

Vegetable and Fruit Intake and Pancreatic Cancer in a Population-Based Case-Control Study in the San Francisco Bay Area

June M. Chan,^{1,2} Furong Wang,¹ and Elizabeth A. Holly¹

Departments of ¹Epidemiology and Biostatistics, and ²Urology, University of California San Francisco, San Francisco, California

Abstract

Pancreatic cancer is one of the most devastating and rapidly fatal cancers, yet little is known about the primary cause and prevention of this disease. We conducted a population-based case-control study to investigate the association between vegetables and fruits and pancreatic cancer. Between 1995 and 1999, 532 cases and 1,701 age- and sex-matched controls completed direct interviews using a semiquantitative food-frequency questionnaire. No proxy interviews were conducted. We observed inverse associations between consumption of total and specific vegetables and fruits and the risk of pancreatic cancer. The odds ratio and 95% confidence interval for the highest versus the lowest quartile of total vegetable intake was 0.45 (0.32-0.62), trend $P < 0.0001$; and for total fruits and fruit juice was 0.72 (0.54-0.98), trend $P = 0.06$. Odds ratios and

95% confidence intervals for the highest versus the lowest quartile of specific vegetables and fruits were: 0.63 (0.47-0.83) for dark leafy vegetables, 0.76 (0.56-1.0) for cruciferous vegetables, 0.59 (0.43-0.81) for yellow vegetables, 0.56 (0.41-0.76) for carrots, 0.51 (0.38-0.70) for beans, 0.46 (0.33-0.63) for onions and garlic, and 0.78 (0.58-1.0) for citrus fruits and juice. Compared with less than five servings per day of total vegetables and fruits combined, the risk of pancreatic cancer was 0.49 (0.36-0.68) for more than nine servings per day. These results suggest that increasing vegetable and fruit consumption, already recommended for the prevention of several other chronic diseases, may impart some protection against developing pancreatic cancer. (Cancer Epidemiol Biomarkers Prev 2005;14(9):2093-7)

Introduction

Pancreatic cancer progresses rapidly and has an extremely high mortality rate. In the U.S., it has the fourth highest cancer fatality rate of all cancers (1). In 2005, it is estimated that ~32,180 pancreatic cancer patients will be diagnosed, with almost an equal number of deaths (1). The 5-year survival rate is low at 4% (1) and is due primarily to late-stage at diagnosis and lack of effective treatment. Very little is known about the epidemiology of pancreatic cancer. Like many cancers, it is age-dependent, often with >90% of patients diagnosed at age 50 or older. The incidence rate is higher in men than in women. The most consistent risk factor for pancreatic cancer is cigarette smoking, that accounts for only ~27% of new cases (2). Thus, further understanding of risk factors that might help to prevent this lethal disease could have substantial public health impact.

Because of the swift fatality rate of this relatively uncommon cancer, studying dietary associations can be challenging in observational epidemiologic studies. Of five prospective studies that have examined fruit and vegetable intake and the risk of pancreatic cancer, one has reported inverse associations (3), whereas others observed inverse associations and confidence intervals (CI) that included unity (4, 5), or no clear association (6, 7). In contrast, at least 11 case-control studies have reported inverse associations for risk of pancreatic cancer and intake of total or specific fruits and vegetables (8-18). Some case-control studies (19-23) and one cohort (24)

also have reported inverse associations for nutrients commonly found in fruits and vegetables (e.g., vitamin C, carotenoids, vitamin E, other common antioxidants, fiber, folate) and risk of pancreatic cancer, whereas an additional study observed inverse trends for vitamin C and carotenoids but these could have been due to chance (25).

Taken together, these studies suggest that vegetables and fruits may impart some protection against risk of incident pancreatic cancer. Several of the studies did not report values for individual vegetables or fruits, had small sample sizes, or used proxy interviews. Thus, to explore these relationships further in a contemporary population of men and women, we conducted a large case-control study of pancreatic cancer in the San Francisco Bay Area. We assessed the association between total and specific fruits and vegetables and the risk of pancreatic cancer among 532 cases and 1,701 age- and sex-matched controls, using data from direct interviews only (no proxy interviews).

