Dietary habits and prostate cancer detection: a case–control study

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Abstract

Background: Many studies have suggested that nutritional factors may affect prostate cancer development. The aim of our study was to evaluate the relationship between dietary habits and prostate cancer detection.

Methods: We studied 917 patients who planned to have transrectal ultrasonography–guided prostatic biopsy based on an elevated serum prostate-specific antigen (PSA) level, a rising serum PSA level or an abnormal digital rectal examination. Before receiving the results of their biopsy, all patients answered a self-administered food frequency questionnaire. In combination with pathology data we performed univariable and multivariable logistic regression analyses for the predictors of cancer and its aggressiveness.

Results: Prostate cancer was found in 42% (386/917) of patients. The mean patient age was 64.5 (standard deviation [SD] 8.3) years and the mean serum PSA level for prostate cancer and benign cases, respectively, was 13.4 (SD 28.2) µg/L and 7.3 (SD 4.9) µg/L. Multivariable analysis revealed that a meat diet (e.g., red meat, ham, sausages) was associated with an increased risk of prostate cancer (odds ratio [OR] 2.91, 95% confidence interval [CI] 1.55–4.87, $p = 0.027$) and a fish diet was associated with less prostate cancer (OR 0.54, 95% CI 0.32–0.89, $p = 0.017$). Aggressive tumours were defined by Gleason score (≥ 7), serum PSA level (≥ 10 µg/L) and the number of positive cancer cores (≥ 3). None of the tested dietary components were found to be associated with prostate cancer aggressivity.

Conclusion: Fish diets appear to be associated with less risk of prostate cancer detection, and meat diets appear to be associated with a 3-fold increased risk of prostate cancer. These observations add to the growing body of evidence suggesting a relationship between diet and prostate cancer risk.

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Introduction

The incidence and mortality rates of prostate cancer vary widely among countries. The lowest prostate cancer incidence and mortality rates are observed in the Far East and on the Indian subcontinent, and the highest rates occur in western Europe, Australia and North America, with up to a 30-fold variation between highest and lowest rates.[1,2] Interestingly, there are differences within the same ethnic groups, such as Japanese living in the United States, who have a 4–5 times higher incidence of prostate cancer than those living in Japan.[3] Environmental and lifestyle factors, including dietary habits, are suggested as determinants. Total energy intake,[4,5] fat intake, especially of animal sources,[5–7] and dairy products and calcium[8,9] have been associated with a positive risk.[10] Among fruits and vegetables with suggested protective effects are tomatoes[11] and yellow-orange and cruciferous vegetables,[12] although other studies[13,14] have not shown this association. A fish diet, with its unique marine omega-3 polyunsaturated fatty acids, has been suggested by some studies[15,16] to protect against prostate cancer although others[17] have found no association. We studied the association between different dietary items and the detection of prostate cancer in a cohort of high-risk men.

Methods

Our study included 1356 patients who underwent transrectal ultrasonography–guided prostatic biopsy at the McGill Prostate Cancer Detection Clinic in Montréal, Que., between August 2003 and November 2006. The indication for biopsy was based on an abnormally elevated serum prostate-specific antigen (PSA) level, a rising serum PSA level or a suspicious digital rectal examination. All men were asked to respond to a self-administered food frequency questionnaire (Appendix 1) before the procedure. Of these patients, 917 (68%) agreed and completed the questionnaire, which measured the number of servings per week among 12 food groups. The questionnaire also included demographic data (i.e., age, marital status, ethnicity, occupation and level of education), smoking habits, alcohol intake, family history of prostate cancer, medical history of general diseases (e.g., diabetes mellitus, liver diseases, heart diseases and arthritis) and local genitourinary conditions (e.g., cystitis, prostatitis,

sexually transmitted infections and vasectomy). Transrectal ultrasonography–guided prostatic biopsy was performed via the standard approach as described by Tanguay and colleagues[18] with a median of 10 biopsy cores (range 6–14). All biopsies were examined by the same uropathologist (L.B.).

