Null Results in Brief

Dietary Acrylamide Intake and Prostate Cancer Risk in a Prospective Cohort of Swedish Men

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Abstract

Background: **Acrylamide is a probable human carcinogen that can be formed in foods prepared at high temperatures. Whereas evidence indicates that acrylamide causes cancer in laboratory animals, epidemiologic data on dietary acrylamide intake in relation to cancer risk are limited and mainly null. We examined the association between dietary acrylamide intake and risk of prostate cancer in a cohort of men.**

Methods: **The Cohort of Swedish Men is a population-based prospective study of 45,306 men who were cancer-free and completed a food frequency questionnaire at enrollment in 1997. Cox proportional hazards models were used to estimate relative risks adjusted for potential confounders.**

Results: **During a mean follow-up of 9.1 years, we ascertained 2,696 incident cases of prostate cancer. We observed no association between acrylamide intake and risk of prostate cancer. Compared with the lowest quintile of acrylamide intake (mean, 23.7 μg/d), the multivariable relative risks (95% confidence interval) for the highest quintile (mean, 49.8 μg/d) were 0.88 (0.70-1.09) for total prostate cancer, 1.07 (0.87-1.32) for localized prostate cancer (n = 1,088), and 0.98 (0.78-1.22) for advanced prostate cancer (n = 951).**

Conclusions: **Results from this prospective study provide no evidence that dietary acrylamide in amounts typically consumed by Swedish men is associated with risk of prostate cancer.** (Cancer Epidemiol Biomarkers Prev 2009;18(6):1939–41)

Introduction

Acrylamide is a small hydrophilic molecule formed in foods prepared at high temperatures (1) and is classified by the IARC as probably carcinogenic to humans (2). High levels of acrylamide have been found in fried and baked potato products as well as in bread, breakfast cereals, and cookies (3). Although studies in animals suggest a dose-response relationship between acrylamide given in drinking water and cancer in multiple organs (4), results from epidemiologic studies generally show no association between dietary acrylamide intake and risk of cancer at various sites (5-15). However, positive associations of acrylamide intake with risk of renal cell, endometrial, and ovarian cancers were observed in a cohort of Dutch men and women (6, 7). To date, only one prospective study (7) and two case-control studies have examined the relation between acrylamide intake and prostate cancer risk (9, 16). We therefore examined the association between acrylamide intake and risk of prostate cancer in a cohort of Swedish men.

Materials and Methods

Study Cohort. The Cohort of Swedish Men began in the autumn of 1997 when all men, ages 45-79 y, who resided in Västmanland and Örebro counties of central Sweden, received a questionnaire that included about 350 items about diet and other lifestyle factors (12, 17). Of the 48,850 men who returned a completed questionnaire, we excluded those with an erroneous or missing National Registration Number, those with implausible values for total energy intake (i.e., 3 SD from the $\log_e$-transformed mean energy intake), and those with a cancer diagnosis (other than nonmelanoma skin cancer) before enrollment. This left 45,306 men for analysis. The study was approved by the Ethics Committee at the Karolinska Institutet in Stockholm, Sweden.

Dietary Assessment. Diet was assessed at baseline using a self-administered food frequency questionnaire on which participants reported their average frequency of consumption of 96 food items over the past year. Participants could choose from eight prespecified frequency categories ranging from "never" to "3 or more times per day." Information on the acrylamide content in Swedish foods was obtained from the Swedish National Food Administration (18) and Svensson et al. (3). Acrylamide intake was calculated by multiplying the frequency of consumption of each food item by its acrylamide content per age-specific serving. Details of the calculation of acrylamide intake have been described elsewhere (13). Acrylamide intake was energy adjusted by using the residual method (19).

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Table 1. Characteristics of participants of the Cohort of Swedish Men (*n* = 45,306) according to quintiles of energy-adjusted acrylamide intake at baseline