Materials and Methods

Study Population. We conducted a population-based case-control study of pancreatic cancer in the San Francisco Bay Area. Details on study design and selection of the study population have been published previously (26-31). In brief, between 1995 and 1999, newly diagnosed patients with adenocarcinoma of the exocrine pancreas in the San Francisco Bay Area were identified through rapid case ascertainment by the Northern California Cancer Center. Eligible cases were 21 to 85 years old at diagnosis, residents of one of six counties of the San Francisco Bay Area, alive when contacts were attempted and could complete an interview in English. Out-of-area cases were identified through clinical records at the University of California San Francisco with the same eligibility requirements except for residency. Among 797 eligible cases, 532 (288 men and 238 women) completed an interview. Diagnoses of pancreatic cancer were confirmed by participants'

Received 4/1/05; revised 6/3/05; accepted 7/6/05.

Grant support: NIH, National Cancer Institute grants CA59706, CA89726, CA72712, CA09889, CA108370 and the Rombauer Pancreatic Cancer Research Fund (to EA Holly, PI).

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Requests for reprints: Elizabeth A. Holly, 3333 California Street, Suite 280, Department of Epidemiology and Biostatistics, Box 1228, University of California San Francisco, San Francisco, CA 94118-1944. Phone: 415-476-3345; Fax: 415-563-4602. E-mail: elizabeth.holly@ucsf.edu

Copyright © 2005 American Association for Cancer Research.

doi:10.1158/1055-9965.EPI-05-0226

physicians and by Surveillance, Epidemiology, and End Results (SEER) abstracts that included histologic confirmation of disease. Control participants, frequency-matched to cases by age within 5-year categories and sex, were selected from the target population using random digit dial. Controls older than 65 years were supplemented by random selection from Health Care Finance Administration lists (now the Centers for Medicare and Medicaid Services). Cases within the six Bay Area counties were interviewed in person, and out-of-area cases and controls were interviewed by telephone. Among 2,525 eligible controls, 1,701 (883 men and 818 women) completed an interview and their data were included in the final analyses. The response rates for eligible participants were 67% for cases and 67% for controls.

Eligible cases and controls usually were interviewed in-person by trained interviewers using one main questionnaire and one supplementary food-frequency questionnaire within 4 months of diagnosis (median = 2.8 months). No proxy interviews were conducted in this study. The study was reviewed and approved by the university institutional review board and written informed consent was obtained from each participant prior to interview. Items in the main questionnaire included demographic factors, smoking history, alcohol consumption, medical history, occupational history, and questions about food preparation, cooking, and changes in eating habits. The study participants were asked about: whether their diet differed between 1 and 10 years prior to the interview; the reasons contributing to the diet changes; how they usually cooked their meats, fish, and vegetables; for vegetable consumption 1 year prior to the interview, what percentage were eaten raw, and what percentage were lightly steamed or still crisp after cooking; and whether they ate much more, much less, or about the same amount of total food as they had 10 years before.

We also used a validated semiquantitative food frequency questionnaire from Harvard University that contained 131 items of commonly eaten foods in the American diet. Participants were asked how often, on average, they consumed the total amount of individual food items, with portion sizes specified, during the year that occurred 1 year before the diagnosis for cases or interview for controls. Seasonal foods were averaged over the entire year. The frequencies of food intake were: never, <1/mo, 1 to 3/mo, 1/wk, 2 to 4/wk, 5 to 6/wk, 1/d, 2 to 3/d, 4 to 5/d, or 6+/d. Food frequency responses were computed as servings per day. Total consumption of vegetables and fruits and subgroups of these foods were computed by adding servings per day of individual food items.

We examined total vegetables as well as the following vegetable categories: dark leafy vegetables, yellow vegetables, light-green vegetables, cruciferous vegetables, tomatoes/tomato products, onions and garlic, beans, potatoes, and carrots. Dark leafy vegetables consisted of spinach, kale, mustard, and chard greens. Yellow vegetables included carrots, corn, yellow squash, yams, and sweet potatoes. Light-green vegetables included iceberg head lettuce, romaine and leafy lettuce, and celery. Cruciferous vegetables consisted of broccoli, cabbage and coleslaw, cauliflower, and Brussels sprouts. The tomatoes/tomato products group included raw tomatoes, tomato juice, tomato sauce, salsa, and picante/taco sauce. The bean group contained tofu/soybeans, peas and lima beans, beans and lentils, and string beans. Potatoes included French-fried potatoes, baked, boiled and mashed potatoes, and potato chips. Carrots included raw and cooked carrots.