The dietary intakes were divided into quintiles based on distributions. To assess recall bias we compared 50 (5.5%) patients who had repeated the questionnaire in their follow-up visits after 3 to 12 months. There was no statistically significant difference between the questionnaire answers in both sessions ($p = 0.11$) using the χ^2 test. We performed univariable and multivariable logistic regression analyses between the highest and lowest quintile of each food group and the detection of prostate cancer, and we estimated the odds ratio (OR) of prostate cancer and 95% confidence interval (CI) for food groups with adjustments for age, ethnicity, level of education, family history of prostate cancer, smoking and alcohol consumption, sexually transmitted infections, cystitis and prostatitis. We compared prostate cancer cases ($n = 386$, 42.1%) and nonsignificant pathology ($n = 268$, 29.2%) after exclusion of cases with high-grade prostatic intraepithelial neoplasia and atypical small acinar proliferation. We defined aggressive prostate cancer by a Gleason score of 7 or

Table 1. Characteristics of study patients

Characteristics	No. (and %) of cases	No. (and %) of controls	Odds ratio (95% CI)	*p* value
Age, yr				
60–64	77 (20.0)	72 (26.9)	1.06 (0.77–1.47)	
65–69	96 (24.9)	68 (25.4)	1.41 (1.03–1.92)	
≥ 70	141 (36.5)	38 (14.2)	3.71 (2.59–5.30)	< 0.001
Ethnicity*				
White	212 (55.0)	151 (56.3)	1.00†	
Black	13 (3.4)	5 (1.9)	2.60 (0.92–7.29)	
Asian	16 (4.2)	22 (8.2)	0.72 (0.38–1.38)	
Hispanic	9 (2.3)	9 (3.4)	1.00 (0.39–2.51)	
Other	97 (25.9)	66 (24.6)	0.63 (0.49–0.81)	0.250
Level of education, yr*				
< 7	60 (15.5)	32 (12.0)	1.00†	
7–11	132 (34.2)	76 (28.4)	1.71 (1.11–2.65)	
≥ 12	152 (39.4)	138 (51.5)	1.10 (0.87–1.38)	0.060
Family history of prostate cancer	23 (6.0)	24 (9.0)	0.95 (0.54–1.69)	0.150
Smoking habit, index,* cigarette packs/yr				
Never smoke	129 (33.4)	102 (38.1)	1.00†	
< 200	35 (9.1)	30 (11.2)	1.16 (0.71–1.89)	
200 to < 400	33 (8.6)	23 (8.6)	1.43 (0.84–2.44)	
≥ 400	94 (24.4)	69 (25.8)	1.36 (0.99–1.85)	0.600
Alcohol, servings/wk*				
No alcohol	41 (10.6)	33 (12.3)	1.00†	
1	39 (10.1)	39 (14.6)	1.00 (0.64–1.55)	
2–3	52 (13.5)	30 (11.2)	1.73 (1.10–2.71)	
4–6	31 (8.0)	29 (10.8)	1.06 (0.64–1.77)	
≥ 7	45 (11.7)	33 (12.3)	1.63 (1.06–2.52)	0.330
Vasectomy‡	70 (18.1)	45 (16.8)	1.09 (0.65–1.78)	0.340
STIs‡	101 (26.2)	65 (24.3)	1.13 (0.59–1.96)	0.230
Cystitis and/or prostatitis‡	58 (15.0)	44 (16.4)	1.23 (0.83–2.12)	0.520

CI = confidence interval; STI = sexually transmitted infection.
*Does not sum to total because of missing values.
†Reference category.
‡Categorized variables.

