

Food Habits and Pancreatic Cancer: A Case-Control Study of the Francophone Community in Montreal, Canada¹

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Abstract

In a population-based case-control study of pancreatic cancer and nutrition among the Francophone population of Montreal (Quebec, Canada), a total of 179 cases and 239 controls matched for age, sex, and language (French) were interviewed between 1984 and 1988. Data on food habits, methods of food preparation and preservation, and related information were obtained through a questionnaire. The study found an increased risk of pancreatic cancer associated with a high consumption of salt [relative risk (RR) = 4.28; 95% confidence interval (CI) = 2.20–8.36], smoked meat (RR = 4.68; CI = 2.05–10.69), dehydrated food (RR = 3.10; 95% CI = 1.55–6.22), fried food (RR = 3.84; 95% CI = 1.74–8.48), and refined sugar (RR = 2.81; 95% CI = 0.94–8.45). An inverse association was found with the consumption of food with no preservatives or additives (RR = 0.08; 95% CI = 0.01–0.59), raw food (RR = 0.28; 95% CI = 0.10–0.75), and food prepared by presto or high-pressure cooking (RR = 0.35; 95% CI = 0.15–0.81), electricity (RR = 0.30; 95% CI = 0.90–0.99), or microwave oven (RR = 0.56; 95% CI = 0.34–0.92). Cooking with firewood was associated with a significantly higher risk for pancreatic cancer (RR = 4.63; 95% CI = 1.15–16.52). The results of this study suggest that food habits may play an important role in the etiology of cancer of the pancreas among French Canadians in Montreal, whereas other food habits may reduce the risk of this disease.

Introduction

Because of its increasing incidence and poor prognosis, cancer of the pancreas is one of the most important malignant diseases in humans. Countries at highest and lowest risk show a 20-fold difference in incidence rate. The highest incidence rates for both males and females are found among African-Americans in Alabama (males, 13.7 of 100,000; females, 11.9 of 100,000). In Canada, the average incidence rates (1983–1987) were 8.8 and 5.8/100,000 for males and females, respectively. In

Quebec, rates for the same years were 10.3 for males and 6.2 for females (1).

Several studies have been carried out on the relation between dietary pattern, nutrition, and cancer of the pancreas, but very little is known about the possible role of "food habits," such as method of preparation and preservation of food, eating habits, and patterns of food consumption. A positive association between fat consumption and increased risk of pancreatic cancer has been reported previously based on epidemiological studies (2–9). Although some studies have also shown increased risk associated with consumption of meat, particularly beef (10–12), other studies found no significant increase in risk related to fat consumption (13) or beef intake (6, 10, 14). Increased consumption of fried food (13), particularly fried and grilled meat (5), has been associated with an increased risk of pancreatic cancer. A positive association between the mortality rate from pancreatic cancer and a high intake of sugar has been reported (7, 9, 13). Consumption of fresh fruits and vegetables has been associated with decreased risk (5, 6, 11, 13, 15).

The SEARCH program has recently undertaken a large, collaborative, case-control study (802 cases and 1669 controls) of nutrition and pancreatic cancer involving five different populations. In the Montreal part of this study (8), positive associations between intake of total fat, particularly saturated fat, and pancreatic cancer were observed. In this paper, we present the results of the study concerning food habits and pancreatic cancer among French Canadians in Montreal.

Materials and Methods

As part of the collaborative study group, we in the Montreal center used a general qualitative questionnaire adjusted for our particular area to include specific questions concerning the food habits of those with pancreatic cancer. These questions concerned containers used for preparation, preservation, and consumption of food, fuel used for cooking, methods of food preservations and food storage, beverages used with meals, temperature at which foods and drinks were consumed, and, finally, frequency of consumption ("never," "rarely," "occasionally," and "very often") of approximately 20 food items and food groups. Food items were preserved food (frozen and canned), dried food (fruits, vegetables, etc.) and dehydrated food (packaged soup, etc.), raw food (natural food, such as fresh fruits and vegetables and foods with no additives and preservatives), cooked food, fried, grilled, and barbecued food, fast food, spiced food, food salted during preparation or at the table or sweetened food (food to which refined sugar had been added), and food containing large quantities of fat.

