Short Communication

Dietary Patterns and Risk of Prostate Cancer in U.S. Men

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Abstract

We prospectively investigated the associations between dietary patterns and risk of prostate cancer in the Health Professionals Follow-up Study. Between 1986 and 2000, 3,002 incident prostate cancer cases were identified in our cohort. Using factor analysis, two major dietary patterns were identified, a prudent and a western dietary pattern. Dietary patterns were not appreciably associated with risk of total prostate cancer. For the highest versus the lowest quintiles, the multivariable relative risk (RR) for the prudent pattern was 0.94 [95% confidence interval (CI), 0.83-1.06], and for the western pattern, the multivariable RR was 1.03 (95% CI, 0.92-1.17). Neither were these associated with risk of advanced prostate cancer [highest versus lowest quintile, prudent pattern (RR, 1.01; 95% CI, 0.68-1.49); western pattern (RR, 1.13; 95% CI, 0.77-1.67)]. Higher western pattern scores were suggestively associated with a greater risk of advanced prostate cancer among older men [highest versus lowest quintile (RR, 1.35; 95% CI, 0.97-1.90)], but not after adding processed meat to the model [highest versus lowest quintile (RR, 1.11; 95% CI, 0.75-1.65)]. We did not find any evidence for a protective association between prudent pattern and risk of prostate cancer. The lack of association between a western dietary pattern as identified by factor analysis in our cohort and prostate cancer risk suggests that dietary risk factors for prostate cancer are likely to differ from those for other conditions, such as cardiovascular disease and type 2 diabetes, that have been associated with a western dietary pattern in this cohort. (Cancer Epidemiol Biomarkers Prev 2006;15(1):167–71)

Introduction

Factor analysis has been used to examine overall dietary patterns and risk of some cancers (1, 2). Instead of examining the association between individual nutrients and risk of disease, this method examines the association between overall diet and risk of disease, taking into account that foods are eaten in combination (3). Epidemiologic studies that have used factor analysis to examine the association between dietary patterns and prostate cancer are sparse (4, 5). Thus, we investigated the association between dietary patterns and risk of prostate cancer in a large cohort of U.S. health professionals. With the large sample size, we were able to address associations by extent of tumor progression (advanced or nonadvanced) and by age at diagnosis as some studies have suggested etiologic differences for these subgroups (6, 7).

Materials and Methods

Study Population. In 1986, 51,129 male U.S. health professionals ages between 40 and 75 years responded to a questionnaire requesting information about their life-style and their medical history, and a 131-item food frequency questionnaire (FFQ). Every 2 years, follow-up questionnaires were mailed to the participants, and every 4 years, the participants were also asked to fill out another FFQ, i.e., in 1990, 1994, and 1998 (8). We excluded men with very high or very low intakes (i.e., <800 or >4,200 kcal/d), those with a high number of blanks on their FFQ (>70 items blank) and men with a history of cancer (except for non–melanoma skin cancer) prior to 1986. These exclusions left 47,725 men, who were followed between 1986 and January 31, 2000. This study was approved by the Human Subjects Committee of the Harvard School of Public Health.

Case Ascertainment. Men who reported a diagnosis of prostate cancer on their follow-up questionnaires, were contacted and asked for permission to review their medical records. The medical records were reviewed by physicians who extracted information on stage and pathology of the prostate cancer. After excluding cases with stage T_{1a} cancers, a total of 3,002 incident prostate cancer cases with information on stage were identified in our cohort by January 31, 2000. Advanced prostate cancer cases were classified as cancers that had either spread regionally to the seminal vesicle or nearby organs, or were metastatic at diagnosis, or fatal by January 2000.

Assessment of Dietary Patterns. Dietary patterns were identified using the same approach as reported in earlier studies from our cohort (9, 10). We applied the residual method to energy-adjust the factor scores (11).

