Null Results in Brief

Cancer Epidemiology, Biomarkers & Prevention

Dietary Acrylamide Intake and Risk of Renal Cell Carcinoma in Two Large Prospective Cohorts

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Abstract

Background: Accumulating evidence suggests that dietary acrylamide intake is not associated with the risk of most cancers in humans. However, a meta-analysis of five epidemiologic studies found a suggestion of an increased risk of kidney cancer with higher dietary acrylamide intake.

Methods: We investigated this association in the prospective Health Professionals Follow-up Study (HPFS; 1986–2014) and Nurses' Health Study (NHS; 1980–2014) cohorts. Dietary acrylamide intake was calculated on the basis of 46 acrylamide-containing foods reported on food frequency questionnaires completed every 4 years. The associations with the incidence of total and fatal renal cell carcinoma (RCC; $n =$ 292/84 HPFS, $n =$ 337/87 NHS) during more than two decades of follow-up were assessed using Cox proportional hazards models adjusting for potential confounders.

Results: There was no association between cumulative average or baseline acrylamide intake and the risk of total or fatal RCC risk in men or women. Acrylamide intake was also not associated with RCC risk among never-smokers, nor was it associated with the risk of clear cell RCC.

Conclusions: Dietary acrylamide was not associated with risk of RCC in two long-term prospective cohorts with repeated measures of dietary intake.

Impact: This analysis of RCC adds to the body of evidence that dietary acrylamide is not an important cancer risk factor in humans. *Cancer Epidemiol Biomarkers Prev; 27(8); 979–82. ©2018 AACR.*

Introduction

Acrylamide has been designated a probable human carcinogen based largely on evidence from animal studies (1). Among its most abundant dietary sources are coffee, French fries, potato chips, cereal, and other foods made from grains. Cigarette smoke and occupational settings are also exposure sources. Epidemiologic evidence suggests that dietary acrylamide is not associated with risk of most cancers (2). However, a meta-analysis of five studies of dietary acrylamide intake and kidney cancer found a borderline significant association, with a stronger association when restricting to two prospective studies (2).

We studied this association in two long-term prospective studies, the Health Professionals Follow-up Study (HPFS) and Nurses' Health Study (NHS), which collect repeated measures of diet over time.

Materials and Methods

Study populations

The HPFS is a cohort of 51,529 male health professionals, ages 40–75 at baseline in 1986. The NHS is a cohort of 121,701 female nurses, ages 30–55 at baseline in 1976. The cohorts have been described (3). These analyses began follow-up in 1986 and 1980 for the HPFS and NHS respectively, when participants completed initial semiquantitative food frequency questionnaires (FFQs). Participants with complete FFQs and no prior cancer at baseline, 47,797 men and 88,767 women, formed the study population. Their dietary intakes of total acrylamide and 46 high-acrylamide foods (among them breads, baked goods, cereal, potatoes, and coffee) were measured every 4 years (4). We used cumulative average intakes as primary exposures and adjusted for energy intake using the residual method (5).

Cancers were identified by self-report or participants' next-of-kin on biennial questionnaires, and confirmed by medical records. Renal cell carcinoma (RCC) cases included pathologically confirmed clear cell, papillary, chromophobe, collecting duct, spindle cell/sarcomatoid, and unclassified RCC (6). Deaths were identified via family and the National Death Index. Follow-up for mortality is >98% complete.

Statistical analysis

Cox models were used to estimate HR and 95% confidence intervals (CIs) for associations between intake of acrylamide and high-acrylamide foods and total and fatal RCC risk. Follow-up ended at the earliest of RCC diagnosis, death date, or end of follow-up (January 2014 HPFS and June 2014 NHS). Analyses were conducted separately in the two cohorts, and meta-analyzed using random effects models. Models were adjusted for the variables described in the table footnotes.

