

Short Communication

A Prospective Study of Diet and Stomach Cancer Mortality in United States Men and Women

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Abstract

Frequent consumption of fruits, vegetables, and whole grains has been associated with a reduced risk of stomach cancer in the majority of case-control studies of these factors; however, prospective studies have been less consistent. We examined the association between selected major food groups (citrus fruits, vegetables, whole grains, and processed meats) and risk of fatal stomach cancer in the Cancer Prevention Study (CPS) II cohort of 1.2 million United States men and women. During 14 years of follow-up, we documented 439 stomach cancer deaths in women and 910 in men after exclusion of individuals with prevalent cancers, inadequate diet information, and recent weight loss at baseline in 1982. After controlling for other risk factors, none of the food groups examined were associated with risk of stomach cancer except for an unexpected increased risk with vegetable consumption in women (relative risk (RR) = 1.25; 95% confidence interval (CI), 0.99–1.58; highest versus lowest tertile, P = 0.06 for trend). A high overall plant food intake (a sum of vegetables, citrus fruit, and whole grains) was associated with reduced risk in men (RR = 0.79; 95% CI, 0.67–0.93; highest versus lowest tertile, P = 0.003 for trend), but not in women (RR = 1.18; 95% CI, 0.93–1.50; P = 0.16 for trend). Of individual foods examined, liver consumption greater than twice/week was associated with an increased risk of fatal stomach cancer in women (RR = 1.96; 95% CI, 1.09–3.53) and men (RR = 1.63; 95% CI, 1.02–2.62) compared with nonconsumers. This study supports a modest role for plant foods in reducing the risk of fatal stomach cancer in men, but not in women.

Introduction

Dietary factors are thought to contribute to the large international variation in stomach cancer rates (1) and to the global decline in stomach cancer incidence over the last half-century (2–4), although certain aspects of this relationship remain unclear. Citrus fruit, vegetables, and whole grains, high in antioxidant vitamins and polyphenols (5), may lower stomach cancer risk by protecting the gastric epithelium from inflammatory responses caused by Helicobacter pylori and by reducing endogenous carcinogenic nitrosamine formation (2, 6). The majority of the >30 published case control studies report an inverse association between one or more of these food groups and stomach cancer (1), whereas prospective studies have been fewer and less consistent (7–16). Consumption of processed meats, which contain nitrosamine precursors, has been inconsistently associated with stomach cancer in both case-control and prospective studies (1).

Although there have been a considerable number of epidemiological studies of diet and stomach cancer, most have been case-control studies that are susceptible to recall bias (2). Previous prospective studies of diet and stomach cancer have generally been small (9–11, 13, 14), thus limiting statistical power to examine risk separately by gender or other potential risk modifiers. In addition, past studies have not simultaneously controlled for important confounders such as socioeconomic status, cigarette smoking, and aspirin use (7, 13–16). The purpose of this study was to evaluate the association of dietary factors, especially citrus fruit, vegetables, whole grains, and processed meats, with risk of fatal stomach cancer in a large prospective cohort of United States men and women.

Materials and Methods

Study Cohort and Follow-up. In 1982, 508,351 men and 676,306 women completed a mailed questionnaire for the ACS’s2 CPS II. The questionnaire obtained information on medical history, demographic characteristics, diet and life-style habits, and medication use. Participants were recruited and enrolled by ACS volunteers in all 50 of the United States, the District of Columbia, and Puerto Rico and were followed-up for vital status through December 31, 1996, as described previously (17). Death certificates or codes for cause of death were obtained for 98.8% of all known deaths. Stomach cancer deaths were defined as International Classification of Diseases-9 codes 150.0–150.9 (18).

We excluded participants from this analysis if they reported prevalent cancer at baseline (except nonmelanoma skin cancer; n = 82,349), if they lost >20 pounds over the previous year (n = 20,797), or if diet information was incomplete (n = 111,466). The final analytic cohort consisted of 533,391 women and 436,654 men in whom 439 and 910 deaths from stomach cancer occurred, respectively.

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2The abbreviations used are: ACS, American Cancer Society; CPS II, Cancer Prevention Study II; BMI, body mass index; CI, confidence interval; RR, relative risk.

