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Breakfast cereals and risk of hypertension in the Physicians' Health Study I

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Summary

Background and aims—Hypertension is a major public health problem. While many dietary factors affect the risk of developing hypertension, limited data are available on the association between consumption of breakfast cereal and incident hypertension. We examined the association between breakfast cereal consumption and the risk of hypertension.

Methods—We prospectively analyzed data from 13,368 male participants of the Physicians' Health Study I. Consumption of breakfast cereals was estimated using an abbreviated food frequency questionnaire and incident hypertension was ascertained through yearly follow-up questionnaires.

Results—The average age of study participants was 52.4 ±8.9 years (range 39.7-85.9) during the initial assessment of cereal intake (1981-1983). During a mean follow up of 16.3 years, 7,267 cases of hypertension occurred. The crude incidence rates of hypertension were 36.7, 34.0, 31.7, and 29.6 cases/1,000 person-years for people reporting breakfast cereal intake of 0, ≤ 1, 2-6, and ≥ 7 servings/week, respectively. In a Cox regression model adjusting for age, smoking, body mass index, alcohol consumption, fruit and vegetable consumption, physical activity, and history of

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Author contribution

Study conception (Kochar, Djoussé); data collection (Djoussé, Gaziano); statistical analyses (Djoussé); drafting the manuscript (Kochar); Critical review for intellectual content (Kochar, Gaziano, Djoussé); obtaining funding (Djoussé, Gaziano); supervision of the study (Gaziano). All authors have read and approved the final manuscript.

Conflict of interest statement

None to declare

diabetes mellitus, hazard ratios (95% CI) for hypertension were 1.0 (reference), 0.93 (0.88-0.99), 0.88 (0.83-0.94), and 0.81 (0.75-0.86) from the lowest to the highest category of cereal consumption, respectively (p for trend <0.0001). This association was strongest for whole grain cereals and was observed in lean as well as overweight or obese participants.

Conclusions—The results of this longitudinal cohort study suggest that whole grain breakfast cereal consumption confers a lower risk of hypertension in middle-aged adult males

Keywords

cereals; hypertension; epidemiology

Introduction

Hypertension (HTN) is a major public health problem.¹ It is an important modifiable risk factor for coronary heart disease, and stroke.² The estimated direct and indirect cost of elevated blood pressure for 2010 was \$76.6 billion.¹ A range of dietary factors, including potassium, magnesium, fiber, vegetable intake and reducing sodium intake etc. have been shown to decrease the risk of HTN.²⁻⁶ Breakfast cereals are an important meal for many Americans, and have a beneficial effect on various cardio-metabolic disorders like diabetes (DM)⁷, obesity⁸ and heart failure.⁹ In a prospective study of 28,926 female participants of the Women's Health Study, as compared to those who consumed <0.5 whole-grain servings/d, the relative risks (RRs) (95% CIs) of incident HTN were 0.93 (0.87- 1.00), 0.93 (0.87- 0.99), 0.92 (0.85- 0.99), and 0.77 (0.66- 0.89), respectively for those consuming 0.5 to <1, 1 to <2, 2 to <4, and 4 whole-grain servings/d.¹⁰ Breakfast cereal was reported as a major source of whole grains in that study. In a randomized controlled trial of 189 participants without history of HTN, anemia, asthma, cancer, or cardiovascular or digestive disease, fortified breakfast cereal significantly decreased plasma homocysteine levels, a known cardiovascular risk biomarker.¹¹ Folic acid, a vitamin commonly used to fortify breakfast cereals, has been shown to decrease the risk of incident HTN.¹² Thus, although data are available on the association between individual components of breakfast cereals and HTN, it is not known whether consumption of breakfast cereal affects the risk of developing HTN. The current study therefore aims to prospectively explore the association between cold breakfast cereal consumption and incidence of HTN among 13,368 US male physicians.

1. Methods

1.1. Study population

This study used data from the Physicians' Health Study (PHS) I, which was a randomized, double blind, placebo-controlled trial to study the effects of low-dose aspirin and beta-carotene for the primary prevention of cardiovascular disease and cancer among US male physicians. A detailed description of the PHS I has been published previously.¹³ Briefly, following the run-in period, 22, 071 subjects were randomized to low-dose aspirin, beta-carotene, both agents, or placebo. For the current project, we used data on 13,368 after exclusion of subjects with prevalent HTN (n=5216), patients with undefined HTN status (n=3242) missing data on breakfast cereal (n=10) or covariates (n=235). Each participant gave written informed consent and the study protocol was approved by the Institutional review Board at Brigham and Women's Hospital.