Table 2. Multivariable odds ratios of food groups and the risk of prostate cancer*

	Quintiles†										
	1		2		3		4		5		
Food	Servings/wk	Risk of prostate cancer, OR‡	Servings/wk	Risk of prostate cancer, OR (95% CI)	Servings/wk	Risk of prostate cancer, OR (95% CI)	Servings/wk	Risk of prostate cancer, OR (95% CI)	Servings/wk	Risk of prostate cancer, OR (95% CI)	*p* value
Dairy products	2	1.00	4	1.44 (0.99–2.18)	6	1.26 (0.94–2.21)	7	1.35 (0.84–1.91)	NA	1.21 (0.74–2.01)	0.240
Red meat, ham, sausages	1	1.00	2	1.55 (0.85–1.69)	4	1.97 (0.74–2.73)	5	2.31 (1.32–2.46)	NA	2.91 (1.55–4.87)	0.027
Chicken	1	1.00	2	0.89 (0.52–1.48)	3	1.02 (0.56–1.84)	4	1.26 (0.58–2.75)	NA	0.67 (0.28–1.53)	0.340
Fish	1	1.00	2	1.23 (0.67–1.45)	3	0.97 (0.95–1.56)	4	0.77 (0.26–0.91)	NA	0.54 (0.32–0.89)	0.017
Bread, pasta, rice, maize	2	1.00	4	1.70 (0.86–3.66)	6	1.81 (0.84–3.86)	7	1.67 (0.91–3.05)	NA	2.22 (0.87–5.66)	0.090
Potatoes	1	1.00	2	1.09 (0.60–1.98)	3	0.65 (0.34–1.25)	4	0.63 (0.30–1.31)	NA	0.57 (031–1.08)	0.080
Any green vegetables	2	1.00	4	1.29 (0.63–2.60)	6	1.66 (0.81–3.40)	7	1.82 (0.87–3.82)	NA	1.60 (0.56–4.57)	0.370
Tomatoes (e.g., fresh, sauce)	2	1.00	4	0.95 (0.56–1.63)	6	0.72 (0.39–1.32)	NA	1.08 (0.54–2.16)	NA	NA	0.810
Pulses (e.g., beans, peas)	2	1.00	4	0.98 (0.50–1.91)	5	1.20 (0.59–2.43)	NA	0.78 (0.34–1.77)	NA	NA	0.550
Fruits (e.g., fresh, juices)	2	1.00	4	1.59 (0.98–2.57)	6	1.15 (0.72–1.83)	7	1.49 (1.17–1.91)	NA	1.03 (0.63–1.66)	0.590
Soy products	2	1.00	4	1.22 (0.60–2.53)	NA	0.98 (0.45–2.14)	NA	NA	NA	NA	0.430
Cakes, dessert, ice cream	1	1.00	3	1.34 (0.92–1.97)	5	1.41 (1.03–1.93)	NA	1.08 (0.75–1.56)	NA	NA	0.470

CI = confidence interval; NA = data is missing or unavailable; OR = odds ratio.
*Adjusted for age, ethnicity, level of education, family history of prostate cancer, smoking and alcohol consumption, sexually transmitted infections, cystitis and prostatitis.
†Expressed as the upper cutoff point.
‡Reference category.

greater, a serum PSA level of 10 µg/L or greater, or 3 or more malignant cores. All statistics were performed using Stata 9.2 (StataCorp).

Results

The mean age was 64.5 (standard deviation [SD] 8.3) years, and the mean serum PSA level for prostate cancer and benign cases was 13.4 (SD 28.2) µg/L and 7.3 (SD 4.9) µg/L, respectively. Table 1 demonstrates the baseline characteristics of both cases and controls with regard to age, ethnicity, level of education, family history of prostate cancer for father or brothers, smoking, alcohol consumption, history of vasectomy, sexually transmitted infections, cystitis and prostatitis. Both groups were similar except for statistically significant differences in the age between cases and controls (OR 3.71, 95% CI 2.59–5.30, $p < 0.001$). The rate of cancer appeared to be higher in African patients and lower in Asian patients but the difference was statistically insignificant.

Multivariable analysis of food groups as shown in Table 2 revealed that a meat diet (e.g., red meat, ham, sausages) was associated with a higher risk of prostate cancer (OR 2.91, 95% CI 1.55–4.87, $p = 0.027$) and a fish diet was associated with less prostate cancer (OR 0.54, 95% CI 0.32–0.89, $p = 0.017$) after adjustment with suspected confounders (e.g., age, ethnicity, family history of prostate cancer).