Cases Ascertainment. During 1984–1988, all French-speaking patients between the ages of 35 and 79 years with a clinical or histological diagnosis of cancer of the pancreas, bile duct, or gallbladder were identified through admission offices, pathology departments, gastroenterological services, and medical record departments of all 19 Francophone hospitals located in

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greater Montreal and serving predominantly French-speaking patients.

Patients with a clinical diagnosis of the cancers of interest were interviewed before confirmation through histological diagnosis was received because, given the rapid progression of these cancers, waiting for the histological diagnosis often makes direct interviews impossible. For some patients, diagnosis was made entirely on the basis of clinical or radiological findings (four patients had a clinical diagnosis of pancreatic cancer that was later found to be incorrect; these patients were excluded from the study group).

Once an eligible case was identified, the attending surgeon or physician was approached for permission to interview the patient. If permission was given, the patient was then contacted by letter, followed by a telephone call to arrange an interview. Proxy interviews were carried out in those cases where the patient was very ill or recently deceased (less than 12 months before interview).

During the period from June 1984 to June 1988, we identified a total of 447 cases of cancer of the pancreas. Of these, 144 (32%) were ineligible: 31 (22%) because of age, 71 (49%) because of date of death (more than 12 months before interview), and 42 (29%) because their place of residence was outside the study region. In the remaining 303 eligible cases, we were unable to obtain physician permission to interview the patient in 32 cases (11%), and, in 29 (9%) instances, patients or their proxy relatives refused to be interviewed. Twenty-one physicians (7%) did not answer our request for permission to interview their patients. We were unable to contact 20 (7%) cases due to wrong addresses and 18 (6%) of the cases who had died during the preceding 12 months and lacked a reliable proxy. Therefore, we interviewed 183 (60%) eligible cases. Four cases (1%) were later excluded because of wrong diagnosis, giving a final total of 179 pancreatic cancer patients (97 males and 82 females) interviewed during 1984–1988 by trained interviewers using a structured questionnaire. Of these cases, 25% were interviewed directly and 75% through proxies. The average period from identification of an eligible case to interview was 6 months, and the matched control was interviewed no longer than 3 months after the interview of the case. Of the cases interviewed, (Table 1) 83% were confirmed histologically; the remaining 17% were diagnosed clinically or radiologically. The overall participation rate for cases was 64% (8).

Controls Ascertainment. Population-based controls, individually matched for age (within 5-year-age-group), sex, place of residence, and language (during our very large study of food habits it was found that French Canadians in Montreal have a distinctive lifestyle and food habits; this led to our decision that controls and cases should be matched for language), were selected from the telephone directory in which the corresponding case was listed (all patients studied had a listed telephone number; 1% of families in the Montreal region do not have a telephone). A page from the telephone directory was randomly selected from the sampling frame, and the names and addresses of 10 individuals with the same first 3-digit telephone numbers as the patient were selected. These residences were then contacted by letter, and the aims of the study explained. Approximately 1 week later, these residences were telephoned to see if they contained an individual who matched the original case for age and sex, and if they would agree to be interviewed. If so, an interview was arranged at the control's home. If not, the procedure was repeated. If more than one eligible control was reached at a given number, one subject was selected randomly

Table 1 Distribution of cases and controls by sex and response status

	Males		Females		Both sexes	
	Direct ^a	Proxy	Direct ^a	Proxy	Direct ^a	Proxy
Cases						
No.	23	74	22	60	45	134
%	12.8	41.3	12.3	33.5	25.1	74.9
Controls						
No.	87	36	112	4	199	40
%	36.4	15.1	46.9	1.6	83.3	16.7
Total						
No.	110	110	134	64	244	174
%	26.3	26.3	32.1	15.3	58.4	41.6

^a Direct and assisted interviews.

as the index control, and information about the remaining control(s) was kept in a data bank for additional use. For cases without a telephone, RDD would have been used to select the control. The overall response rate for controls was 47% (Table 1).