Characteristics	Quintile of acrylamide intake, μg/d				
	<28.3	28.3-33.1	33.2-37.6	37.7-43.3	≥43.4
No. of participants	9,068	9,063	9,074	9,037	9,064
Age (y)	63.5	62.1	60.3	58.7	56.8
Postsecondary education (%)	16.9	15.7	17.6	16.2	14.1
Never smoker (%)	34.2	37.4	38.4	37.5	34.4
Body mass index (kg/m^2)	26.0	25.8	25.6	25.7	25.8
Height (cm)	177.1	177.2	177.5	177.4	177.1
Exercise ≥2 h/wk (%)	56.5	60.0	60.6	59.2	58.3
History of diabetes (%)	5.9	5.8	5.5	6.1	8.6
Family history of prostate cancer (%)	9.1	9.4	9.0	8.9	8.3
Daily dietary intake					
Total energy (kcal)	2,690	2,730	2,702	2,652	2,515
Acrylamide (μg)	23.7	30.9	35.4	40.3	49.8
Alcohol (g)	12.3	10.8	10.3	9.5	8.3
Calcium (mg)	1,335	1,262	1,219	1,179	1,118
Red meat (g)	108	105	104	102	97

NOTE: Data are age-standardized to the age distribution of the study cohort at baseline. All values are means if not otherwise indicated.

Case Ascertainment and Follow-up. Incident cases of prostate cancer were identified by linkage of the study population (using the National Registration Number) with the National Swedish Cancer Registry and the Regional Cancer Registry that recorded all cancer diagnoses in the study area. Follow-up for cancers is estimated to be almost 100% complete (20). Information on tumor-node-metastasis stage, Gleason grade, and value of prostate specific antigen (PSA) at prostate cancer diagnosis was obtained from the Swedish Prostate Cancer Quality Registry. We divided the prostate cancers into localized disease (T_1-T_2, N_{X-0}, M_{X-0}, PSA <20, or Gleason grade ≤7) and advanced disease (T_3-T_4, N_{X-1}, M_{X-1}, PSA >100, or Gleason grade >7). Information on dates of death for deceased participants was obtained from the Swedish Death Registry.

Statistical Analysis. Participants contributed person-time from January 1, 1998 to the date of diagnosis of prostate cancer, death, December 31, 2007 (for total prostate cancer analysis), or December 31, 2006 (for analysis of localized and advanced prostate cancer). Age-adjusted and multivariable Cox proportional hazards models were used to estimate relative risks and 95% confidence intervals for each quintile of acrylamide intake compared with

Table 2. Relative risks (95% confidence intervals) for prostate cancer according to quintiles of acrylamide intake in the Cohort of Swedish Men, 1998-2007

Acrylamide intake, μg/d	Overall				Never smokers			
	Cases	Person-years	RR (95% CI)*	RR (95% CI)†	Cases	Person-years	RR (95% CI)*	RR (95% CI)†
Total prostate cancer								
<28.3	610	78,867	1.00	1.00	245	27,165	1.00	1.00
28.3-33.1	613	81,565	1.06 (0.94-1.18)	0.86 (0.71-1.04)	257	30,344	1.03 (0.86-1.22)	1.01 (0.84-1.20)
33.2-37.6	559	83,032	1.05 (0.94-1.18)	1.02 (0.84-1.23)	232	31,882	0.96 (0.80-1.15)	0.95 (0.79-1.14)
37.7-43.3	485	83,959	1.00 (0.89-1.13)	0.90 (0.73-1.10)	200	31,182	0.94 (0.78-1.14)	0.93 (0.77-1.13)
≥43.4	429	85,365	1.00 (0.89-1.14)	0.88 (0.70-1.09)	154	28,534	0.90 (0.73-1.11)	0.91 (0.74-1.13)
P for trend‡			0.78	0.34			0.20	0.28
Localized prostate cancer								
<28.3	234	72,239	1.00	1.00	105	24,819	1.00	1.00
28.3-33.1	271	74,416	1.23 (1.03-1.46)	1.20 (1.01-1.43)	114	27,642	1.07 (0.82-1.39)	1.07 (0.82-1.39)
33.2-37.6	224	75,647	1.11 (0.92-1.33)	1.09 (0.90-1.31)	104	29,015	1.00 (0.76-1.32)	1.02 (0.77-1.34)
37.7-43.3	194	76,391	1.05 (0.87-1.27)	1.04 (0.86-1.27)	94	28,347	1.03 (0.78-1.36)	1.04 (0.78-1.38)
≥43.4	165	77,517	1.02 (0.83-1.25)	1.07 (0.87-1.32)	66	25,888	0.90 (0.66-1.23)	0.92 (0.67-1.27)
P for trend‡			0.61	0.99			0.46	0.56
Advanced prostate cancer								
<28.3	237	72,239	1.00	1.00	89	24,819	1.00	1.00
28.3-33.1	201	74,416	0.91 (0.75-1.09)	0.91 (0.75-1.09)	79	27,642	0.88 (0.65-1.20)	0.87 (0.64-1.18)
33.2-37.6	202	75,647	1.01 (0.84-1.22)	1.02 (0.84-1.24)	80	29,015	0.94 (0.69-1.27)	0.94 (0.69-1.28)
37.7-43.3	169	76,391	0.95 (0.78-1.16)	0.97 (0.79-1.18)	61	28,347	0.84 (0.60-1.16)	0.83 (0.59-1.16)
≥43.4	142	77,517	0.94 (0.76-1.16)	0.98 (0.78-1.22)	42	25,888	0.74 (0.51-1.07)	0.75 (0.51-1.10)
P for trend‡			0.72	0.99			0.11	0.15