As regards the factors of aggressive tumours, none of the food groups were found to be associated with a higher Gleason score, a higher serum PSA level or a higher number of cancer cores in our cohort as shown in Table 3.

Discussion

In our study we examined the possible association of different dietary habits with prostate cancer detection. A statistically significant associated risk of prostate cancer was found with a meat-containing diet (OR 2.91) and a fish diet was found to be associated with less prostate cancer (OR 0.54). In our cohort there were 35% and 18% of cases present in the fourth and fifth quintiles of meat diet, respectively, and 25% and 14% of controls were present in the fourth and fifth quintiles, respectively. On the other

hand, 11% and 8% of cases were present in the fourth and fifth quintiles of fish diet, respectively, and 14% and 10.5% of controls were present in the fourth and fifth quintiles, respectively. The fourth and fifth quintiles of meat diet presented 5 and greater than 5 servings per week, respectively, and the fourth and fifth quintiles of fish diet presented 4 and greater than 4 servings per week, respectively. The relationship between prostate cancer development and either total meat and fish or the specific fatty acids as marine omega-3 polyunsaturated fatty acids and omega-6 polyunsaturated fatty acids present in animal sources, was studied in several epidemiological and experimental studies.[19,20] In vivo and in vitro studies suggest that omega-3 polyunsaturated fatty acids may protect against prostate cancer, whereas omega-6 polyunsaturated fatty acids stimulate malignant cell growth.[21–23] Those studies may explain our observations of the protective effect of a high intake of fish and the positive association between a high intake of different types of meat and prostate cancer detection.

Although there exists some evidence of the protective effect of tomatoes and green vegetables against prostate cancer,[13] we did not find any statistically significant association between those types of food with prostate cancer. Stram and coauthors[14] performed a large multiethnic study on the effect of fruits, vegetables and micronutrients and the incidence of prostate cancer and, surprisingly, they also did not find any significant association. In our cohort we observed an association between potatoes and low rates of cancer, and bread, pasta, rice and maize trended toward an association with a higher rate of cancer. Although these associations approached statistical significance ($p = 0.08$ and $p = 0.09$, respectively) it is possible that significance could be achieved with a greater number of patients. In addition, since the main component of both food groups is starch, it is possible that the apparently protective effect of potatoes is due to other associated dietary habits.

With respect to aggressive prostate cancer we examined the association of the same dietary habits with a high Gleason score (≥ 7), higher number of cancer cores (≥ 3) or higher serum PSA level (≥ 10). These criteria were chosen as they are commonly

Table 3. Multivariable odds ratios of food groups and the incidence of aggressive prostate cancer

	Quintiles*; odds ratio (95% confidence interval)								
	Gleason score ≥ 7; *n* = 188, 48.70%			No. of cancer cores ≥ 3; *n* = 235, 60.88%			Serum PSA level ≥ 10 µg/L; *n* = 84, 21.76%		
Food	Q1†	Q5	*p* value	Q1†	Q5	*p* value	Q1†	Q5	*p* value
Dairy products	1	1.16 (0.68–1.97)	0.58	1	0.93 (0.54–1.60)	0.81	1	0.76 (0.43–1.35)	0.35
Red meat, ham, sausages	1	1.09 (0.65–2.45)	0.47	1	0.77 (0.44–1.36)	0.37	1	0.97 (0.54–1.76)	0.94
Chicken	1	1.04 (0.59–1.84)	0.59	1	0.96 (0.54–1.72)	0.90	1	1.05 (0.54–2.04)	0.87
Fish	1	1.44 (0.68–3.03)	0.33	1	1.04 (0.65–1.33)	0.12	1	0.91 (0.39–2.15)	0.84
Bread, pasta, rice, maize	1	0.92 (0.55–1.53)	0.76	1	1.06 (0.63–1.78)	0.80	1	0.80 (0.46–1.39)	0.43
Potatoes	1	1.17 (0.63–2.15)	0.61	1	1.11 (0.60–2.05)	0.60	1	1.49 (0.75–2.94)	0.24
Any green vegetables	1	0.89 (0.65–2.14)	0.27	1	1.09 (0.69–2.25)	0.46	1	1.20 (0.62–2.32)	0.58
Tomatoes (e.g., fresh, sauce)	1	1.27 (0.72–2.23)	0.39	1	1.16 (0.66–2.02)	0.60	1	1.25 (0.66–2.39)	0.48
Pulses (e.g., beans, peas)	1	1.86 (0.86–3.99)	0.11	1	2.89 (0.98–8.16)	0.06	1	1.42 (0.61–3.41)	0.39
Fruits (e.g., fresh, juices)	1	1.55 (0.91–2.62)	0.10	1	1.28 (0.76–2.17)	0.34	1	1.09 (0.93–3.78)	0.09
Soy products	1	1.03 (0.88–1.21)	0.66	1	0.90 (0.65–1.98)	0.23	1	1.13 (0.76–1.89)	0.11
Cakes, desserts, ice cream	1	0.95 (0.55–1.62)	0.86	1	0.70 (0.41–1.22)	0.22	1	1.78 (0.93–3.39)	0.08

