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Dietary fiber intake and retinal vascular caliber in the Atherosclerosis Risk in Communities Study[1,2,3]

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Abstract

Background—Dietary fiber appears to decrease the risk of cardiovascular morbidity and mortality. Microvascular abnormalities can be observed by retinal examination and contribute to the pathogenesis of various cardiovascular diseases. The impact of dietary fiber on the retinal microvasculature is not known.

Objective—We aimed to examine the association between dietary fiber intake and retinal vascular caliber.

Design—At the third visit (1993–1995) of the Atherosclerosis Risk in Communities (ARIC) Study, a population-based cohort of adults in 4 US communities, the retinal vascular caliber of 10 659 participants was measured and summarized from digital retinal photographs. Usual dietary intake during the same period was assessed with a 66-item food-frequency questionnaire.

Results—After control for potential confounders including hypertension, diabetes, lipids, demographic factors, cigarette smoking, total energy intake, micronutrients intake, and other cardiovascular disease risk factors, higher intake of fiber from all sources and from cereal were significantly associated with wider retinal arteriolar caliber and narrower venular caliber. Participants in the highest quintile of fiber intake from all sources had a 1.05-μm larger arteriolar caliber (*P* for trend = 0.012) and a 1.11-μm smaller venular caliber (*P* for trend = 0.029).

Conclusions—Dietary fiber was related to wider retinal arteriolar caliber and narrower venular caliber, which are associated with a lower risk of cardiovascular disease. These data add to the growing evidence of the benefits of fiber intake on various aspects of cardiovascular pathogenesis.

Keywords

Dietary fiber; cardiovascular diseases; micro-circulation; retinal abnormalities; cereal

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INTRODUCTION

Dietary fiber intake is associated with a reduced risk of cardiovascular diseases, including ischemic heart disease (1–7), stroke (2,7–9), peripheral arterial disease (10), hypertension (11), and atherosclerosis (12–14). The underlying mechanisms of the effect of dietary fiber on the cardiovascular system remain poorly understood, although previous studies have shown that fiber intake can affect blood pressure, systemic inflammation, serum lipid concentrations, postprandial absorption of carbohydrates, insulin sensitivity, fibrinolysis, coagulation, and endothelial cell function (15–21).

Microvascular dysfunction has long been implicated as a possible pathogenic factor in the development of various cardiovascular disorders (22). Observation of retinal vascular caliber may convey important information regarding the state of the micro-circulation in the eyes and in other vascular beds (23). Several recent prospective studies have shown that a narrower retinal arteriolar diameter independently predicts incident severe hypertension (24), coronary heart disease (25,26), and diabetes mellitus (27,28). A wider retinal venular diameter has been associated with an increased risk of stroke, cerebral infarction (29), and cerebral small vessel disease (30).

We hypothesized that a higher intake of dietary fiber is associated with a wider retinal arteriolar and a narrower venular caliber. We examined this hypothesis in a population-based cohort of middle-aged men and women. We also examined potential modifying effects of cardiovascular disease risk factors, including sex, smoking status, diabetes status, hypertension, and physical activity.

SUBJECTS AND METHODS

Subjects

The design and objectives of the Atherosclerosis Risk in Communities (ARIC) Study have been reported in detail (31). Briefly, the ARIC Study is a prospective epidemiologic study of new and established risk factors for atherosclerosis and community trends in coronary heart disease. The study population was selected as a probability sample of 15 792 men and women aged 45–64 y in Forsyth County, NC; Jackson, MS; selected suburbs of Minneapolis, MN; and Washington County, MD. Eligible participants were interviewed at home and then invited to a baseline clinical examination in 1987–1989. Three further examinations were carried out at approximately 3-y intervals, and participants were contacted annually by telephone between visits to the clinic.

Participants for the current analysis are limited to 12 887 who attended the third visit of the ARIC study cohort (1993–1995), at which time the retinal examinations occurred. This represented 86% of cohort survivors. We excluded persons who were of an ethnicity other than African American or white (n = 38) and who were missing data on retinal vascular caliber (n = 1849) or dietary fiber (n = 341). The final study sample consisted of 10 659 adults. The Institutional Review Board of the 4 participating centers approved the study.