1.2. Assessment of breakfast cereal consumption

Information about consumption of cold breakfast cereals was self-reported using an abbreviated food questionnaire during enrollment (1981-1983). A detailed description of the assessment of breakfast cereal intake in the PHS has been published.^{9, 13} Briefly,

participants were asked to report their average consumption of cold breakfast cereals (1 cup) during the past year. Possible response categories included “rarely/never”, “1-3/month”, “1/week”, “2-4/week”, “5-6/week”, “daily”, and “2+/day”. In addition, the brand of cereals consumed was queried at baseline. We used an algorithm developed by Jacobs and colleagues¹⁴ to classify breakfast cereals into whole grain and refined grain. Specifically, breakfast cereals that contain at least 25% of oat or bran were classified as whole grain. Information on breakfast cereal consumption was obtained at baseline, at 18 weeks and 24, 48, 72, 96, and 120 months after randomization.

1.3. Ascertainment of incident HTN

A questionnaire was mailed to each participant every 6 months during the first year and has been mailed annually thereafter to obtain information on incident outcomes including HTN. HTN was defined as systolic blood pressure of 140+, diastolic blood pressure of 90+, or treatment for elevated blood pressure.¹⁵

1.4. Other variables

Information on age, height, weight, body mass index, cigarette smoking, fruit and vegetable consumption, HTN, history of DM, alcohol consumption, and physical activity was collected at baseline. Incidence of major chronic disease was ascertained through annual follow-up questionnaires.

1.5. Statistical analyses

We used total breakfast cereals as main exposure. However, we conducted stratified analyses by whole grain vs. refined breakfast cereals. Since the distribution of total, refined, and whole grain cereals was skewed to the right, we did not use quintiles to categorize cereal consumption. We grouped adjacent categories to allow sufficient number of person-times per category and to maintain a gradient of exposure as previously described.⁹ Thus, we classified each subject into one of the following categories of breakfast cereals: rarely or never, ≤ 1 , 2-6, and 7+ servings/week. We calculated person-time of follow up from baseline until the first occurrence of a) HTN, b) death, or c) date of receipt of last follow-up questionnaire. Within each breakfast cereal group, we calculated the incidence rate of HTN by dividing the number of HTN cases by the corresponding person-time. We used Cox proportional hazard models to compute multivariable adjusted hazard ratios with corresponding 95% confidence intervals using subjects in the cereal category of “rarely/never” as the reference group. Assumptions for the proportional hazard models were tested (by including main effects and product terms of covariates and a logarithmic transformed time factor) and were met (all p values >0.05). We obtained p value for linear trend by treating cereal variable as ordinal (taking values of 0, 1, 2, and 3 from the lowest to the highest category of cereal intake). The initial model controlled for age. Fully adjusted model adjusted for age, smoking (never, past and current smokers), body mass index (BMI) (<25 , 25-29.9, ≥ 30 kg/m²), alcohol consumption (<1 , 1-4, 5-6, 7+ drinks/week), fruit and vegetable consumption (<4 , 4-5, 6-7, and 8+ servings/day), physical activity (rarely/never, ≤ 1 , 2-4, and 5+ times per week), and history of DM. To examine the influence of BMI on the cereal-HTN association, we conducted stratified analyses according to BMI Categories (<25 , and ≥ 25). We then repeated the main analysis using updated cereal consumption at 24, 48, 72, 96, and 120 months as time-dependent variable. All analyses were completed using PC SAS, version 9.1 (SAS Institute, NC) and the significance level was set at 0.05.

2. Results

The mean age was 52.4 ± 8.9 (range 39.7-85.9) years among the 13,368 male participants. Higher intake of breakfast cereals was associated with increased physical activity; higher

consumption of fruit and vegetables; and lower prevalence of current smoking and current alcohol drinking (**Table 1**). The crude incidence rates of HTN were 36.7, 34.0, 31.7, and 29.6 cases/1,000 person-years for people reporting breakfast cereal intake of 0, ≤ 1 , 2-6, and 7+ servings/week respectively. From the lowest to the highest category of breakfast cereal intake, age-adjusted hazard ratios (95% CI) for HTN were 1.0 (reference), 0.92(0.87-0.98), 0.84(0.79-0.90) and 0.75(0.71-0.81) respectively (p for trend <0.0001) (**Table 2**). Additional adjustment for smoking, BMI, alcohol consumption, fruit and vegetable consumption, physical activity, and history of DM had only a modest influence on the hazards ratios with a 19% lower risk of HTN among people consuming 7+ servings/week of breakfast cereals compared to those who did not consume breakfast cereals (**Table 2**). The association between breakfast cereal and incident HTN was mostly evident and strongest for whole grain (p for trend <0.0001) than with refined cereal where no statistically significant association was observed in the highest category of refined cereal intake [RR= 0.86(95% CI 0.74-1.00)] (**Table 3**). Using updated cereal as time-varying covariate did not alter the results (HR: 0.99(0.92-1.05), 0.93(0.87-1.00), 0.85(0.80-0.91)). Being lean or overweight/obese did not affect the association between breakfast cereal intake and incident HTN (**Table 4**).

