

Meat-Related Mutagens and Pancreatic Cancer: Null Results from a Clinic-Based Case–Control Study

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Abstract

Background: Pancreatic cancer is a devastating disease for which the role of dietary factors remains inconclusive. The study objective was to evaluate risk of pancreatic cancer associated with meat preparation methods and meat-related mutagen consumption using a clinic-based case–control design.

Methods: There were 384 cases and 983 controls; subjects provided demographic information and completed a 144-item food frequency questionnaire, which was used to estimate meat mutagen intake using the National Cancer Institute's CHARRED database (Bethesda, MD). Logistic regression was used to calculate ORs and 95% confidence intervals (CI), adjusted for factors including age, sex, cigarette smoking, body mass index, and diabetes mellitus.

Results: Overall, the findings were null with respect to meat mutagen intake and pancreatic cancer.

Conclusions: The results do not support an association between well-done meat or meat-related mutagen intake and pancreatic cancer and contrast with generally increased risks reported in previous studies.

Impact: These data contribute to evidence about pancreatic cancer and potentially carcinogenic compounds in meat. *Cancer Epidemiol Biomarkers Prev*; 22(7); 1336–9. ©2013 AACR.

Introduction

Authors of The World Cancer Research Fund Second Expert Report (1) evaluated literature on pancreatic cancer risk factors and concluded that current evidence suggests that red meat increases the risk. For meat mutagens and meat preparation/doneness preference, the evidence from 2 cohort and two case–control (2–6) studies has generally shown positive associations between pancreatic cancer and increasing intake of well-done grilled/barbecued meat, heterocyclic amines (HCA), and a mutagenicity activity index (MAI; revertants/grams of daily meat intake) based on mutagenicity in the Salmonella-based Ames Assay (7).

Our objective was to evaluate meat-related mutagen consumption for association with pancreatic cancer using a clinic-based case–control design. This study used a protocol to rapidly identify and enroll cases that were seen at the Mayo Clinic (Rochester, MN).

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Materials and Methods

Study population description

This study was approved by the Mayo Clinic Institutional Review Board. The study population has been described in detail elsewhere (8).

Dietary data from FFQ

Participants were asked to complete a 144-item food frequency questionnaire (FFQ). Details are given in our previous report (8).

Meat mutagens

Meat-related responses from the FFQ and a meat-cooking module were used with a database, CHARRED (9), developed at the National Cancer Institute (Bethesda, MD) to estimate average intake of meat-related mutagens and the MAI. The database reports on the 3 most mass abundant of 15-plus identified HCAs known to accumulate in cooked meat, whereas the MAI is a more general measure of DNA-damaging potential.

Statistical analysis

Reported intake of grilled/barbecued and broiled red meat was analyzed by categories of doneness preferences. Intake in controls was split into quartiles with the reference group consisting of those who reported no intake. For meat-related mutagens and associations with pancreatic cancer, a logistic regression model was used to calculate ORs and 95% confidence intervals (CI)

Table 1. Selected meat doneness preference categories associated with pancreatic adenocarcinoma

	Quartile				<i>P</i> _{trend}
	1	2	3	4	
Total red meat – grilled/barbecued, g/day^{c,a}					0.003
Cases	51	156	107	70	
Median (range)	0	2.13 (0.11–2.72)	3.74 (2.75–8.02)	11.4 (8.08–80.51)	
OR (95% CI)	1.00 (ref)	0.98 (0.64–1.48)	0.76 (0.49–1.17)	0.53 (0.34–0.84)	
Total red meat – broiled, g/day^{c, b}					0.03
Cases	272	52	31	29	
Median (range)	0	0.79 (0.11–1.02)	1.87 (1.08–3.4)	5.44 (3.57–32.77)	
OR (95% CI)	1.00 (ref)	0.86 (0.59–1.26)	0.58 (0.37–0.90)	0.67 (0.42–1.06)	

^aTotal red meat not grilled/barbecued (continuous).