Measurement of retinal vascular caliber

The procedures for retinal photography and the assessment of photographs were described in detail previously (32). Briefly, photographs of the retina were taken from a randomly selected eye after 5 min of dark adaptation. Trained graders, masked to all participant characteristics, used a standardized protocol to evaluate the photographs for microvascular signs.

Retinal arteriolar and venular calibers were measured with a computer-assisted technique, whereby photographs were digitized with a high-resolution scanner, and the diameters of all

arterioles and venules in an area half to one disc diameter from the optic disc were measured. These diameters were summarized as the central retinal artery equivalent (CRAE) and the central retinal venular equivalent (CRVE), which represented average calibers of retinal arterioles and venules, respectively. A smaller CRAE value represents narrower retinal arterioles, and a higher CRVE value represents wider venular diameters. Quality control procedures were previously reported (32). For the retinal vascular caliber, reliability coefficients were 0.84 for within-grader and 0.79 for between-grader agreement.

Dietary assessment

The usual dietary intake of the participants at the third visit over the preceding year was assessed by using a 66-item semi-quantitative food-frequency questionnaire. The questionnaire was a modified version of the 61-item instrument designed and validated by Willett et al for self-administration. The correlation coefficient of energy-adjusted crude fiber between the questionnaire and four 1-wk dietary records was 0.58 (33). To improve data quality and completeness, the questionnaire was administered by trained interviewers. Participants were asked to report the frequency of consumption of each food on the basis of 9 categories, which ranged from never or <1 time/mo to ≥6 times/d. Interviewers also obtained additional information, including the brand name of the breakfast cereal usually consumed. All dietary factors in our analysis were adjusted for total energy by using the residual method (34).

Other covariates

Blood pressure was measured with a random-zero sphygmomanometer according to a standardized protocol (35). We used the average values over the first 3 examinations (9-y mean blood pressure) to approximate the long-term blood pressure level. Hypertension was defined as a systolic blood pressure of ≥140 mm Hg, a diastolic blood pressure of ≥90 mm Hg, or the use of antihypertensive medication during the previous 2 wk. Diabetes mellitus was defined as a fasting glucose concentration of ≥126 mg/dL (7.0 mmol/L), a nonfasting glucose concentration of ≥200 mg/dL (11.1 mmol/L), or a self-reported history of or treatment for diabetes. Anthropometric measures (weight and height) were determined by trained, certified technicians who followed a detailed, standardized protocol (35). BMI was calculated as weight (kg)/[height squared (m)]. Blood collection and processing for concentrations of HDL cholesterol, LDL cholesterol, and triacylglycerol are described elsewhere (35). Trained and certified interviewers also collected information on age, ethnicity, sex, smoking, alcohol consumption status, medical history, occupation, education, and physical activity. We used the sports index, derived from the survey of Baecke et al (36), as a measure of physical activity. The index ranged from 1 (low) to 5 (high) for physical activity from sports during leisure time.

Statistical analysis

For this analysis, CRAE and CRVE were used in combination with fiber intake data from the same period in a cross-sectional analysis. SAS (version 9.1.2; SAS, Cary, NC) software was used for all statistical analyses. The distributions of CRAE and CRVE were continuous and relatively normally distributed in this population; therefore, we used linear regression models to examine the association of retinal vascular caliber with fiber intake. We analyzed energy-adjusted intake of fiber according to quintiles.

To assess for confounding, multivariate linear regression models were used. Our base model adjusted for age, sex, race and center. Several known and potential confounding factors were included in the multivariate models, either as indicator variables [sex, race, center, smoking status (never, former, and current smokers), occupation, education, alcohol intake, diabetes status, and hypertension] or continuous variables [age, smoking years, age at which smoking started, cigarettes smoked per day, BMI, physical activity, long-term systolic and diastolic blood pressure, serum lipids (HDL, LDL, and triacylglycerol), dietary factors from both food

and supplements (total energy intake, glycemic index, carotenoids, folate, n–3 fatty acids, and vitamins B-6, B-12, C, and E), and other sources of fiber (total fiber intake not adjusted for the specific fiber types)]. Because CRAE and CRVE are correlated and might be confounders for each other (37), we included CRAE and CRVE in the models simultaneously (23,38). Taking the lowest quintile of fiber intake as the reference, we estimated the difference of CRAE and CRVE with fiber intake after adjustment for the abovementioned covariates. In addition, we also conducted the stratified analysis by sex, smoking status, diabetes status, hypertension, and physical activity.