3. Discussion

3.1. Breakfast cereal and HTN

In this study, we found an inverse association between breakfast cereal consumption and incident HTN in US male physicians. Such relation was strongest and mostly observed with whole grain cereal and observed in lean as well as overweight and obese subjects. To the best of our knowledge, this is the first prospective study examining the association between breakfast cereal and incident HTN in a large cohort of males.

Our data are consistent with many other population based studies on the effects of diet on HTN. The Dietary Approaches to Stop HTN (DASH) diet, which consists of higher amounts of potassium, magnesium and fiber, has been shown to lower blood pressure.¹⁶ In the Health Professionals Follow-Up Study, a cohort of 31,684 men, the relative risk (RR) of HTN was 0.81 (95% CI: 0.75-0.87) in the highest compared with the lowest quintile (p for trend, 0.0001) of whole grain consumption.¹⁷ However, in addition to cold breakfast cereal, that study included in the category of whole grains various other sources of whole grain, such as dark bread, cooked brown rice, and pasta.¹⁷ In the Coronary Artery Risk Development in Young Adults (CARDIA) Study, consisting of 4,304 male and female participants, the relative risks of HTN were 1.0 (reference), 0.83 (95% CI: 0.68- 1.01), 0.83 (0.67- 1.02), 0.82 (0.65- 1.03), and 0.64 (0.53- 0.90) from the lowest to the highest quintile of plant food (fruit, vegetables, nuts, legumes, and whole- and refined-grain products) intake, respectively, adjusting for age, sex, race, education, center, energy intake, physical activity, alcohol intake, baseline smoking, vitamin supplement use (p for trend=0.01).¹⁸

Similarly, in a cohort of 5,880 Spanish men and women older than 20 years of age, as compared to the lowest quintile of cereal fiber intake, the highest quintile was associated with a 40% decreased risk of HTN (RR=0.6, 95% CI-0.3-1.0), p for trend 0.05).¹⁹ Short term randomized trials on the effect of oat bran or oat cereals on HTN have shown mixed results; some suggesting a role of oat bran or oat cereals on reducing blood pressure²⁰⁻²², while others have failed to find such benefit.²³ In a study of 28,926 female participants from the Women's Health Study, multivariable adjusted RR's of HTN in subjects consuming <0.5 , 0.5 to <1 , 1 to <2 , 2 to <4 , and ≥ 4 whole-grain servings/day were 1.00 (reference), 0.96 (0.89- 1.03), 0.95 (0.88- 1.02), 0.92 (0.85- 0.99), 0.89 (0.82- 0.97), respectively, p for trend= 0.007.¹⁰ However, in contrast with our study, that study did not show any significant beneficial effect of refined grain consumption; the corresponding RR's for HTN were 1.00

(reference) 0.97 (0.90- 1.04) 0.94 (0.87- 1.01) 0.99 (0.91- 1.07) 0.97 (0.89- 1.06) respectively, p for trend= 0.80.¹⁰

The discrepancy with our findings merits some comments. Although the overall trend for the inverse association between increasing frequency of refined grain breakfast cereal and incident HTN was statistically significant, there was lack of statistical significance in the intake of 7+ servings/week of refined breakfast cereal [RR: 0.87(0.75-1.01)]. Alternative explanation could be misclassification of whole grain cereal as refined grain cereal, thereby inflating the true effect of refined breakfast cereal on incident HTN. It is also possible that some participants were consuming more than one type of breakfast cereal (i.e. both whole grain and refined cereal). Failure to remember the correct cereal brand could also have led to this misclassification. Unfortunately, we did not ask detailed questions on cereal brand and the number of cold cereal consumed to further assess this issue.

3.2. Possible biological mechanisms

Whole grain cereal consumption has been shown to prevent postprandial impairment of vascular reactivity in response to a high-fat meal²⁴, attenuate gene expression of inflammatory markers like interleukin (IL)-10 receptor alpha and tumor necrosis factor-alpha in subcutaneous adipose tissue¹⁸, increase insulin sensitivity²⁵, and decrease abdominal obesity.²⁰ All these effects may ultimately decrease the risk of developing HTN. Vitamins including folate, commonly found in breakfast cereals have been associated with decreased risk of incident HTN.¹²

3.3. Study limitations

Our study has some limitations. First, we used a simple food questionnaire to collect dietary information. Thus, we were not able to control for total energy intake and other nutrients, including fiber content, potassium, and magnesium in the diet. Second, although salt intake is an important risk factor for hypertension, we did not have data on this variable and were not able to adjust for this variable in our analyses. Third, there is a possibility of inaccurate reporting of breakfast cereals because these data were self-reported. Fourth, the fact that our sample consists of male physicians who may have different behaviors than the general population limits the generalization of our findings. It is possible that those on a healthy diet, including daily consumption of cereals, are more likely to maintain other healthy lifestyle measures such as regular physical activity, abstinence from smoking, etc. Lastly, there remains a possibility that residual confounding or confounding by unmeasured factors could explain our findings. Nevertheless, the large sample size, the longer duration of follow-up, the robustness of our findings in sensitivity analyses, and the fact that participants were physicians who could recognize early signs of HTN are strengths of the present study.