Statistical Analysis. The Mantel-Haenzel estimator was used to calculate age-adjusted relative risks (RR; ref. 12). We used the Cox proportional hazards model to simultaneously adjust for several potential confounders (13). RRs were adjusted for known and suspected nondietary risk factors for prostate cancer: age, height, smoking, family history of prostate cancer in first-degree relatives, race, history of vasectomy, vigorous exercise, alcohol intake, and body mass index as well as total energy intake. We computed trend tests by using the median of each quintile of dietary pattern as exposure score. Associations were examined using the cumulatively updated dietary pattern

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scores (i.e., the average of all existing dietary pattern scores calculated from the three FFQs up to the beginning of each follow-up period; ref. 14). Because previous analyses in our cohort have shown that associations between dietary risk factors and risk of prostate cancer might vary by body mass index and age, we also conducted analyses stratified by body mass index and age (6, 7, 15). Interaction tests were done by including a product term with either age (binary variable, <65 versus ≥65 years) or body mass index (<26 versus ≥26 kg/m^2) and diet pattern score (continuous variable, using median values in each quintile) in the multivariable models. All reported *P* values were two-sided.

Results

The two dietary patterns that emerged have been described in more detail in previous publications (9, 10). In brief, the first factor corresponded to high intakes of fruits, vegetables, whole grains, fish, and poultry, and was labeled the prudent pattern. The second factor represented intakes of meat products (red meat and processed meat), refined grains and high-fat dairy, and was labeled the western pattern. The baseline characteristics of the study population are shown in Table 1. Men in the higher quintiles of prudent pattern were younger and more likely to engage in regular physical exercise and to be of Southern European origin. They were also less likely to be smokers. Men in the higher quintiles of the western pattern were more likely to be older and to smoke and less likely to be of Southern European origin, or to exercise regularly. Men in the highest quintile of (non–energy-adjusted) prudent and western pattern scores tend to have higher energy intake than men in the lowest quintile (data not shown).

Relative risks according to quintiles of cumulatively updated prudent and western pattern score are shown in Table 2. We found little association between the prudent pattern scores and risk of total, organ-confined and advanced prostate cancer. There was also no evidence for an association between western pattern scores and risk of total, organ-confined, and advanced prostate cancer. We also investigated the associations between dietary pattern scores and risk of prostate cancer after stratification by age (<65 and ≥65 years). Stratification by age indicated no evidence for a protective association between prudent pattern and organ-confined or advanced cancer. Associations between western pattern and organ-confined prostate cancer also did not differ by age (data not shown). Table 3 shows the relative risk of advanced prostate cancer and meat intake and western pattern by age. Among those ≥65 years of age, we observed a modest but nonsignificant positive association between western pattern scores and risk of advanced prostate cancer.

We did not find any evidence for a conclusive interaction between body mass index (<26 versus ≥26) and western pattern with regard to risk of advanced prostate cancer among older men ($P_{interaction}$ = 0.86).

We also examined whether the association between western pattern score and advanced prostate cancer risk observed among older men could be explained in part by either red or processed meat intake, two factors previously shown to be associated with advanced prostate cancer risk in this cohort (16). The positive associations between processed meat and advanced prostate cancer seemed to be restricted to older men, whereas the positive associations between red meat and advanced prostate cancer seemed to be restricted to younger men. Adjusting for western pattern did not diminish these associations; if anything, the positive associations between red meat intake and advanced prostate cancer in younger men became slightly stronger. Adding red meat intake to the multivariable models did not appreciably change the association between western pattern and advanced prostate cancer risk in older men, but adding processed meat to the model eliminated the positive association with western pattern and risk of advanced prostate cancer. Neither red meat intake nor processed meat intake were associated with risk of organ-confined prostate cancer (data not shown). When we examined associations between the main contributors for

Table 1. Baseline characteristics of the study population by quintiles of energy-adjusted dietary pattern scores (Health Professionals Follow-up Study, 1986)