We also examined the following fruit categories: citrus fruits, berries, apples and apple-related products, fruit juice, and total fruit consumed with and without fruit juice. Citrus fruits included orange, grapefruit, orange juice, and grapefruit juice. Strawberries and blueberries comprised the berry group. Fresh apples or pears, applesauce, and apple juice and cider

were categorized in the apples and apple-related product group. Fruit juice included apple juice or cider, orange juice, grapefruit juice, and other fruit juice. Total fruit without fruit juice contained oranges, grapefruits, apples or pears, apple-sauce, strawberries, blueberries, raisins or grapes, prunes, bananas, cantaloupes, avocado, peaches, apricots, and plums. The data from 2,227 participants (526 cases and 1,701 controls) were included in the final analyses after the exclusion of six case participants whose dietary questionnaire had missing responses for >10 items.

Statistical Methods. We conducted χ^2 tests to compare the proportions of cases and controls in different categories of consumption of vegetables and fruits. Odds ratios (OR) and 95% CI were computed from unconditional logistic regression models and used as an estimate of the relative risk (hereafter called risk) of developing pancreatic cancer by consumption groups. We examined consumption of total and specific vegetables and fruits in quartiles and in categories. Quartile cutoffs were based upon the distribution of intake among the controls with the lowest intake category used as the reference group. Results for men and women were similar, thus we combined analyses. We conducted linear tests for trend using Wald's test applied to index variables for the quartiles. Effect modification of the relationship between vegetable or fruit intake and risk of pancreatic cancer was assessed for energy intake in total calories, body mass index, cigarette smoking, physical activity, race, diabetes, and family history of pancreatic cancer. When no interaction effect was observed, the confounding effects of these factors were further investigated. Only total energy intake affected the association between vegetables and fruits and risk of pancreatic cancer. Therefore, the primary multivariate model was adjusted for total calories and the matching factors of sex and age at diagnosis for cases or interview for controls. All statistical tests were two-sided and considered statistically significant when $P \leq 0.05$. Statistical analyses were conducted using SAS software V8 (SAS Institute, Inc., Cary, NC).

Age at pancreatic cancer diagnosis for cases or interview for controls was categorized as <50, 50 to 59, 60 to 69, 70 to 79, and 80+ years. Total caloric intake was categorized into quartiles using the following cutoffs: <1,439, 1,439 to 1,810, 1,811 to 2,265, and >2,265 kcal per day. To investigate the potential effects of measurement error, we conducted additional analyses excluding participants with extremely low (<500 kcal/d) or high (>3,500 kcal/d) caloric intake. The results were essentially the same as the primary results and these participants were retained in the main analyses.

Body mass index was estimated from adult weight and height [weight (kg)/height (m)²] as a measure of body size. Body mass index was examined in quartiles using the following cutoffs: <22.2, 22.2 to 24.2, 24.3 to 26.6, and >26.6 kg/m². Smokers were defined as participants who had smoked >100 cigarettes in their lifetime, or a pipe or cigar for at least once a month for ≥ 6 months. We examined smoking using the following categories: never smokers, former cigarette smokers, and current cigarette smokers. We asked about the frequency of nonoccupational physical activity conducted for at least 30-minute intervals. Exercise frequency was grouped as <1/mo, 2 to 4/mo, 2 to 3/wk, or at least 1/d. Participants self-reported their race selecting from the following categories: White, Black/African-American, Asian/Pacific Islander, or Other.

Results

Sociodemographic characteristics of case and control participants are provided in Table 1. Vegetables were inversely associated with the risk of pancreatic cancer (Table 2). Compared with the lowest quartile of intake of total vegetables, the OR for the highest quartile was 0.45 (95% CI,

Table 1. Sociodemographic characteristics of 526 incident cases of pancreatic cancer and 1,701 controls in the San Francisco Bay Area, CA

	Pancreatic cancer cases, n (%)	Control participants, n (%)
Age		
<50	46 (9)	164 (10)
50-59	119 (23)	438 (26)
60-69	169 (32)	473 (28)
70-79	156 (30)	498 (29)
80+	36 (7)	128 (8)
Sex		
Men	288 (55)	883 (52)
Women	238 (45)	818 (48)
Race		
White	438 (83)	1,471 (86)
Black/African-American	45 (9)	78 (5)
Asian/Pacific Islander	34 (6)	119 (7)
Others	9 (2)	33 (2)
Hispanic origin		
Yes	25 (5)	114 (7)
No	501 (95)	1,585 (93)
Education		
<High school	229 (44)	534 (31)
College	200 (38)	754 (44)
Graduate work	97 (28)	413 (24)
Marital status		
Never married	22 (4)	116 (7)
Married or living as married	344 (65)	1,044 (61)
Widowed	75 (14)	242 (14)
Divorced	78 (15)	272 (16)
Separated	7 (1)	27 (2)

0.32-0.62), trend $P < 0.0001$. Similar inverse associations were observed after excluding potatoes from analyses.