To be acceptable, a control must have been alive when the patient's cancer was diagnosed. Living controls were interviewed directly. If a control had died between the time of diagnosis of the matched case and his/her date of interview, a proxy control interview was conducted.

Interviews for both cases and controls were carried out in the respondent's home. If either the case or control was hospitalized at the time of the scheduled interview and seemed unlikely to be available for a home interview within 2 weeks, an in-hospital interview was attempted. If a patient was very ill, whether at home or in hospital, the interview was carried out in the presence of, and with the help of, any family members or other persons who were available and likely to have relevant information. The detailed study methodology of the study has been published elsewhere (8). A total of 239 population-based control subjects (123 males and 116 females) were interviewed in this study; 83% were interviewed through direct interviews and 17% by proxy.

Questionnaires. All information was obtained through questionnaires containing core questions as well as questions on food frequency and food habits and administered in a standardized manner to all cases and controls at the home of the study subject by trained interviewers.

Results

A total of 179 Francophones with pancreatic cancer and 239 controls matched for age, sex, place of residence, and language were interviewed. The mean age at diagnosis was 63.9 years for cases and 62.1 years at time of selection for controls. For statistical analysis, conditional logistic regression was used to estimate relative risk and the CI³ was adjusted for age and sex. Food intake and related food habits were categorized as taking place "never," "rarely," "once in a while," "often," and "very often." The relative risk and 95% CI for each category are estimated, along with a test for trend.

It was found that total fat consumption was an important risk factor, with an OR of 2.97 (highest to lowest quartile) and 95% CI of 1.02–8.62. The risk was stronger for saturated fat

³ The abbreviations used are: CI, confidence interval; RR, relative risk; OR, odds ratio.

Table 2 Relative risk of pancreatic cancer associated with the intake of major nutrients (significant) adjusted for age, sex, lifetime cigarette consumption, response status, and total energy intake

Total energy is not adjusted for itself. For total fat, saturated fat, and total carbohydrates, the adjustment for energy has been replaced by an adjustment for other sources of energy.

Nutrient	Exposure category				Continuous exposure highest/lowest quartile
	Q ¹	Q ²	Q ³	Q ⁴	
Total energy					
OR	1.00	1.12	1.15	2.16	2.07
95% CI		0.53–2.35	0.53–2.49	0.97–4.81	0.97–4.43
Total fat					
OR	1.00	0.69	1.91	2.24	2.97
95% CI		0.29–1.65	0.71–5.16	0.74–6.73	1.02–8.62
Saturated fat					
OR	1.00	1.10	2.54	4.32	5.02
95% CI		0.46–2.60	0.89–7.23	1.37–13.7	1.63–15.4
Cholesterol					
OR	1.00	1.15	1.64	2.24	2.31
95% CI		0.53–2.51	0.67–4.05	0.83–6.05	0.87–6.11

(OR = 5.02; 95% CI = 1.63–15.4). Although total energy intake, as well as dietary cholesterol consumption appeared to increase risk (Table 2), and a number of micronutrients were apparently associated with reduction of risk, these were not statistically significant (8).

Table 3 contains details of the frequency pattern of each variable as well as RR, 95% CI, and *P* for trend. There was an apparent increase in risk of pancreatic cancer associated with a high intake of smoked food. The RR for frequency consumption reported as “often,” compared with “never” was 4.68 (95% CI = 2.05–10.69), and the difference between cases and controls was statistically significant (*P* < 0.01). Salted food intake also appeared to be a major risk factor, showing an RR of 9.94 (95% CI = 3.79–26.06). It was found that cases used more salt both during the preparation of food (RR = 3.81; 95% CI = 1.64–8.83) and at the table (RR = 4.28; 95% CI = 2.20–8.36), and differences from controls were statistically significant. We also found that higher risks were associated with more frequent consumption of fried food (RR for the category of “often” consumers as compared with “never” consumers was 3.84 with 95% CI of 1.74–8.48), higher intake of dehydrated food (RR = 3.10; 95% CI = 1.55–6.22), and higher frequency of consumption of refined sugar (RR = 2.81; 95% CI = 0.94–8.45).