Given that the measurement error of dietary assessment may bias our findings, we repeated our analysis with the dietary data at the first visit (1987–1989). We also examined the association of fiber intake with frank retinal microvascular abnormalities such as arteriovenous nicking and retinopathy.

RESULTS

The descriptive characteristics of the ARIC participants at visit 3 stratified by quintiles of energy-adjusted total dietary fiber are shown in Table 1. Participants with a higher fiber intake generally had a higher intake of carotenoids ($P < 0.001$), folate ($P < 0.001$), n–3 fatty acids ($P < 0.001$), and vitamins B-6 ($P < 0.001$), B-12 ($P < 0.009$), C ($P < 0.001$), and E ($P < 0.001$). Subjects in the highest quintile of fiber intake were generally slightly older ($P < 0.001$), had lower BMI values ($P < 0.001$) and diastolic blood pressure ($P < 0.001$), were more likely to be female ($P < 0.001$), had more physical activity ($P < 0.001$), and were less likely to be current drinkers ($P < 0.001$), smokers ($P < 0.001$), or diabetes patients ($P < 0.001$).

The mean (±SEM) retinal arteriolar caliber was 162.3 ± 0.2 μm, and the venular caliber was 193.1 ± 16.7 μm. Consistent with previous literature (36), we found that sex, age, BMI, alcohol drinking, smoking status, physical activity, blood pressure, and serum lipids (HDL and triacylglycerol) independently predicted retinal vascular caliber in our analysis (data not shown).

We found a statistically significant dose-response relation between CRAE and dietary fiber from all sources and from cereal (Table 2). After adjustment for CRVE, age, sex, race, center, BMI, smoking, alcohol drinking, occupation, education, physical activity, diabetes status, and other dietary factors (multivariate model 1), total fiber consumption was positively associated with arteriolar caliber (P for trend = 0.002); CRAE was 1.42 μm higher (95% CI: 0.42, 2.42 μm) in the highest quintile of intake than in the lowest quintile. Sports activity accounted for most of the difference between base model and multivariate model 1 (change in slope: −10%). After further adjustment for current hypertension, long-term systolic and diastolic blood pressure and lipids (HDL, LDL, and triacylglycerol) (multivariate model 2), the dose-response relation for total fiber attenuated (change in slope compared with base model: −30%) but remained significant (P for trend = 0.012); CRAE was 1.05 μm higher (95% CI: 0.09, 2.01 μm) in the highest quintile of intake than in the lowest quintile. A similar pattern of relation with CRAE was found for cereal fiber. The association of fruit fiber with CRAE was not significant in multivariate model 1 (P for trend = 0.114), although it became significant after further adjustment for current hypertension, long-term systolic and diastolic blood pressure, and lipids (multivariate model 2) (P for trend = 0.028). Vegetable fiber was not significantly associated with CRAE in either base model or after multivariate analyses (data not shown).

Similarly, we found significantly inverse dose-response associations between CRVE and fiber intake from all sources and from cereal, both before and after adjustment for covariates (Table 3). After adjustment for CRAE, age, sex, race, center, BMI, smoking, alcohol drinking, occupation, education, physical activity, diabetes, and dietary factors (multivariate model 1),

the difference of CRVE in the highest quintile was −1.31 μm (95% CI: −2.27, −0.35 μm) relative to the lowest quintile of total fiber intake (*P* for trend = 0.011). Smoking and physical activity accounted for most of the difference between base model and multivariate model 1 (change in slope: −56%). The inverse association of total fiber with CRVE remained significant (change in slope compared with base model: −62%; *P* for trend = 0.029) after further adjustment for current hypertension, long-term systolic and diastolic blood pressure, and lipids (multivariate model 2); the CRVE was 1.11 μm lower (95% CI: 0.15, 2.08 μm) in the highest quintile of intake than in the lowest quintile. A similar pattern of relation with CRVE was found for cereal fiber. The association with CRVE was marginally significant for fruit fiber (*P* for trend = 0.066 in multivariate model 1) and was not significant for vegetable fiber.

We examined whether sex, smoking status, diabetes, hypertension, and physical activity modified the associations of total fiber with arteriolar caliber (Table 4). We found no significant interaction terms. Similar patterns were found for venular caliber.