Individual vegetables also were inversely associated with the risk of pancreatic cancer (Table 2). Compared with the lowest quartile of intake, the OR for the highest quartile was 0.63 (95% CI, 0.47-0.83) for dark leafy vegetables, 0.76 (95% CI, 0.56-1.0) for cruciferous vegetables, 0.59 (95% CI, 0.43-0.81) for yellow vegetables, 0.56 (95% CI, 0.41-0.76) for carrots, 0.51 (95% CI, 0.38-0.70) for beans, and 0.46 (95% CI, 0.33-0.63) for onions and garlic. Light-green vegetables (trend $P = 0.03$) and tomatoes/tomato products (trend $P = 0.06$) were inversely associated with the risk of pancreatic cancer but most of their CIs overlapped unity. Potatoes were the only vegetable positively associated with pancreatic cancer risk, although the relationship could have been due to chance. When we examined this association further, it seemed that French-fried

potatoes and potato chips specifically were associated with an increased risk, suggesting that cooking methods, fat content, or other components of these foods may underlie the positive association (data not shown).

There was a suggestion that consuming raw vegetables reduced the risk of pancreatic cancer more than eating cooked vegetables. OR comparing more than or equal to two servings per week versus less than or equal to three servings per month was 0.50 (95% CI, 0.29-0.86) for raw spinach versus 0.92 (95% CI, 0.59-1.4) for cooked spinach. ORs were 0.62 (95% CI, 0.49-0.79) for consumption of raw carrots and 0.86 (95% CI, 0.65-1.1) for cooked carrots (data not shown in tables).

Decreased risks were observed with an increasing amount of total fruits and fruit juice intake and the OR for the highest quartile of intake was 0.72 (95% CI, 0.54-0.98), trend $P = 0.06$ (Table 3). Compared with the lowest quartile of intake of citrus fruits and juice, the OR for the highest quartile was 0.78 (95% CI, 0.58-1.0).

In Table 4, we report on categories of intake of fruits and vegetables and pancreatic cancer risk. Compared with participants who ate less than three servings of vegetables per day, participants eating more than five servings had a reduced risk of pancreatic cancer (OR, 0.47; 95% CI, 0.35-0.62; trend $P < 0.0001$). Eating more than four servings of fruits per day compared with less than two servings per day reduced the risk of pancreatic cancer by ~25%. Consuming more than nine servings per day of vegetables and fruits combined also was inversely associated with risk (OR, 0.49; 95% CI, 0.36-0.68) when compared with less than five servings per day (trend $P < 0.0001$).

Regarding eating habits, more cases than controls reported use of animal fat in preparing their vegetables 1 year before diagnosis for cases or interview for controls ($P = 0.01$). There were more cases than controls who had maintained their same dietary habits from 10 years ago (35% versus 28%, $P = 0.03$), and more controls had changed their dietary habits towards a more healthy diet that included more raw vegetables ($P < 0.01$) and fruits ($P < 0.01$).

Discussion

In this large case-control study, vegetable consumption was inversely associated with risk of developing pancreatic cancer. The risk of pancreatic cancer for people consuming more than five servings per day of vegetables was half that of low consumers. Specifically, dark leafy vegetables, cruciferous vegetables, yellow vegetables, beans, onions and garlic, and carrots were associated with a reduced risk of pancreatic cancer. Some raw vegetables also seemed to be more strongly

Table 2. ORs and 95% CIs by quartile of vegetable intake in a case-control study of pancreatic cancer in the San Francisco Bay Area, CA

