAD comparing the top to bottom quintile of fiber intake in a prospective study (RR = 0.87, 95% CI 0.77–0.97) in Finnish male smokers; separate estimates for cereal, fruit and vegetable fiber were not available (8). The main food source of dietary fiber in that study was rye bread so that the results are also probably due to cereal fiber. Our results demonstrate that it is important to evaluate the different types of fiber in relation to PAD risk because the associations vary considerably.

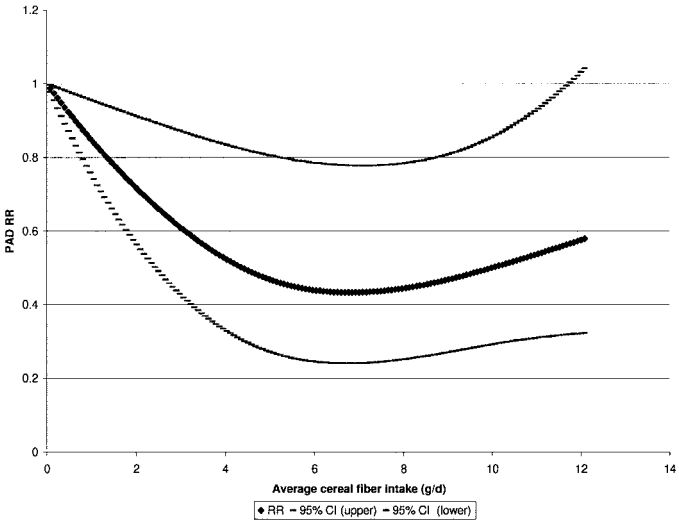

FIGURE 1 Multivariate association between cereal fiber intake and peripheral arterial disease (PAD) risk in men. RR, relative risk.

It has been hypothesized that the apparent protective effect of fiber intake against CHD is mediated by lowered cholesterol especially due to soluble fiber (9), and lowered plaminogen activator inhibitor type 1 and factor VII activity (27). PAD results mainly from atherosclerotic narrowing of the blood vessel lumen. LDL are taken up by monocytes in the intima of the blood vessels, becoming foam cells, and leading to the formation of plaque. Increased cytosolic triglycerides are associated with oxidative stress and can cause endothelial dysfunction (28). Thus, increased serum LDL and triglycerides increase the risk of PAD (29). Other factors that increase PAD risk are hypertension (4), smoking (5) and insulin resistance (29). It has been hypothesized that fiber intake improves insulin sensitivity by slowing the absorption of nutrients from the gut (30), reducing serum glucose levels (31), producing

TABLE 3

Subgroup analysis of cumulatively averaged energy-adjusted total fiber and cereal fiber intake and incidence of peripheral arterial disease in men (relative risks and 95% CI)[1]

		Quintiles of cereal fiber intake					
	n	1	2	3	4	5	*P* value
Median intake, *g/d*		2.7	4.1	5.4	7.1	10.3	
Age < 65 y	57	1.00	0.84 (0.55–1.28)	0.78 (0.50–1.23)	0.56 (0.33–0.94)	0.69 (0.42–1.13)	0.07
Age ≥ 65 y	251	1.00	0.45 (0.24–0.84)	0.52 (0.29–0.94)	0.72 (0.42–1.24)	0.64 (0.37–1.11)	0.52
No supplemental vitamin E	172	1.00	0.69 (0.44–1.12)	0.75 (0.46–1.23)	0.78 (0.47–1.29)	0.81 (0.49–1.34)	0.57
Supplemental vitamin E	136	1.00	0.73 (0.42–1.29)	0.61 (0.35–1.08)	0.55 (0.31–0.98)	0.57 (0.32–1.00)	0.07
Past and current smokers	215	1.00	0.71 (0.46–1.10)	0.73 (0.47–1.13)	0.89 (0.59–1.37)	0.74 (0.47–1.17)	0.39
Never smokers	74	1.00	0.55 (0.26–1.19)	0.67 (0.32–1.41)	0.35 (0.15–0.82)	0.62 (0.30–1.28)	0.27
BMI < 25, *kg/m*^{2}	120	1.00	0.76 (0.42–1.38)	0.63 (0.33–1.21)	0.34 (0.20–0.77)	0.78 (0.43–1.43)	0.34
BMI ≥ 25, *kg/m*^{2}	188	1.00	0.63 (0.40–0.98)	0.70 (0.45–1.10)	0.75 (0.48–1.17)	0.63 (0.39–1.04)	0.15

[1] Adjusted for age in months, smoking (never smokers, past smokers who had smoked for <20 years, 20–30 years, and >30 years, and current smokers who smoked 1–14, 15–24, or ≥25 cigarettes per day), BMI <21, 21–22.9, 23–24.9, 25–29.9 and 30+ kg/m^2, alcohol never users to those consuming 0.1–4.9, 5.0–14.9, 15.0–29.9, and 30+ g/d, energy, hypertension, hypercholesterolemia, family history of early heart disease, physical activity in quintiles of metabolic equivalents.

SCFA by gut bacteria and consequently improving glucose metabolism (32).

The inverse association between cereal fiber intake and PAD risk is probably not entirely due to serum cholesterol reduction. Serum cholesterol reduction from cereal fiber intake could not explain the observed 29% reduction in risk for CHD in this cohort (10). Because plasminogen activator inhibitor has not been implicated in the causation of PAD (33), the lower risk of PAD among men with high cereal fiber intake may in part be related to increased insulin sensitivity. Improved glucose metabolism is associated with lower LDL, blood pressure and triglycerides, and higher HDL (9). Each of these factors has been shown to be independently associated with PAD. Foods sources of cereal fiber also contain magnesium and chromium which are associated with improved insulin sensitivity (34,35), and folate which has been inversely associated with PAD risk (23).

Vitamin E has also been shown to prevent LDL oxidation and increase lipoprotein lipase activity (36). Therefore, it is plausible that vitamin E intake would enhance the association between cereal fiber and PAD risk. We observed a slightly stronger association between cereal fiber intake and PAD risk among men who took vitamin E supplements. The association between PAD and cereal fiber intake was not linear, both in the quintile and spline analyses. We observed a threshold of risk reduction at intakes of 5 g/d of cereal fiber. Liu et al. found a similar threshold for the association of whole grain and CHD in the fourth quintile of intake (median cereal fiber of quintile, 5 g/d) among never smokers (16). If the action of cereal fiber were the result of improved insulin-related mechanisms then its effect would be limited by the extent to which impaired glucose metabolism contributes to PAD. Glucose intolerance has been shown to have approximately a two-fold higher risk of PAD in men (4).

In conclusion, we observed that increased dietary cereal fiber intake in a population including smokers and nonsmokers was associated with reduced risk of PAD in men. Increasing cereal fiber in the diet could contribute to the prevention of PAD.

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