PSA = prostate-specific antigen.
*Expressed as the lowest and highest quintiles.
†Reference category.

used in the clinic to differentiate low-risk from higher risk cancers. Although there was a statistically insignificant association between a high intake of pulses and a high Gleason score and a higher number of cancer cores ($p = 0.11$ and $p = 0.06$, respectively), we did not find any statistically significant association between dietary habits and aggressive prostate cancer. It is possible that bias due to biopsy sampling limitations in the identification of aggressive cancer is another reason we did not find significant relationships.

Case–control studies are considered susceptible to information bias more than cohort studies are[24] since cases may be more careful than controls in searching their memory and may infer from known or suspected causes of their disease. To avoid this bias we asked all patients to answer the questionnaire before they received the results of their biopsies. In addition, there are several methods to assess dietary habits. Since developed in the 1950s, self-administered food frequency questionnaires have been considered appropriate methods for dietary assessment in nutritional epidemiology studies since they measure average long-term habitual dietary intake.[25] Self-administered food frequency questionnaires have been validated in many studies compared with 24-hour recalls, food diaries or records of varying length, as well as biomarkers or calculating total energy intake and comparing it with energy expenditure.[26–30] We assessed our questionnaire for variability by asking some patients to answer it again after a variable period of time and we observed no significant difference.

The weaknesses of our study include the short and incomplete nature of the food frequency questionnaire without home confirmation, as well as the fact that the study population comprised men at high risk of prostate cancer who were referred to the centre for biopsy. As such, this study may not apply to the general population.

Conclusion

Fish-containing diets appear to be protective against prostate cancer, and meat diets are associated with a 3-fold increased risk of prostate cancer detection. None of the dietary groups were found to be associated with aggressive prostate cancer on biopsy. These observations add to the growing body of evidence suggesting a relationship between diet and prostate cancer risk.

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Appendix 1. The self-administered food frequency questionnaire

1. Date of birth
2. Marital status
3. Ethnic background
4. Occupation
5. Level of education
6. Family history of prostate cancer
   - History of prostate cancer in biological father
   - History of prostate cancer in biological brothers (how many?)
   - History of prostate cancer in biological sons (how many?)
7. Smoking
   - Age of starting
   - Age of stopping
   - Number of cigarettes per day
8. Dietary intake (how many servings per week?)
   - Dairy products
   - Red meat, ham, sausages
   - Chicken
   - Fish
   - Bread, pasta, rice, maize
   - Potatoes
   - Any green vegetables
   - Tomatoes (fresh, sauce)
   - Pulses (beans, peas, etc.)
   - Fruits (fresh, juices, etc.)
   - Soy products
   - Cakes, dessert, ice cream
   - Alcohol
9. The history of the following diseases and its duration
   - Infection of the bladder
   - Infection of the prostate
   - Cancer of the prostate
   - Diabetes
   - Liver disease
   - Arthritis
   - Heart disease
   - Hypertension
   - Vasectomy
   - Previous prostate biopsy
   - Sexually transmitted diseases (genital warts, gonorrhea, syphilis)