^bTotal red meat not broiled (continuous).

^cAdjusted for age, sex, usual adult BMI (continuous), smoking (never, quit 15+ years, quit < 15 years, current), pack-years (continuous), diabetes mellitus (no diabetes mellitus, diabetes mellitus 3+ years), education (less than high school, high school, post-high school <4 years, post-high school 4+ years), race (White non-Hispanic, Black non-Hispanic, other), total white meat (continuous).

of pancreatic cancer adjusting for age, sex, usual adult body mass index (BMI; kg/m²), diabetes mellitus (none and those with diabetes diagnosis <3 years before cancer; diagnosis ≥3 years before cancer), energy intake (per 1,000 kcal), number of drinks of alcohol per week, education (<high school, high school, post-high school <4 years, post-high school 4+ years), race (non-Hispanic White, non-Hispanic Black, other), cigarette smoking status (never, quit 15+ years, quit < 15 years, current), pack-years (continuous), and pack-years squared (continuous). All statistical significance tests were 2-sided; *P* values < 0.05 were considered significant. All analyses were generated using SAS software [Version (9.2); ref. 10].

Results

Compared with controls, cases were more likely to have a personal history of diabetes, be slightly older, be male, and have ever smoked cigarettes. Usual adult BMI was similar in the 2 groups. Using the same group of cases and controls, we previously conducted a sensitivity analysis for demographic characteristics comparing cases that did and did not complete the questionnaire and determined the 2 groups were similar (8).

Controls had significantly higher reported consumption of both grilled/barbecued and broiled meat than cases (Table 1) with OR (95% CI) for the highest versus lowest intake categories of 0.53 (0.34–0.84) and 0.67 (0.42–1.06), respectively.

Median carcinogen intake ranges OR, 95% CI, and trend test of OR across quintiles were calculated (Table 2). Overall, these findings were null. The observed difference in intake and corresponding ORs for white

meat [0.71 (0.51, 0.98)] and for nitrates derived from processed meat [0.26 (0.17, 0.40)] indicates that controls had a significantly higher reported intake of each.

Discussion

Given the previous literature, we hypothesized that there would be positive associations between pancreatic cancer and estimated intake of well-done grilled/barbecued meat, heterocyclic amines, benzo(a)pyrene, and the MAI. However, in general, our results were null with inverse associations between pancreatic cancer and intake of grilled/barbecued and broiled red meat, and nitrate derived from processed meat. Because more than 90% of dietary nitrate intake is from vegetables (11) and because the CHARRED database only assesses mutagen-related intake from meat, we cannot assess overall nitrate intake with pancreatic cancer.

Because meat mutagens (e.g., PhIP, MeIQx, and DiMeIQx) need to be metabolically activated before they form DNA adducts and initiate potential carcinogenic changes (12), there may be positive associations between pancreatic cancer and the HCA meat mutagens among subgroups of individuals in our study with particular polymorphisms in metabolism/antioxidant genes. We will be examining this possibility in future research.

Each of the numerous steps involved in estimating meat-borne carcinogen intake for individuals is prone to measurement error and exposure misclassification including reported intake from a FFQ and laboratory-based carcinogen measurements in specific food samples. We sought to avoid potential biases from assessing diet in individuals with pancreatic cancer (or other conditions) who may have recently changed their intake of meat, by removing participants who reported changing their diet

Table 2. Total meat and meat-related mutagens associated with pancreatic adenocarcinoma