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Results

In the HPFS, 292 cases of RCC were diagnosed during a median follow-up of 27.2 years. In the NHS, 337 cases were diagnosed during a median follow-up of 33.9 years. At baseline, those with the highest dietary acrylamide were younger, had less hypertension, and were more likely smokers than those with lower intakes (Table 1).

Multivariable models showed no association between dietary acrylamide and RCC risk in men (top vs. bottom quartile HR, 1.09; 95% CI, 0.77–1.55; P_{trend}, 0.96) or women (HR, 0.85; 95% CI, 0.61–1.17; P_{trend}, 0.39; Table 2). Results remained null when meta-analyzed (top quartile P_{diff}, 0.30; HR, 0.95; 95% CI, 0.74–1.22; P_{trend}, 0.58). In men, restriction to never-smokers yielded results more suggestive but nonsignificant (HR, 1.59; 95% CI, 0.93–2.72; P_{trend}, 0.09). The meta-analysis of never-smokers showed nonsignificant heterogeneity between the cohorts (top quartile P_{diff}: 0.26), and the combined results were null (HR, 1.27; 95% CI, 0.85–1.91; P_{trend}, 0.13). Results for fatal RCC were similarly suggestive but nonsignificant in men (HR, 1.82; 95% CI, 0.94–3.52; P_{trend}, 0.13) and null in the cohorts combined (top quartile P_{diff}, 0.26; HR, 1.38; 95% CI, 0.84–2.28; P_{trend}, 0.14). There was no association between dietary acrylamide and clear cell RCC. Baseline acrylamide intake and cumulative average intakes of high-acrylamide food groups, breads, baked goods, cereal, potatoes, and coffee, were not significantly associated with RCC risk in either cohort or when meta-analyzed.

Discussion

We found no association between dietary acrylamide intake and RCC risk in two cohorts with >2 decades of follow-up. A meta-analysis of five studies with 1,802 cases found an RR of 1.20 (95% CI, 1.00–1.45) for the highest versus lowest categories, with an RR of 1.48 (95% CI, 1.09–2.00) for the two prospective cohort studies (2). The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study found no significant association based on 184 cases and higher acrylamide intakes than in our cohorts, driven mainly by coffee (7). The Netherlands Cohort Study found a significant association based on 339 cases and a similar distribution of acrylamide intake to our cohorts (8). However, the major source of variation in acrylamide intake was Dutch spiced cake, which is an uncommon source of acrylamide in other populations. With 629 RCC cases, our cohorts had more cases than the previous prospective studies combined (523 cases). Our study also benefited from repeated measures of diet, which better estimate long-term intakes and reduce random within-person measurement error (5).

Table 1. Age-adjusted characteristics of the study population at baseline (1980 for the NHS and 1986 for the HPFS) according to quartiles of energy-adjusted dietary acrylamide intake