In conclusion, our data show an inverse association between whole grain breakfast cereals and HTN. If confirmed in other studies, consumption of whole grain breakfast cereal, along with other life style changes may help lower the risk of developing HTN.

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Table 1

Characteristics of 13,368 participants according to categories of cereal intake in the Physicians' Health Study^a

Variables	Categories of cereal intake			
	None (n=4,200)	≤1 / week (n=3,104)	2-6 / week (n=3,384)	7+ / week (n=2,680)
Age (y)	51.8±8.5	51.6±8.9	52.4±8.8	54.0±9.5
Body mass index (kg/m ²)	24.7±2.7	24.8±2.7	24.4±2.5	24.0±2.3
Vegetable intake (servings / day)	2.2±1.2	2.3±1.1	2.5±1.1	2.5±1.2
Current smoking (%)	15.6	11.1	7.9	5.8
Alcohol 1+/week (%)	75.1	73.7	72.9	71.4
Physical activity 1+/week (%)	83.3	89.1	91.3	90.4
History of DM (%)	2.14	2.22	1.65	2.31
Randomized to aspirin (%)	50.4	49.0	49.9	50.0

^aContinuous variables are shown as mean ± SD; categorical variables as %

Table 2

Hazard ratios (95% CI) for HTN according to breakfast cereal intake in the Physicians' Health Study

Cereal intake (servings/week)	Cases	Crude incidence rate (per 1,000 person-years)	Hazards Ratio (95% CI)	
			Age adjusted	Model 1 ^a
0	2,410	36.7	1.0	1.0
≤1	1,715	34	0.92(0.87-0.98)	0.93(0.88-0.99)
2-6	1,798	31.7	0.84(0.79-0.90)	0.88(0.83-0.94)
7+	1,344	29.6	0.75(0.71-0.81)	0.81(0.75-0.86)
p for linear trend			<0.0001	<0.0001

^a Adjusted for age, smoking (never, past and current smokers), BMI (<25, 25-29.9, ≥30), alcohol consumption (<1, 1-4, 5-6, 7+ drinks/week), fruit and vegetable consumption (<3, 3-4, 5-6, 7-13, 14+ servings/week), physical activity (<1, 1+/week), and history of DM.

Table 3

Hazard ratios (95% CI) of HTN according to type of breakfast cereals in the Physicians' Health Study ^a

Cereal intake (servings/week)	Missing cereal type		Refined grain		Whole grain	
	Cases	HR (95 % CI)	Cases	HR (95 % CI)	Cases	HR (95 % CI)
0	2,410	1.0	2,410	1.0	2,410	1.0
≤1	721	1.0(0.92-1.08)	271	0.91(0.80-1.03)	723	0.89(0.82-0.97)
2-6	424	0.95(0.86-1.06)	260	0.86(0.76-0.98)	1,114	0.87(0.81-0.94)
7+	219	0.80(0.69-0.91)	191	0.86(0.74-1.00)	934	0.80(0.74-0.86)
p for trend		0.005		0.003		<0.0001

^a Adjusted for age, smoking (never, past and current smokers), BMI (<25, 25-29.9, ≥30), alcohol consumption (<1, 1-4, 5-6, 7+ drinks/week), fruit and vegetable consumption (<3, 3-4, 5-6, 7-13, 14+ servings/week), physical activity (<1, 1+/week), and history of DM.

Table 4Hazard ratios (95% CI) of HTN by body mass index (BMI) categories in the Physicians' Health Study ^a

Whole grain Cereal intake (servings/week)	BMI < 25 kg/m ²		BMI ≥25 kg/m ²	
	Cases	RR (95 % CI)	Cases	RR (95 % CI)
0	1,294	1.0	1,116	1.0
≤1	889	0.93(0.86-1.02)	826	0.93(0.85-1.01)
2-6	1,048	0.86(0.79-0.93)	750	0.93(0.85-1.02)
7+	891	0.81(0.75-0.89)	453	0.80(0.72-0.90)
p for trend		<0.0001		0.0003

^a Adjusted for age, smoking (never, past and current smokers), alcohol consumption (<1, 1-4, 5-6, 7+ drinks/week), fruit and vegetable consumption (<3, 3-4, 5-6, 7-13, 14+ servings/week), physical activity (<1, 1+/week), and history of DM.