Using the dietary data at the first visit (1987–1989), we found similar associations of dietary fiber with wider retinal arteriolar caliber and narrower venular caliber as we did with diet at visit 3 (1993–1995) when the retinal exams were done. We found no significant association of fiber intake with arteriovenous nicking or retinopathy.

DISCUSSION

In this cross-sectional analysis of a population-based cohort of middle-aged adults, we found significant associations of higher fiber intake from all sources and from cereal with wider retinal arteriolar caliber and narrower venular caliber. These associations were not explained by other dietary factors, including antioxidants, B vitamins, n–3 fatty acids, glycemic index, and fruit and vegetable fiber or by a large array of risk factors for this condition, including smoking, physical activity, hypertension, diabetes, and serum lipids.

Several mechanisms could underlie the associations we observed. Fiber intake may reduce known risk factors for smaller retinal arteriolar caliber and wider venular caliber. The primary risk factor for retinal arteriolar narrowing is hypertension (39). Several clinical trials and prospective studies suggest that fiber may protect against hypertension (40–42). In our analysis, the effect of fiber intake on CRAE or CRVE attenuated after adjustment for current hypertension and long-term blood pressure, which supports the hypothesis that the protective effect of fiber on arteriolar narrowing or venular widening may be mediated, in part, through its direct or indirect effects on blood pressure. Fiber intake may also reduce dyslipidemia, which is a risk factor for retinal microvascular abnormalities (39); attenuation of the association between dietary fiber and retinal vascular caliber when serum lipids were included in the regression model supports this potential mechanism. In addition, higher cereal fiber intake has been associated with reduced incident diabetes in the ARIC cohort (43), which is related with retinal venular widening (39). However, it should be noted that the significant associations between dietary fiber and retinal vascular caliber remained after we carefully controlled for hypertension, long-term blood pressure, lipids, and diabetes, which suggests that other mechanism may also play a role in the protective effect of dietary fiber. For example, fiber intake appears to reduce systemic inflammation, an important contributor to arteriolar narrowing and venular widening (19–21,39); however, the markers of systemic inflammation, such as C-reactive protein, fibrinogen, and white blood cell count, were not available for most subjects at the third visit of the ARIC Study. Moreover, fiber intake was found to benefit endothelial cell function (18); several small clinical studies have suggested that endothelial dysfunction may influence retinal vascular caliber (44,45). Fiber consumption may also replace intake of other foods with potentially detrimental effects on the microcirculation. Another

possibility is that some constituents of dietary fiber, such as trace elements, may reduce cardiovascular disease risk (46).

As in most observational studies, residual confounding is possible. However, we found significant associations of dietary fiber with retinal vascular caliber after detailed adjustment for known and potential cardiovascular disease risk and protective factors (eg, hypertension, long-term blood pressure, lipids, diabetes, smoking, physical activity, alcohol intake, total energy intake, glycemic index, n–3 fatty acids, antioxidant vitamins, and specific sources of fiber), which suggests an independent role of dietary fiber in the etiology of retinal microvascular abnormalities. Although the concern may be raised that a diet high in fiber might be a marker of a healthy lifestyle, including less frequent smoking (Table 1), we carefully adjusted for smoking [smoking status (current, past, and never smokers), smoking years, age at which smoking started, and cigarettes smoked per day]. Although residual confounding by smoking could occur despite our careful control, we also found a protective effect of fiber in never smokers, which suggests that the benefits of fiber intake are not due to the correlation with smoking behavior (47).

In adjusted analyses, we found significant associations for total fiber and fiber from cereal, but not for vegetable fiber. The lack of an association of retinal vascular caliber and vegetable fiber is consistent with several prior reports on other cardiovascular outcomes (3–6,9), which suggests that the effect of dietary fiber may vary depending on the food sources. However, the biological mechanisms for these differences are unclear.

We found no significant association of fiber with arteriovenous nicking and retinopathy, which suggests that fiber might be protective in the earlier stages of pathogenesis. The heterogeneity of these associations may reflect different pathophysiologic processes related with specific retinal microvascular signs (48).

On stratification by hypertension, subjects with hypertension were the smaller group. Although we did not observe a significant effect of fiber among subjects with hypertension (Table 4), there was no suggestion of interaction. This finding suggests limited power for this stratified analysis. However, it is possible that the effect of hypertension on retinal vascular caliber may dominate to such an extent that the additional exposure to fiber does not enhance effects in the same pathways.