		Baseline dietary acrylamide intake quartile (μg/day)							
		Men (HPFS)				Women (NHS)			
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	Quartile 1	Quartile 2	Quartile 3	Quartile 4
	Range:	≤14.64	14.65–20.16	20.17–27.46	≥27.47	≤10.19	10.20–15.05	15.06–20.80	≥20.81
Characteristic	Median:	11.06	17.42	23.23	35.11	7.12	12.65	17.63	25.80
Number		12,484	12,027	11,774	11,512	22,593	22,147	22,041	21,986
Mean age, years (SD)[a]		57.1 (9.7)	55.2 (9.7)	53.8 (9.5)	51.5 (9.2)	48.3 (7.1)	47.2 (7.2)	46.4 (7.1)	45.1 (6.9)
Mean BMI, kg/m^2 (SD)		25.4 (3.5)	25.5 (3.3)	25.5 (3.2)	25.7 (3.4)	24.6 (4.7)	24.4 (4.6)	24.3 (4.4)	24.3 (4.4)
Diagnosis of hypertension		24.4%	21.8%	20.8%	20.8%	19.7%	17.0%	14.8%	13.4%
Diabetes		3.1%	3.1%	3.3%	3.1%	3.1%	2.3%	2.1%	1.7%
Smoking status									
Never		51.9%	48.7%	44.6%	41.7%	49.1%	47.2%	42.6%	35.6%
Past, quit >10 years before baseline		29.0%	30.2%	31.7%	30.5%	17.0%	17.1%	16.3%	13.8%
Past, quit ≤10 years before baseline		11.2%	12.0%	13.7%	14.7%	11.7%	10.9%	11.5%	11.1%
Current		7.9%	9.1%	10.1%	13.2%	22.2%	24.8%	29.6%	39.5%
Mean pack-years of smoking (SD)[b]		23.9 (19.0)	24.9 (19.0)	25.5 (19.2)	27.9 (20.1)	19.0 (16.5)	19.2 (16.4)	20.5 (16.6)	23.0 (17.0)
Nulliparous		—	—	—	—	6.3%	5.9%	5.5%	5.7%
Mean parity, number of children (SD)[c]		—	—	—	—	3.1 (1.5)	3.2 (1.5)	3.2 (1.5)	3.2 (1.5)
Mean (SD) nutrient & food intakes									
Total calories, kcal/day		1,997 (641)	2,061 (615)	1,931 (569)	1,943 (640)	1,569 (509)	1,615 (504)	1,576 (473)	1,499 (513)
Alcohol, g/day		11.8 (17.2)	12.1 (16.0)	11.1 (14.2)	10.0 (13.6)	6.5 (11.4)	6.6 (11.0)	6.4 (10.1)	5.7 (9.3)
Breads, servings/day[d]		1.6 (1.3)	2.0 (1.5)	2.1 (1.6)	2.1 (1.6)	1.3 (1.0)	1.5 (1.1)	1.7 (1.2)	1.7 (1.3)
Baked goods, servings/week[e]		4.9 (6.6)	6.4 (7.8)	6.3 (7.5)	6.4 (7.5)	2.5 (3.2)	3.8 (4.8)	4.6 (6.1)	5.5 (7.4)
Cereal, servings/week		2.1 (2.5)	2.7 (2.8)	3.1 (3.1)	3.4 (4.6)	1.7 (2.4)	2.1 (2.6)	2.1 (2.8)	2.1 (3.2)
Potatoes, servings/week[f]		2.7 (2.4)	3.4 (2.4)	3.8 (2.5)	5.5 (3.6)	2.3 (2.2)	3.0 (2.4)	3.4 (2.5)	4.8 (3.8)
Coffee, cups/day[g]		1.0 (1.2)	1.7 (1.5)	2.3 (1.8)	2.8 (2.1)	0.8 (1.0)	1.8 (1.6)	2.7 (1.8)	3.6 (1.9)

NOTE: Percentages may not add up as expected due to rounding.

Abbreviation: BMI, body mass index.

[a]Not adjusted for age.

[b]Among 24,396 male ever smokers and 49,822 female ever smokers.

[c]Among 82,158 parous women.

[d]Breads include white bread, rye bread, other dark bread, English muffins/bagels/rolls, muffins/biscuits, pancakes/waffles, crackers, pizza, tortillas, pretzels, breakfast bars, energy bars, and high-protein bars.

[e]Baked goods include cookies, cake, pie, brownies, doughnuts, and sweet rolls/coffee cake/other pastries.

[f]Potatoes include baked/boiled/mashed potatoes, French fries, and potato chips.

[g]Coffee includes regular, decaffeinated, and dairy coffee drinks.