An inverse association with risk of pancreatic cancer was observed with consumption of raw food, such as fresh fruits and vegetables (RR = 0.28; 95% CI = 0.10–0.75) and natural food (fresh foods and foods with no additives and preservatives, or previous preparation; RR = 0.08; 95% CI = 0.01–0.59).

In considering methods of cooking and food preparation, a lower risk was observed for individuals who used electricity (RR = 0.30; 95% CI = 0.90–0.99), steam or presto (pressure cookers; RR = 0.35; 95% CI = 0.15–0.81), or microwave ovens for cooking (RR = 0.56; 95% CI = 0.34–0.92). A small number of both cases and controls in the study region still cooked on wood stoves and it was found that more frequent use of wood as fuel source was associated with higher risk (RR = 4.63; 95% CI = 1.15–16.52) for pancreatic cancer.

Discussion

The results of this study among French Canadians support earlier findings regarding the role of fat in the etiology of pancreatic cancer. The positive association with frequent consumption of smoked food (meat) suggested in this study is interesting. Polycyclic aromatic hydrocarbons, which have been linked with cancer, are formed during incomplete combustion of organic material. Among the various foods studied which contain polycyclic aromatic hydrocarbons, smoked products such as smoked meat are the most popular. Several epidemiological studies in different countries have indicated the possible association between increased incidence rates of gastric cancer and high consumption of smoked meat (16, 17). We detected an RR of 1.68 for those individuals who consumed smoked meat once in a while, whereas the difference between those who never consumed smoked food and those who consumed it often is 4.68, which is statistically significant.

It has been suggested that a high intake of sodium chloride (salt) plays a role in the etiology of stomach cancer (18, 19). In this study, we found that a high intake of salted food and salt increases the risk of pancreatic cancer significantly. This has been previously reported only by one case-control study (20) and a statistical analysis of food pattern and cancer incidence study. Our findings offer support for these reports and suggest that further studies are needed on the role of salt in the etiology of pancreatic cancer.

The formation of mutagens during the generation of heat and grilling of food, particularly fish and meat, was first reported by Sugimura *et al.* in 1977 (22) and Commoner *et al.* in 1978 (23). These mutagenic substances have been demonstrated to be carcinogenic when tested on laboratory animals (24, 25). One cohort (10) and three case-control (5, 13, 26) studies have reported that frequent consumption of deep-fried food, particularly meat, increases the risk of pancreatic cancer. We found that those who rarely consume fried food have an RR of 1.92 when compared with those who never consume it. Rates were 2.28 and 3.84, respectively, for those who consumed fried food once in a while and often, indicating a dose response.

Our study indicates that cases consumed dehydrated food, such as powdered soup, more frequently than controls. Perhaps the long process of dehydration causes certain changes (creatinine) in the composition of the original food. It could also be that those subjects who frequently consume dehydrated food seldom consume raw or untreated food. This finding has not been reported before and needs careful interpretation and additional study.

Our data suggest that refined sugar plays a role in the etiology of pancreatic cancer, supporting published reports (10, 14). An international correlation study (27) found an association between refined sugar intake and mortality from pancreatic cancer. Two case-control studies (13, 28) reported that cases consumed higher amounts of refined sugar and sugared drinks, whereas another study (26) demonstrated a decreased risk of pancreatic cancer among those who drank low-calorie soda. We found increased risk associated with frequent consumption of refined sugar, with a clear dose response.