Servings per day	OR (95% CI)*				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Trend P
Total fruits and vegetables	1.0	0.83 (0.62-1.1)	0.70 (0.52-0.94)	0.47 (0.34-0.65)	<0.0001
Total vegetables	1.0	0.80 (0.61-1.1)	0.69 (0.51-0.92)	0.45 (0.32-0.62)	<0.0001
Total vegetables without potatoes	1.0	0.89 (0.68-1.2)	0.62 (0.46-0.83)	0.47 (0.34-0.64)	<0.0001
Dark leafy vegetables	1.0	0.74 (0.56-0.96)	0.90 (0.68-1.2)	0.63 (0.47-0.83)	0.01
Light-green vegetables	1.0	1.1 (0.84-1.5)	0.77 (0.58-1.0)	0.80 (0.60-1.1)	0.03
Cruciferous vegetables	1.0	0.94 (0.71-1.3)	0.87 (0.66-1.2)	0.76 (0.56-1.0)	0.06
Yellow vegetables	1.0	0.93 (0.71-1.2)	0.85 (0.64-1.1)	0.59 (0.43-0.81)	0.001
Carrots	1.0	0.86 (0.66-1.1)	0.73 (0.56-0.95)	0.56 (0.41-0.76)	0.0001
Tomatoes/tomato products	1.0	1.2 (0.88-1.5)	0.86 (0.64-1.1)	0.81 (0.61-1.1)	0.06
Beans	1.0	0.94 (0.71-1.2)	0.71 (0.54-0.93)	0.51 (0.38-0.70)	<0.0001
Onions and garlic	1.0	0.94 (0.72-1.2)	0.92 (0.71-1.2)	0.46 (0.33-0.63)	<0.0001
Potatoes	1.0	1.3 (0.96-1.8)	1.1 (0.80-1.5)	1.4 (1.0-1.9)	0.15

*Adjusted for age, sex and energy intake.

Table 3. ORs and 95% CIs by quartile of fruit intake in a case-control study of pancreatic cancer in the San Francisco Bay Area, CA

Servings per day	OR (95% CI)*				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Trend <i>P</i>
Total fruits and fruit juice	1.0	0.85 (0.64-1.1)	0.90 (0.68-1.2)	0.72 (0.54-0.98)	0.06
Total fruits	1.0	0.94 (0.71-1.3)	0.97 (0.73-1.3)	0.85 (0.63-1.2)	0.35
Total fruit juice	1.0	0.99 (0.75-1.3)	0.98 (0.74-1.3)	0.72 (0.54-0.98)	0.05
Citrus fruits and juice	1.0	0.83 (0.63-1.1)	0.96 (0.73-1.3)	0.78 (0.58-1.0)	0.20
Fresh apple, apple juice and sauce	1.0	0.94 (0.70-1.3)	0.93 (0.70-1.2)	1.1 (0.79-1.4)	0.74
Berries	1.0	1.4 (1.1-1.7)	0.90 (0.65-1.3)	0.98 (0.74-1.3)	0.52

*Adjusted for age, sex and energy intake.

inversely associated with risk than their cooked counterparts. Total fruits and juice intake also were associated with a reduced risk of pancreatic cancer. Our results indicated that controls were more likely to have changed their dietary habits during the 10 years prior to interview, and in particular that they started consuming more raw or lightly cooked vegetables and fruits. In contrast, cases tended to make fewer changes in their vegetable and fruit consumption patterns.

Several case-control studies and at least one cohort study have observed inverse associations for total or specific vegetable and fruit intake and the risk of pancreatic cancer, even though these reports have had different study designs. Some did not have total energy adjustment, whereas others had smaller sample sizes (*n* for cases <150) or used proxy interviews (3, 4, 7, 9-11, 14, 16, 17, 20, 22). Our results were consistent with those of several previous case-control studies (8-12, 14-16, 18) and one cohort (3) that observed inverse associations for total and specific vegetables and pancreatic cancer risk. Similar to our results, at least 11 case-control studies (8-11, 13-18, 20) and one cohort study (3) have observed reduced risks of pancreatic cancer associated with total or specific fruit consumption. At least one study observed protective effects only among men (18). However, other cohort studies (4-7) and one case-control study (12) observed no statistically significant association between fruits and pancreatic cancer risk, although nearly all had risk estimates below unity.