NOTE: The follow-up period for analysis of localized and advanced prostate cancer was from January 1998 through December 2006.
Abbreviations: RR, relative risk; 95% CI, 95% confidence interval.
*Adjusted for age (continuous).
†Adjusted for age (continuous), education (less than high school, high school graduate, more than high school), smoking status (never, past, current), body mass index (<23.0, 23.0-24.9, 25.0-29.9, ≥30.0 kg/m^2), height (continuous), physical activity (in quintiles), history of diabetes (yes/no), family history of prostate cancer (yes/no) and intakes of total energy (continuous), alcohol (in quintiles), dietary calcium (in quintiles), and red meat (in quintiles).
‡The test for trend was calculated by using the median intake of acrylamide in each quintile as a continuous variable.

the lowest quintile for total, localized, and advanced prostate cancers. The covariates chosen for inclusion in the multivariable model were based on previously identified risk factors for prostate cancer, as well as those that were statistically significantly associated with prostate cancer in the Cohort of Swedish Men. Multivariable models included age, education, smoking status, body mass index, height, physical activity, history of diabetes, family history of prostate cancer, and intakes of total energy, alcohol, calcium, and red meat.

Because smoking is an important source of acrylamide exposure (21, 22), we conducted subgroup analyses for never smokers. All P values presented are two-sided and $P < 0.05$ was considered statistically significant. The study had ~80% power to detect a relative risk of >1.17 for the highest versus lowest quintile ($\alpha = 0.05$).

Results

The mean (± SD) daily intake of acrylamide in the study population was 36.1 ± 9.6 μg. Major contributors to acrylamide intake were coffee (23%), whole grain soft bread (17%), whole grain crisp bread (8%), white bread (7%), cookies/buns (7%), breakfast cereals (6%), wafers/crackers (6%), fried potato (6%), and potato crisps (4%). Compared with men with a low acrylamide intake, those with high intakes tended to be younger and were less likely to have a postsecondary education (Table 1). Moreover, they were slightly more likely to have diabetes and had lower intakes of alcohol, calcium, and red meat.

During a mean follow-up of 9.1 years (412,788 person-years), from 1998 through 2007, 2,696 prostate cancer cases were diagnosed among 45,306 eligible participants. The number of localized and advanced prostate cancer cases ascertained through 2006 was 1,088 and 951, respectively. We found no significant association between acrylamide intake and risk of total, localized, or advanced prostate cancer (Table 2). In never smokers, acrylamide intake was nonsignificantly inversely associated with advanced prostate cancer risk after adjustment for other risk factors (P for trend = 0.15).

Discussion

In this prospective cohort of Swedish men, we found no evidence that acrylamide intake is positively associated with the risk of prostate cancer. As in our study, no association between acrylamide intake and prostate cancer risk was observed in the Netherlands Cohort Study (7), a Swedish population-based case-control study (16), and an Italian-Swiss hospital-based case-control study (9). The Swedish case-control study also did not show any association between hemoglobin adducts of acrylamide and prostate cancer (16). However, as in the present study, the Netherlands Cohort Study showed a nonsignificant inverse relation between acrylamide intake and advanced prostate cancer risk in never smokers (7).

Strengths of this study include its prospective and population-based design, a large sample size, and the completeness of follow-up through linkage to various population-based Swedish registers. We cannot exclude measurement error due to self-reported diet as a contributor to the lack of observed association between acrylamide intake and prostate cancer. Furthermore, large variations in acrylamide content have been found between different brands of the same food and even between different production batches within the same brand (3).

In summary, we found no evidence that dietary acrylamide in amounts typically consumed by Swedish men is positively associated with prostate cancer risk.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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