The limitations of our analysis should be noted. We used a food-frequency questionnaire to characterize dietary fiber intake. Although fiber intake assessed by the food-frequency questionnaire was reasonably well correlated with intake measured by diet records, measurement error likely limited our ability to detect associations. In addition, caution must be made when interpreting the findings described herein that the current analyses were cross-sectional; thus, a temporal relation between fiber intake and retinal vascular caliber cannot be established. However, it should be noted that ARIC subjects would not have been aware of their retinal vascular caliber in advance and thus could not have changed their diet based on this result.

A major strength of our analysis was that it was based on carefully collected data on retinal abnormalities in a large cohort of the general population from 4 US communities. ARIC is also one of the largest studies of risk factors for these retinal microvascular signs. Confounding by hypertension, lipids, and diabetes was addressed by direct measurements made during the ARIC visit, and detailed data were available on other potential confounders.

In summary, in this cross-sectional analysis, a higher intake of fiber from all sources and from cereal was related to wider retinal arteriolar caliber and narrower venular caliber, both of which have been found to be associated with a lower risk of cardiovascular disease. These associations

were independent of smoking, hypertension, diabetes, serum lipids, and other risk factors for cardiovascular disease. These data add to the evidence of a protective role for fiber in various aspects of the pathogenesis of cardiovascular disease.

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TABLE 1

Characteristics of participants of the Atherosclerosis Risk in Communities (ARIC) Study at the third visit (1993–1995) by quintiles of energy-adjusted total dietary fiber[1]

	Quintiles			
	1 (lowest)	3	5 (highest)	*P* for trend[2]
Dietary intake[3]				
Total fiber intake (g)	10.00 ± 0.06[4]	16.84 ± 0.02	26.84 ± 0.14	<0.001
Cereal fiber (g)	2.52 ± 0.03	3.43 ± 0.03	4.28 ± 0.06	<0.001
Fruit fiber (g)	1.54 ± 0.03	3.16 ± 0.04	5.14 ± 0.08	<0.001
Vegetable fiber (g)	2.32 ± 0.04	4.68 ± 0.04	9.09 ± 0.11	<0.001
Carotenoids (IU)	4350 ± 95	8365 ± 115	15 549 ± 281	<0.001
Folate (μg)	255.1 ± 4.0	338.4 ± 4.2	440.3 ± 5.0	<0.001
Vitamin B-6 (mg)	3.1 ± 0.2	4.8 ± 0.3	5.5 ± 0.4	<0.001
Vitamin B-12 (μg)	9.2 ± 0.2	10.0 ± 0.3	10.1 ± 0.3	0.009
Vitamin C (mg)	182.2 ± 5.2	229.3 ± 5.9	317.6 ± 7.2	<0.001
Vitamin E (mg)	60.8 ± 3.2	75.8 ± 3.8	101.2 ± 4.4	<0.001
n–3 fatty acids (g)	0.201 ± 0.006	0.261 ± 0.005	0.335 ± 0.007	<0.001
Subject characteristics				
Age (y)	52.8 ± 0.1	53.7 ± 0.1	54.6 ± 0.1	<0.001
Female sex (%)	40.3	60.0	62.2	<0.001
BMI (kg/m^2)	28.7 ± 0.1	28.7 ± 0.1	28.0 ± 0.1	<0.001
Black race (%)	21.5	19.3	20.9	0.253
Drinker status				
Current drinker (%)	64.2	51.7	44.7	<0.001
Former drinker (%)	18.8	22.4	24.6	<0.001
Never drinker (%)	17.0	25.9	30.7	<0.001
Smoking status				
Current smoker (%)	27.5	15.3	12.8	<0.001
Former smoker (%)	40.9	41.6	40.8	0.570
Never regular (%)	31.6	43.0	46.4	<0.001
Sports index	2.38 ± 0.02	2.55 ± 0.02	2.68 ± 0.02	<0.001
Systolic blood pressure (mm Hg)	121.8 ± 0.3	121.0 ± 0.3	121.2 ± 0.3	0.442
Diastolic blood pressure (mm Hg)	73.3 ± 0.2	72.3 ± 0.2	71.7 ± 0.2	<0.001
Diabetes (%)	11.9	15.3	15.3	<0.001

[1] n = 10 659.