Table 2. HR and 95% CI for quartiles of energy-adjusted dietary acrylamide intake and risk of total RCC in the full cohorts and among never-smokers, and risk of fatal RCC and clear cell RCC in the full cohorts

	Men (HPFS)			Women (NHS)		
	# Cases	Simple HR (95% CI)[a]	Multivariable HR (95% CI)[b]	# Cases	Simple HR (95% CI)[a]	Multivariable HR (95% CI)[b]
Total RCC						
Full cohort						
Quartile 1	66	1.00 (ref.)	1.00 (ref.)	82	1.00 (ref.)	1.00 (ref.)
Quartile 2	86	1.32 (0.95–1.82)	1.32 (0.95–1.84)	87	0.94 (0.69–1.27)	0.93 (0.69–1.27)
Quartile 3	68	1.04 (0.73–1.46)	1.01 (0.71–1.43)	96	1.02 (0.76–1.38)	1.01 (0.75–1.36)
Quartile 4	72	1.21 (0.86–1.70)	1.09 (0.77–1.55)	72	0.87 (0.63–1.19)	0.85 (0.61–1.17)
P_{trend}		0.54	0.96		0.47	0.39
Never-smokers						
Quartile 1	25	1.00 (ref.)	1.00 (ref.)	39	1.00 (ref)	1.00 (ref.)
Quartile 2	30	1.16 (0.68–2.00)	1.24 (0.72–2.14)	42	1.01 (0.65–1.57)	1.00 (0.64–1.55)
Quartile 3	33	1.37 (0.80–2.34)	1.42 (0.83–2.44)	41	1.08 (0.69–1.68)	1.07 (0.68–1.67)
Quartile 4	34	1.63 (0.96–2.78)	1.59 (0.93–2.72)	29	1.06 (0.65–1.73)	1.05 (0.64–1.71)
P_{trend}		0.06	0.09		0.76	0.79
Fatal RCC						
Full cohort						
Quartile 1	16	1.00 (ref.)	1.00 (ref.)	24	1.00 (ref.)	1.00 (ref.)
Quartile 2	24	1.68 (0.89–3.19)	1.71 (0.90–3.25)	19	0.81 (0.44–1.49)	0.79 (0.43–1.45)
Quartile 3	20	1.51 (0.77–2.94)	1.48 (0.76–2.90)	21	0.93 (0.51–1.68)	0.89 (0.49–1.61)
Quartile 4	24	2.02 (1.06–3.85)	1.82 (0.94–3.52)	23	1.13 (0.63–2.02)	1.09 (0.60–1.97)
P_{trend}		0.05	0.13		0.59	0.68
Clear cell RCC						
Full cohort						
Quartile 1	38	1.00 (ref.)	1.00 (ref.)	58	1.00 (ref.)	1.00 (ref.)
Quartile 2	53	1.36 (0.89–2.07)	1.34 (0.87–2.04)	61	0.91 (0.64–1.31)	0.92 (0.64–1.33)
Quartile 3	42	1.04 (0.67–1.62)	0.98 (0.62–1.53)	59	0.88 (0.61–1.27)	0.88 (0.61–1.27)
Quartile 4	46	1.25 (0.81–1.94)	1.09 (0.70–1.70)	54	0.92 (0.63–1.34)	0.92 (0.63–1.35)
P_{trend}		0.56	0.91		0.66	0.67

[a]Stratified by age in months and calendar time.

[b]Additionally adjusted for BMI (<23, 23–<25, 25–<27, and ≥27 kg/m^2), history of hypertension (yes and no), history of diabetes (yes and no), smoking status (analyses including smokers only; never, former/quit >10 years ago, former/quit ≤10 years ago, and current), pack-years (analyses including smokers only; continuous), duration of nonaspirin nonsteroidal anti-inflammatory drug use (<5 years and ≥5 years), energy intake (continuous), alcohol consumption (quartiles), and parity (NHS only; 0, 1–2, 3, and ≥4 children).

In conclusion, our results suggest there is not an important association between acrylamide intake and RCC risk, adding to the body of evidence that dietary acrylamide is not an important risk factor for cancer in humans.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Disclaimer

The authors assume full responsibility for analyses and interpretation of these data.

Authors' Contributions

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Development of methodology: R.E. Graff, E. Cho
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): E. Cho, M.A. Preston
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): R.E. Graff, E. Cho, M.A. Preston, A. Sanchez, K.M. Wilson
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