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Dietary Assessment. Our dietary questionnaire has been described previously (19). Briefly, it asked about consumption of 32 foods using the following wording: “On average, how many days per week do you eat the following foods?” Main exposures included gender-specific tertiles of the following: “vegetables” (a sum of reported frequencies for green leafy vegetables, tomatoes, cabbage/broccoli/brussels sprouts, carrots, and squash/corn); “citrus fruit” (citrus fruits/juices); “whole grains” (brown rice/whole wheat/barley, bran/corn muffins, oatmeal/shredded wheat/barley cereals); and “processed meats” (smoked meats, frankfurters/sausage, fried bacon, and ham). We also created a score representing higher intakes of potentially beneficial plant foods (“plant food”) by summing the frequencies of reported vegetables, citrus fruit, and whole grains. Individual foods, and a separate question on intake of “raw vegetables” were also examined.

Statistical Analyses. We used Cox proportional hazards models (20) to examine the association between dietary factors and stomach cancer mortality while adjusting for other potential risk factors. The time-axis used was follow-up time since enrollment in 1982. Age-adjustment was accomplished by stratifying on exact year of age at enrollment within each Cox model (21). Covariates were modeled using dummy variables. Multivariate models included terms for educational attainment, race, cigarette smoking history, aspirin use, vitamin C use, multivitamin use, family history of stomach cancer, and BMI in kg/m². Variables examined but included, because they did not confound the association between diet and disease, were history of stomach problems (defined as a history of gastric or duodenal ulcers, chronic indigestion, regular use of antacids or regular use of Tagamet), exercise level, use of sniff or chewing tobacco, alcohol use, menopausal status, and history of estrogen use.

We examined whether the relationship between diet and fatal stomach cancer varied by level of education, history of stomach problems, vitamin supplement use, smoking, attained age, BMI, family history of stomach cancer, regular aspirin use, and major change in diet over the previous 10 years. The likelihood ratio test was used to test for interaction (22). In addition, we conducted lag analyses excluding the first 4 years of follow-up to remove early cases in whom the relationship between diet and cancer may have been biased from changes in diet attributable to undiagnosed stomach cancer. Trend tests were conducted by assigning a numeric value from 1 to 5 to each quintile and modeling trend as a continuous variable.

Results
Baseline characteristics of CPS II men and women, according to food group tertiles, are provided in Table 1. Men and women who reported more frequent consumption of citrus fruit, vegetables, and whole grains and lower consumption of processed meat were, on average, slightly older, more educated, less likely to smoke, more likely to be vitamin C users, and less likely to be obese. For frequency of foods consumed per week, women reported more citrus fruit (4.3 ± 2.8) and vegetables (11.6 ± 6.0) compared with men (fruit, 3.8 ± 2.8; vegetables, 10.6 ± 5.8) and less processed meat (women, 2.1 ± 2.1; men, 2.8 ± 3.8); whole grain intake was similar (women, 3.5 ± 3.8; men, 3.4 ± 3.8).

In men, more frequent consumption of citrus fruit, vegetables and whole grains was associated with a decreased risk of stomach cancer, and intake of processed meats was associated with increased risk, in analyses adjusted only for age (Table 2). After controlling for important risk factors, the associations with food groups no longer remained. However, compared with men in the lowest tertile, men in the top two tertiles of the plant food score had a reduced risk of fatal stomach cancer (RR = 0.76; 95% CI, 0.65–0.90, and RR = 0.79; 95% CI, 0.67–0.93; P = 0.003 for trend). Of individual foods examined in men (data not shown), cabbage (RR = 0.82; 95% CI, 0.62–1.04; P = 0.03 for trend) and carrots (RR = 0.86; 95% CI, 0.69–
In women, we observed no association between any food group or plant food score and stomach cancer risk in age-adjusted or multivariate models, except for an unexpected increase in vegetable consumption (RR = 1.58; 95% CI, 1.33–1.90). In men, a stronger decrease in whole-grain products was associated with decreased risk of fatal stomach cancer (RR = 1.70; 95% CI, 1.34–2.16). Plant foods, sum of citrus fruit, vegetables, and whole grain intake. Tertiles: men (<13.5, 13.5 to <21.5, and 21.5+); women (<15.5, 15.5 to <23.5, and 23.5+).

Because frequent consumption of liver was associated with an increased risk of fatal stomach cancer in both men and women, we adjusted further for factors associated with liver consumption (e.g., being foreign-born or having migrant parents) in addition to related factors already in the models (nonwhite race, less education, and older age). This did not alter our findings.