[2] Logistic regression and general linear models were used for categorical and continuous variables, respectively. For categorical variables with >2 levels (drinker status and smoking status), *P* values are for comparisons of the indicated level with all other levels combined.

[3] All dietary factors were energy-adjusted and were from both food and supplements.

[4] $\bar{x}$ ± SEM (all such values).

TABLE 2

Differences in retinal arteriolar caliber (μm) across increasing quintiles of energy-adjusted fiber intake compared with the lowest quintile[1]

Model[2]	Quintiles of energy-adjusted fiber intake					*P* for trend[3]	Change in slope compared with base model
	1 (lowest)	2	3	4	5		
							%
Total fiber							
Median intake (g)	10.77	14.41	16.80	19.58	24.80		
Base model	0	0.48 (−0.37, 1.34)	0.55 (−0.30, 1.41)	1.37 (0.50, 2.23)	1.56 (0.69, 2.44)	<0.001	—
Multivariate model 1	0	0.52 (−0.36, 1.40)	0.53 (−0.36, 1.43)	1.29 (0.37, 2.21)	1.42 (0.42, 2.42)	0.002	−10
Multivariate model 2	0	0.19 (−0.65, 1.03)	0.36 (−0.50, 1.22)	0.92 (0.03, 1.8)	1.05 (0.09, 2.01)	0.012	−30
Fiber from cereal							
Median intake (g)	1.52	2.37	3.07	3.94	5.73		
Base model	0	0.06 (−0.79, 0.91)	1.05 (0.20, 1.90)	1.41 (0.56, 2.26)	2.57 (1.72, 3.43)	<0.001	—
Multivariate model 1	0	0.13 (−0.73, 1.00)	1.05 (0.17, 1.93)	1.52 (0.63, 2.40)	2.45 (1.54, 3.36)	<0.001	−5
Multivariate model 2	0	−0.18 (−1.01, 0.66)	0.62 (−0.23, 1.47)	1.06 (0.21, 1.92)	1.56 (0.69, 2.44)	<0.001	−34
Fiber from fruit							
Median intake (g)	0.85	1.91	2.85	3.93	5.93		
Base model	0	0.92 (0.06, 1.77)	0.73 (−0.13, 1.58)	1.50 (0.64, 2.37)	1.07 (0.20, 1.94)	0.015	—
Multivariate model 1	0	0.83 (−0.05, 1.70)	0.68 (−0.20, 1.56)	1.31 (0.41, 2.21)	0.79 (−0.14, 1.71)	0.114	−31
Multivariate model 2	0	0.58 (−0.26, 1.42)	0.55 (−0.30, 1.39)	1.16 (0.30, 2.02)	0.94 (0.05, 1.83)	0.028	−8

[1] n = 10 659. 95% CIs in parentheses.

[2] Base model adjusted for central retinal venular equivalent, age, sex, race, and center; multivariate model 1 adjusted for central retinal venular equivalent, age, sex, race, center, BMI, smoking (smoking status, smoking years, age at which smoking started, and cigarettes smoked per day), alcohol intake, occupation, education, physical activity, diabetes status, dietary factors from both food and supplements (total energy intake, glycemic index, carotenoids, folate, n–3 fatty acids, and vitamins B-6, B-12, C, and E), and other sources of fiber (total fiber intake not adjusted for the specific fiber types); multivariate model 2 adjusted as for model 1 and for hypertension, long-term systolic and diastolic blood pressure, and lipids (HDL, LDL, and triacylglycerol).

[3] Based on quintiles scaled by the quintile medians.

TABLE 3

Differences in retinal venular caliber (μm) across increasing quintiles of energy-adjusted fiber intake compared with the lowest quintile[1]