We observed the strongest inverse associations for onions and garlic, beans, carrots, yellow vegetables, dark leafy vegetables, and cruciferous vegetables. Nutrients underlying these associations that previously have been inversely associated with pancreatic cancer risk include fiber (9, 15, 16, 20, 22),

Table 4. Total number of daily servings of vegetables and fruits in a case-control study of pancreatic cancer in the San Francisco Bay Area, CA

Servings per day	Cases (<i>n</i> = 526)	Controls (<i>n</i> = 1,701)	OR* (95% CI)
Total vegetables			
<3	192	557	1.0 (Ref.)
3-5	206	599	0.82 (0.64-1.0)
>5	128	545	0.47 (0.35-0.62)
Trend <i>P</i>			<0.0001
Total fruits			
<2	234	787	1.0 (Ref.)
2-4	218	664	0.97 (0.78-1.2)
>4	74	250	0.76 (0.55-1.0)
Trend <i>P</i>			0.15
Total vegetables and fruits			
<5	190	554	1.0 (Ref.)
5-9	245	798	0.71 (0.56-0.90)
>9	91	349	0.49 (0.36-0.68)
Trend <i>P</i>			<0.0001

*Adjusted for age, sex, and energy intake.

folate (5, 9, 24), and antioxidants (e.g., carotenoids, vitamin E, and vitamin C; refs. 9, 10, 15, 22). Nutrients commonly found in fruits and vegetables have been inversely associated with several other cancers including pancreatic cancer (32). Potential mechanisms of action include antioxidant protection against free-radical damage to DNA and polyunsaturated fats (e.g., vitamin C, carotenoids, tocopherols, and selenium), apoptosis (e.g., indole-3 carbinol in cruciferous vegetables), enhancing immune function (e.g., carotenoids, vitamin C, and vitamin E), modulating hormonal pathways linked to cancer, such as sex hormones (e.g., soy and lignans) or insulin-like growth factor (e.g., lycopene), inhibiting cellular proliferation (e.g., carotenoids), and ensuring proper DNA methylation and gene expression (e.g., folate; refs. 18, 23, 32, 33).

In a nested case-control study within the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study, men in the highest versus the lowest tertile of serum folate had approximately half the risk of pancreatic cancer (24). Additionally, in a large case-control study of 802 cases of pancreatic cancer and 1,669 controls, dietary fiber, β -carotene, and vitamin C consumption were all strongly associated with an ~60% to 65% lower risk of pancreatic cancer (22).

A Canadian dietary study of intake of the carotenoid lycopene was related to a 31% reduced risk of pancreatic cancer in men after adjustment for other nutrients and lifestyle factors (23). This effect was strongest among men and there was no statistically significant association for any major carotenoid and pancreatic cancer risk among women (23). Other carotenoids were not associated with pancreatic cancer risk overall, although there was a statistically significant interaction between carotenoid consumption and smoking history and risk of pancreatic cancer. β -Carotene and total carotenoids were inversely associated with risk among never smokers (OR, 0.57 and 0.58, respectively; *P* = 0.02 for each), but not among past or current smokers.

The stronger association in our study for raw spinach and raw carrots versus their cooked counterparts is consistent with a report on food preparation methods and pancreatic cancer (34). Raw food consumption was statistically significantly inversely associated with a 70% decreased risk of pancreatic cancer in this study that included 179 cases and 239 controls. A recent review on raw versus cooked vegetables and cancer that included >30 case-control and cohort studies published in the past 10 years concluded that raw vegetables more often were inversely associated with risk of various cancers when compared with cooked vegetables (35). Raw vegetables may impart more benefit than cooked vegetables due to their potential increased nutrient content, lower glycemic index, higher level of enzymes important for phytochemical production, and increased insoluble fiber content. However, it also was noted that cooking vegetables kills harmful microbes, increases bioavailability of certain carotenoids, and often improves digestibility.

The strengths of the current study include its large sample size (532 cases and 1,701 controls). We could identify only two

previous studies in the literature that included a greater number of cases (6, 22). We also conducted direct interviews with participants, included detailed information on other life-style factors, and data on food preparation and changes in dietary habits. In this study, we used no proxy interviews and had a comprehensive validated semiquantitative food-frequency questionnaire that minimized potential effects of measurement error.

This study also had limitations that should be considered. Due to the high mortality rate of the disease, many ($n = 742$) of the patients with pancreatic cancer died before they could be contacted and no dietary information was available on these fatal cases. As in most case-control studies, there is potential for recall bias. At the same time, most cohort studies that have examined pancreatic cancer risk and diet have been limited by the small number of cases observed (3-5, 7) or lack of detailed dietary assessment (6). Our results were somewhat consistent with those of a few prospective studies that have observed inverse associations for folic acid, a nutrient often found in dark green leafy vegetables (5, 24), or that had suggestive inverse associations for vegetables, fruits, β -carotene, and vitamin C (4). The observation that controls rather than cases were more likely to have changed their diets in the previous decade argues against the likelihood that the observed associations were due entirely to recall bias among the cases, as control participants reported having changed their diets towards more healthy choices over time.