Inclusion of all four food groups in the multivariate models did not change our results for each food group. Analyses excluding the first 4 years of follow-up were similar to the overall analyses for both genders. The relationship between dietary factors and stomach cancer mortality was not modified by education level, attained age, BMI, vitamin use, or aspirin use in men or women. For men with a positive family history of stomach cancer, consuming whole-grain products >4 days/week versus <1 was associated with lower risk (RR = 0.31; 95% CI, 0.15–0.64) compared with those with no family history of stomach cancer (RR = 0.96; 95% CI, 0.81–1.12; P = 0.004 for interaction). In both men and women, the relation between diet and stomach cancer risk was modified by a history of stomach problems at baseline. In men, a stronger decrease in risk with higher plant food intake was observed among those who had a history of stomach problems at baseline (RR = 0.56; 95% CI, 0.40–0.78) compared with those without

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Table 2  Risk of fatal stomach cancer by major food groups—CPS II men and women, 1982–1996

<table>
<thead>
<tr>
<th>Food group</th>
<th>(Reference)</th>
<th>2</th>
<th>3</th>
<th>P</th>
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<tbody>
<tr>
<td>Citrus fruit/juice</td>
<td>1.00</td>
<td>0.94</td>
<td>0.99</td>
<td></td>
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<tr>
<td>Men, cases (n)</td>
<td>156</td>
<td>188</td>
<td>188</td>
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<tr>
<td>Age-adjusted</td>
<td>1.00</td>
<td>0.85</td>
<td>0.88</td>
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<tr>
<td>Multivariate-adjusted</td>
<td>1.00</td>
<td>0.90</td>
<td>0.87</td>
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<tr>
<td>Women, cases (n)</td>
<td>336</td>
<td>283</td>
<td>291</td>
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<tr>
<td>Age-adjusted</td>
<td>1.00</td>
<td>0.83</td>
<td>0.89</td>
<td></td>
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<tr>
<td>Multivariate-adjusted</td>
<td>1.00</td>
<td>0.90</td>
<td>0.89</td>
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<tr>
<td>Whole grains</td>
<td>319</td>
<td>337</td>
<td>337</td>
<td></td>
</tr>
<tr>
<td>Men, cases (n)</td>
<td>143</td>
<td>143</td>
<td>143</td>
<td></td>
</tr>
<tr>
<td>Age-adjusted</td>
<td>1.00</td>
<td>1.00</td>
<td>1.05</td>
<td></td>
</tr>
<tr>
<td>Multivariate-adjusted</td>
<td>1.00</td>
<td>1.10</td>
<td>0.97</td>
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<tr>
<td>Plant foods</td>
<td>360</td>
<td>260</td>
<td>290</td>
<td></td>
</tr>
<tr>
<td>Men, cases (n)</td>
<td>152</td>
<td>153</td>
<td>143</td>
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<tr>
<td>Age-adjusted</td>
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<td>0.92</td>
<td>0.83</td>
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<tr>
<td>Multivariate-adjusted</td>
<td>1.00</td>
<td>1.14</td>
<td>0.97</td>
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</tr>
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</table>

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* Adjusted for age, education, smoking, BMI, multivitamin and vitamin C use, aspirin use, race, and family history.

* Plant foods, sum of citrus fruit, vegetables, and whole grain intake. Tertiles: men (<13.5, 13.5 to <21.5, and 21.5+); women (<15.5, 15.5 to <23.5, and 23.5+).
stomach problems (RR = 0.87; 95% CI 0.73–1.05; P = 0.003 for interaction). Conversely, risk of fatal stomach cancer with higher plant food intake was higher among women with stomach problems (RR = 2.11; 95% CI 1.12–3.97) compared with those without stomach problems (RR = 1.08; 95% CI 0.84–1.38; P = 0.13 for interaction).

Discussion
In this large prospective cohort of United States men and women, none of the food groups we examined were independently related to stomach cancer risk. However, in men, a diet pattern high in potentially beneficial plant foods (citrus fruit, vegetables, and whole grains combined) was associated with a lower risk of fatal stomach cancer. In women, plant foods were not associated with a reduced risk of fatal stomach cancer. Consistent with our diet patterns, the relationship between plant foods and stomach cancer mortality was related to a modestly lower risk of stomach cancer only among men in our study. The lack of findings in women and the increased risk with liver consumption deserve additional investigation. Future studies should examine stomach cancer risk by gender, history of stomach problems and precursor lesions, anatomical subsite, and, if possible, H. Pylori status.

Acknowledgments
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References


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