	Quintiles					P _{trend}
	1	2	3	4	5	
Total meat^a						
Total red meat						
Cases	153	144	125	190	172	0.62
Median (range)	1.00 (ref)	0.85 (0.63–1.15)	0.72 (0.53–0.98)	1.00 (0.74–1.34)	0.85 (0.62–1.15)	
OR (95% CI)	13.59 (0.8–19.26)	24.06 (19.28–28.49)	32.48 (28.5–37.13)	42.61 (37.16–51)	62.69 (51.02–158.47)	
Total white meat						
Cases	167	194	155	167	101	0.02
Median (range)	6.42 (0–9.18)	11.4 (9.19–13.71)	16.46 (13.72–20.17)	24.73 (20.19–31.79)	40.87 (31.8–171.77)	
OR (95% CI)	1.00 (ref)	1.36 (1.02–1.81)	0.98 (0.73–1.33)	1.16 (0.86–1.55)	0.71 (0.51–0.98)	
Meat-related mutagens^b						
MeIQx, ng/day						
Cases	81	74	71	86	68	0.84
Median (range)	4.82 (0–8.61)	12.6 (8.62–16.38)	21.61 (16.39–27.5)	36.37 (27.53–47.76)	68.38 (47.78–541.55)	
OR (95% CI)	1.00 (ref)	0.92 (0.62, 1.36)	0.92 (0.63, 1.36)	1.01 (0.69, 1.47)	0.91 (0.62, 1.35)	
PhIP, ng/day						
Cases	67	84	69	81	79	0.60
Median (range)	7.72 (0–14.89)	24.4 (14.9–34.17)	45.31 (34.26–58.3)	77.04 (58.37–102.11)	162.2 (102.4–883.92)	
OR (95% CI)	1.00 (ref)	1.29 (0.87, 1.91)	1.01 (0.68, 1.51)	1.23 (0.83, 1.82)	1.15 (0.78, 1.71)	
diMeIQx, ng/day						
Cases	82	69	68	77	84	0.81
Median (range)	0.18 (0–0.43)	0.69 (0.43–0.98)	1.33 (0.98–1.72)	2.35 (1.73–3.1)	4.41 (3.11–33.4)	
OR (95% CI)	1.00 (ref)	0.83 (0.56–1.23)	0.82 (0.55–1.21)	0.89 (0.61–1.31)	1.02 (0.70–1.49)	
Mutagenic activity, revertant colonies/day						
Cases	80	80	55	70	95	0.66
Median (range)	803.93 (0–1386.84)	2004.63 (1386.91–2573.39)	3303.56 (2586.32–4195.92)	5089.08 (4199.96–6340.38)	9129.41 (6362.03–92590.62)	
OR (95% CI)	1.00 (ref)	1.05 (0.72–1.53)	0.67 (0.44–1.01)	0.87 (0.58–1.28)	1.21 (0.83–1.75)	
Benzo(a)pyrene, ng/day						
Cases	77	76	81	77	69	0.67
Median (range)	1.33 (0–3.82)	6.68 (3.84–10.13)	14.35 (10.16–20.94)	26.91 (21.03–39.79)	57.73 (39.81–293.26)	
OR (95% CI)	1.00 (ref)	0.96 (0.65–1.41)	0.98 (0.67–1.44)	0.97 (0.66–1.44)	0.90 (0.61–1.33)	
Nitrate from processed meat – measured, mg/day						
Cases	125	79	72	60	48	<.0001
Median (range)	0.01 (0–0.02)	0.03 (0.02–0.05)	0.06 (0.05–0.08)	0.1 (0.08–0.14)	0.26 (0.14–1.1)	
OR (95% CI)	1.00 (ref)	0.57 (0.40–0.83)	0.48 (0.33–0.70)	0.38 (0.26–0.57)	0.26 (0.17–0.40)	

^aAdjusted for age, sex, usual adult BMI (continuous), cigarette smoking (ever, former, never), diabetes mellitus (no diabetes mellitus, diabetes mellitus 3+ years), education (less than high school, high school, post-high school <4 years, post-high school 4+ years), race (non-Hispanic White, non-Hispanic Black, other).

^bChanged the adjustment for cigarette smoking (never, quit < 15 years, current), and additionally adjusted for pack-years (continuous), pack-years squared (continuous).

within the last 5 years. However, this also reduced the sample size and our power to detect potential effects.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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