Conclusion

We observed strong inverse associations for pancreatic cancer risk and intake of vegetables and fruits. These results indicate that consuming a diet high in vegetables and fruits, already recommended for the prevention of several other chronic diseases, might also help prevent the occurrence of this highly fatal cancer.

References

- Jemal A, Murray T, Ward E, et al. Cancer statistics, 2005. *CA Cancer J Clin* 2005;55:10-30.
- Silverman DT, Dunn JA, Hoover RN, et al. Cigarette smoking and pancreas cancer: a case-control study based on direct interviews. *J Natl Cancer Inst* 1994;86:1510-6.
- Mills PK, Beeson WL, Abbey DE, Fraser GE, Phillips RL. Dietary habits and past medical history as related to fatal pancreas cancer risk among Adventists. *Cancer* 1988;61:2578-85.
- Shibata A, Mack TM, Paganini-Hill A, Ross RK, Henderson BE. A prospective study of pancreatic cancer in the elderly. *Int J Cancer* 1994; 58:46-9.
- Stolzenberg-Solomon RZ, Pietinen P, Taylor PR, Virtamo J, Albanes D. Prospective study of diet and pancreatic cancer in male smokers. *Am J Epidemiol* 2002;155:783-92.
- Coughlin SS, Calle EE, Patel AV, Thun MJ. Predictors of pancreatic cancer mortality among a large cohort of United States adults. *Cancer Causes Control* 2000;11:915-23.
- Zheng W, McLaughlin JK, Gridley G, et al. A cohort study of smoking, alcohol consumption, and dietary factors for pancreatic cancer (United States). *Cancer Causes Control* 1993;4:477-82.
- Silverman DT, Swanson CA, Gridley G, et al. Dietary and nutritional factors and pancreatic cancer: a case-control study based on direct interviews. *J Natl Cancer Inst* 1998;90:1710-9.
- Baghurst PA, McMichael AJ, Slavotinek AH, et al. A case-control study of diet and cancer of the pancreas. *Am J Epidemiol* 1991;134:167-79.
- Bueno de Mesquita HB, Maisonneuve P, Runia S, Moerman CJ. Intake of foods and nutrients and cancer of the exocrine pancreas: a population-based case-control study in the Netherlands. *Int J Cancer* 1991;48:540-9.
- Norell SE, Ahlbom A, Erwald R, et al. Diet and pancreatic cancer: a case-control study. *Am J Epidemiol* 1986;124:894-902.
- Olsen GW, Mandel JS, Gibson RW, Wattenberg LW, Schuman LM. A case-control study of pancreatic cancer and cigarettes, alcohol, coffee and diet. *Am J Public Health* 1989;79:1016-9.
- Falk RT, Pickle LW, Fontham ET, Correa P, Fraumeni JF, Jr. Life-style risk factors for pancreatic cancer in Louisiana: a case-control study. *Am J Epidemiol* 1988;128:324-36.
- Gold EB, Gordis L, Diener MD, et al. Diet and other risk factors for cancer of the pancreas. *Cancer* 1985;55:460-7.
- Ji BT, Chow WH, Gridley G, et al. Dietary factors and the risk of pancreatic cancer: a case-control study in Shanghai China. *Cancer Epidemiol Biomarkers Prev* 1995;4:885-93.
- Lyon JL, Slattery ML, Mahoney AW, Robison LM. Dietary intake as a risk factor for cancer of the exocrine pancreas. *Cancer Epidemiol Biomarkers Prev* 1993;2:513-8.
- La Vecchia C, Negri E, D'Avanzo B, et al. Medical history, diet and pancreatic cancer. *Oncology* 1990;47:463-6.
- Nkondjock A, Krewski D, Johnson KC, Ghadirian P. Dietary patterns and risk of pancreatic cancer. *Int J Cancer* 2005;114:817-23.
- Olsen GW, Mandel JS, Gibson RW, Wattenberg LW, Schuman LM. Nutrients and pancreatic cancer: a population-based case-control study. *Cancer Causes Control* 1991;2:291-7.
- Howe GR, Jain M, Miller AB. Dietary factors and risk of pancreatic cancer: results of a Canadian population-based case-control study. *Int J Cancer* 1990; 45:604-8.