Model[2]	Quintiles of energy-adjusted fiber intake					*P* for trend[3]	Change in slope compared with base model
	1 (lowest)	2	3	4	5		
							%
Total fiber							
Median intake (g)	10.77	14.41	16.80	19.58	24.80		
Base model	0	−1.50 (−2.33, −0.66)	−1.52 (−2.36, −0.68)	−2.27 (−3.12, −1.43)	−2.83 (−3.68, −1.98)	<0.001	—
Multivariate model 1	0	−0.68 (−1.52, 0.17)	−0.43 (−1.29, 0.43)	−0.79 (−1.67, 0.10)	−1.31 (−2.27, −0.35)	0.011	−56
Multivariate model 2	0	−0.51 (−1.35, 0.34)	−0.29 (−1.15, 0.58)	−0.60 (−1.49, 0.28)	−1.11 (−2.08, −0.15)	0.029	−62
Fiber from cereal							
Median intake (g)	1.52	2.37	3.07	3.94	5.73		
Base model	0	−1.00 (−1.83, −0.17)	−1.95 (−2.79, −1.12)	−1.97 (−2.80, −1.14)	−3.21 (−4.05, −2.38)	<0.001	—
Multivariate model 1	0	−0.38 (−1.22, 0.45)	−0.82 (−1.67, 0.02)	−0.68 (−1.53, 0.17)	−1.39 (−2.27, −0.52)	0.002	−58
Multivariate model 2	0	−0.23 (−1.07, 0.61)	−0.75 (−1.60, 0.11)	−0.57 (−1.42, 0.29)	−1.16 (−2.04, −0.27)	0.009	−64
Fiber from fruit							
Median intake (g)	0.85	1.91	2.85	3.93	5.93		
Base model	0	−1.07 (−1.91, −0.24)	−1.56 (−2.40, −0.73)	−1.85 (−2.70, −1.01)	−2.39 (−3.25, −1.54)	<0.001	—
Multivariate model 1	0	−0.03 (−0.87, 0.81)	−0.16 (−1.01, 0.69)	−0.24 (−1.10, 0.63)	−0.76 (−1.65, 0.13)	0.066	−65
Multivariate model 2	0	0.01 (−0.83, 0.85)	−0.12 (−0.97, 0.73)	−0.23 (−1.10, 0.63)	−0.88 (−1.77, 0.02)	0.032	−59

[1] n = 10 659. 95% CIs in parentheses.

[2] Base model adjusted for central retinal artery equivalent, age, sex, race, and center; multivariate model 1 adjusted for central retinal artery equivalent, age, sex, race, center, BMI, smoking (smoking status, smoking years, age at which smoking started, and cigarettes smoked per day), alcohol intake, occupation, education, physical activity, diabetes status, dietary factors from both food and supplements (total energy intake, glycemic index, carotenoids, folate, n–3 fatty acids, and vitamins B-6, B-12, C, and E), and other sources of fiber (total fiber intake not adjusted for the specific fiber types); multivariate model 2 adjusted as for model 1 and for hypertension, long-term systolic and diastolic blood pressure, and lipids (HDL, LDL, and triacylglycerol).

[3] Based on quintiles scaled by the quintile medians.

TABLE 4

Adjusted differences in retinal arteriolar caliber (μm) between the highest and lowest quintiles of energy-adjusted intakes of total fiber, by sex, smoking status, diabetes status, hypertension, and physical activity[1]

	Adjusted differences[2]	*P* for interaction[3]
Sex		
Female (*n* = 5947)	0.68 (−0.68, 2.03)	0.744
Male (*n* = 4712)	1.37 (−0.03, 2.78)	
Smoking status		
Never or past (*n* = 8790)	1.22 (0.17, 2.28)	0.242
Current (*n* = 1864)	0.80 (−1.63, 3.22)	
Diabetes status		
No (*n* = 9096)	1.08 (0.05, 2.11)	0.678
Yes (*n* = 1515)	1.01 (−1.71, 3.72)	
Hypertension		
No (*n* = 6409)	1.59 (0.36, 2.83)	0.656
Yes (*n* = 4197)	0.48 (−1.04, 2.00)	
Sports index		
<2.5 (*n* = 4893)	1.69 (0.28, 3.10)	0.305
≥2.5 (*n* = 5720)	0.26 (−1.07, 1.59)	

[1] *n* = 10 659. 95% CIs in parentheses.

[2] Comparison of the highest with the lowest quintiles of energy-adjusted intakes after adjustment for central retinal venular equivalent, age, sex, race, center, BMI, smoking (smoking status, smoking years, age at which smoking started, and cigarettes smoked per day), alcohol intake, occupation, education, physical activity, diabetes status, hypertension, long-term systolic and diastolic blood pressure, lipids (HDL, LDL, and triacylglycerol), and dietary factors from both food and supplements (total energy intake, glycemic index, carotenoids, folate, n–3 fatty acids, and vitamins B-6, B-12, C, and E).

[3] Likelihood ratio test for interaction (effect modification) by sex, smoking, diabetes, hypertension, or physical activity.