We found diminished risk associated with the consumption of raw and natural foods, such as fresh fruits and vegetables. Decreased risk of pancreatic cancer has been associated with increased consumption of fresh fruits and vegetables (5, 6, 9, 26, 28), possibly because of dietary fiber, vitamin C, and β -carotene. In our study, consumption of foods that were uncooked or without preservatives decreased the risk of pancreatic cancer significantly; frequent consumers of such foods had

Table 3 Comparison of the food habits between cases and controls, adjusted for age and sex: RR of often versus never

Variable	Frequency	Case	Control	RR	95% CI	P (trend)
Smoked food (meat)	Never	55	89	1.00		
	Rarely	44	88	0.84	0.51–1.40	
	Once in a while	48	49	1.68	0.98–2.87	
	Often	27	10	4.68	2.05–10.69	<0.01
Salted food	Never	28	66	1.00		
	Rarely	66	90	1.83	1.05–3.18	
	Once in a while	38	49	1.99	1.06–3.74	
	Often	19	27	1.79	0.83–3.88	
	Very often	27	7	9.94	3.79–26.06	<0.01
Salt (food preparation)	Never	37	65	1.00		
	Rarely	47	68	1.21	0.70–2.11	
	Once in a while	71	94	1.36	0.82–2.99	
	Often	23	11	3.81	1.64–8.83	0.0098
Salt (table)	Never	85	159	1.00		
	Rarely	27	28	1.82	1.00–3.30	
	Once in a while	31	36	1.71	0.97–3.01	
	Often	35	16	4.28	2.20–8.36	<0.0001
Fried food	Never	41	93	1.00		
	Rarely	69	92	1.92	1.15–3.18	
	Once in a while	33	37	2.28	1.22–4.24	
	Often	22	15	3.84	1.74–8.48	
	Very often	13	2	16.71	3.54–78.83	<0.01
Dehydrated food	Never	56	104	1.00		
	Rarely	52	61	1.64	0.99–2.70	
	Once in a while	38	53	1.37	0.80–2.35	
	Often	27	18	3.10	1.55–6.22	<0.01
Refined sugar	Never	6	11	1.00		
	Rarely	24	56	0.84	0.27–2.59	
	Once in a while	46	75	1.26	0.42–3.72	
	Often	41	52	1.71	0.56–5.18	
	Very often	61	45	2.81	0.94–8.45	<0.01
Raw food	Never	13	7	1.00		
	Rarely	36	26	0.77	0.27–2.25	
	Once in a while	29	38	0.40	0.14–1.16	
	Often	51	75	0.37	0.14–1.01	
	Very often	49	93	0.28	0.10–0.75	<0.01
Natural food	Never	164	188	1.00		
	Rarely	8	18	0.52	0.22–1.26	
	Once in a while	1	15	0.08	0.01–0.59	
	Often	2	10	0.23	0.05–1.06	<0.01

70–75% less chance of developing pancreatic cancer as compared with those who never consumed raw and natural foods.

It is important to consider some potential methodological problems and limitations in this study, which could have biased observed results. Extensive use was made of proxy respondents, particularly for cases. Proxy status was included as a variable in the analysis of nutrient intake, but not in the food habits study. However, because proxies were used for both cases and controls, any bias introduced in this study should have been reduced. As well, in our main analysis of nutrition and pancreatic cancer (8), the relative risk related to various nutrients was generally similar for proxy and nonproxy respondents.

Selection bias may have occurred because participation rates were low (64% for cases and 47% for controls) and because we have no information concerning the characteristics of nonparticipant subjects. Recall bias is another methodological limitation that should be considered. Cases may recall their diets differently from controls because of the stress of diagnosis and treatment of cancer, but this differential recall is unlikely to be a major source of bias (8, 29). As well, except for nutrients (fat), the data are adjusted for only age and sex.

In conclusion, food habits (such as methods of food preparation and preservation) and frequent consumption of certain foods (such as smoked meat, fried food, dehydrated food,

refined sugar, and salted food) may play important role in the etiology of pancreatic cancer. Other food habits, such as consumption of fresh fruits and vegetables and raw food, may reduce the risk. Additional studies are needed to clarify the possible role of these factors in the etiology of pancreatic cancer.

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