- Zatonski W, Przewozniak K, Howe GR, et al. Nutritional factors and pancreatic cancer: a case-control study from south-west Poland. *Int J Cancer* 1991;48:390-4.
- Howe GR, Ghadirian P, Bueno de Mesquita HB, et al. A collaborative case-control study of nutrient intake and pancreatic cancer within the search programme. *Int J Cancer* 1992;51:365-72.
- Nkondjock A, Ghadirian P, Johnson KC, Krewski D. Dietary intake of lycopene is associated with reduced pancreatic cancer risk. *J Nutr* 2005; 135:592-7.
- Stolzenberg-Solomon RZ, Albanes D, Nieto FJ, et al. Pancreatic cancer risk and nutrition-related methyl-group availability indicators in male smokers. *J Natl Cancer Inst* 1999;91:535-41.
- Ghadirian P, Simard A, Baillargeon J, Maisonneuve P, Boyle P. Nutritional factors and pancreatic cancer in the Francophone community in Montreal, Canada. *Int J Cancer* 1991;47:1-6.
- Hoppin JA, Tolbert PE, Holly EA, et al. Pancreatic cancer and serum organochlorine levels. *Cancer Epidemiol Biomarkers Prev* 2000;9:199-205.
- Slebos RJ, Hoppin JA, Tolbert PE, et al. K-ras and p53 in pancreatic cancer: association with medical history, histopathology, and environmental exposures in a population-based study. *Cancer Epidemiol Biomarkers Prev* 2000;9:1223-32.
- Duell EJ, Holly EA, Bracci PM, et al. A population-based, case-control study of polymorphisms in carcinogen-metabolizing genes, smoking, and pancreatic adenocarcinoma risk. *J Natl Cancer Inst* 2002;94:297-306.
- Duell EJ, Holly EA, Bracci PM, Wiencke JK, Kelsey KT. A population-based study of the Arg399Gln polymorphism in X-ray repair cross-complementing group 1 (XRCC1) and risk of pancreatic adenocarcinoma. *Cancer Res* 2002; 62:4630-6.
- Holly EA, Eberle CA, Bracci PM. Prior history of allergies and pancreatic cancer in the San Francisco Bay area. *Am J Epidemiol* 2003;158:432-41.
- Duell EJ, Holly EA. Reproductive and menstrual risk factors for pancreatic cancer: a population-based study of San Francisco Bay Area women. *Am J Epidemiol* 2005;161:741-7.
- McCullough ML, Giovannucci EL. Diet and cancer prevention. *Oncogene* 2004;23:6349-64.
- Potter JD, Steinmetz K. Vegetables, fruit and phytoestrogens as preventive agents. *IARC Sci Publ* 1996;61-90.
- Ghadirian P, Baillargeon J, Simard A, Perret C. Food habits and pancreatic cancer: a case-control study of the Francophone community in Montreal, Canada. *Cancer Epidemiol Biomarkers Prev* 1995;4:895-9.
- Link LB, Potter JD. Raw versus cooked vegetables and cancer risk. *Cancer Epidemiol Biomarkers Prev* 2004;13:1422-35.

Cancer Epidemiology, Biomarkers & Prevention

Vegetable and Fruit Intake and Pancreatic Cancer in a Population-Based Case-Control Study in the San Francisco Bay Area

June M. Chan, Furong Wang and Elizabeth A. Holly

Cancer Epidemiol Biomarkers Prev 2005;14:2093-2097.

Updated version Access the most recent version of this article at:
<http://cebp.aacrjournals.org/content/14/9/2093>

Cited articles This article cites 34 articles, 8 of which you can access for free at:
<http://cebp.aacrjournals.org/content/14/9/2093.full#ref-list-1>

Citing articles This article has been cited by 10 HighWire-hosted articles. Access the articles at:
<http://cebp.aacrjournals.org/content/14/9/2093.full#related-urls>

E-mail alerts [Sign up to receive free email-alerts](#) related to this article or journal.

Reprints and Subscriptions To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions To request permission to re-use all or part of this article, use this link
<http://cebp.aacrjournals.org/content/14/9/2093>.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.