Quintile	Prudent pattern			Western pattern		
	Q1	Q3	Q5	Q1	Q3	Q5
Age (y)	51.5	54.3	55.7	55.9	53.9	52.4
Ancestry, Northern European (%)	72.4	69.4	66.5	67.0	68.9	73.7
Southern European (%)	21.9	23.8	26.3	24.8	23.7	21.5
Other (%)	4.8	5.2	5.7	6.4	5.5	3.8
Body mass index (kg/m^2)	25.0	25.0	24.8	24.2	25.1	25.4
Physical activity (MET/wk*)	14.9	19.9	26.7	28.1	19.3	14.9
Current smokers (%)	16.7	8.5	5.5	3.3	8.2	18.4
History of vasectomy (%)	22.0	23.0	21.1	20.0	23.3	23.2
Family history of prostate cancer, first-degree relatives (%)	5.6	5.6	5.2	5.4	5.6	5.5
Dietary intake (d)						
Alcohol (g/d)	14.4	10.8	10.0	9.6	11.5	13.2
Total protein (g)	84.4	92.7	100.6	98.1	91.3	88.7
Total saturated fat (g)	28.2	24.7	19.9	18.7	24.7	29.5
Total polyunsaturated fat (g)	12.3	13.4	13.7	12.4	13.2	14.0
α-Linoleic fatty acid (g)	1.0	1.1	1.1	1.0	1.1	1.2
Lycopene (mcg)	6,024	10,165	15,482	11,197	10,556	9,363
Zinc (mg)	18.1	21.0	24.6	23.7	20.5	19.1
Vitamin E (IU)	66.1	99.3	140	136	101	71.2
Fructose (g)	23.8	25.7	30.9	33.3	26.1	21.0
Vitamin D (IU)	308	366	418	470	357	275
Calcium (mg)	822	902	968	1,057	878	778
Phosphorus (mg)	1,293	1,399	1,491	1,541	1,376	1,282

NOTE: Standardized for age at baseline: Q1, lowest quintile; Q3, medium quintile; Q5, highest quintile.
*Metabolic equivalent hours per week.

Table 2. Relative risk of prostate cancer by stage and quintiles of cumulative updated dietary prudent and western pattern scores (Health Professionals Follow-up Study, 1986-2000)

	Quintile prudent pattern score					*P* for trend
	1 (low)	2	3	4	5 (high)	
Prudent pattern						
Total prostate cancer						
Cases/person-years	474/12,0662	545/120,012	680/119,486	658/118,527	645/117,762	
Age-adjusted RR	1.00	0.98 (0.87-1.11)	1.12 (0.99-1.26)	1.01 (0.90-1.14)	0.95 (0.84-1.07)	0.36
Multivariate RR*	1.00	0.97 (0.86-1.10)	1.10 (0.98-1.24)	1.01 (0.90-1.14)	0.95 (0.84-1.07)	0.37
Organ-confined prostate cancer						
Cases/person-years	275/120,662	304/120,012	396/119,486	368/118,527	353/117,762	
Age-adjusted RR	1.00	0.96 (0.81-1.13)	1.14 (0.98-1.33)	0.99 (0.85-1.17)	0.91 (0.78-1.07)	0.28
Multivariate RR*	1.00	0.93 (0.79-1.09)	1.09 (0.93-1.28)	0.97 (0.82-1.13)	0.89 (0.76-1.05)	0.15
Advanced prostate cancer						
Cases/person-years	77/120,662	80/120,012	111/119,486	103/118,527	113/117,762	
Age-adjusted RR	1.00	0.91 (0.64-1.30)	1.02 (0.72-1.43)	1.05 (0.76-1.47)	1.01 (0.73-1.41)	0.89
Multivariate RR*	1.00	0.89 (0.65-1.22)	1.12 (0.84-1.51)	0.98 (0.73-1.34)	1.05 (0.78-1.42)	0.60
Western pattern						
Total prostate cancer						
Cases/person-years	678/117,816	629/118,960	608/119,767	556/120,049	531/119,858	
Age-adjusted RR	1.00	0.99 (0.89-1.10)	1.03 (0.93-1.15)	1.01 (0.90-1.13)	1.02 (0.91-1.15)	0.66
Multivariate RR*	1.00	0.98 (0.88-1.10)	1.03 (0.92-1.16)	1.00 (0.89-1.13)	1.02 (0.91-1.15)	0.62
Organ-confined prostate cancer						
Cases/person-years	375/117,816	362/118,960	352/119,767	308/120,049	299/119,858	
Age-adjusted RR	1.00	1.02 (0.89-1.18)	1.07 (0.83-1.43)	0.99 (0.85-1.16)	1.01 (0.86-1.18)	0.94
Multivariate RR*	1.00	1.02 (90.88-1.18)	1.08 (0.93-1.25)	1.00 (0.85-1.16)	1.05 (0.90-1.23)	0.63
Advanced prostate cancer						
Cases/person-years	108/117,816	93/118,960	101/119,767	88/120,049	94/119,858	
Age-adjusted RR	1.00	0.93 (0.70-1.22)	1.09 (0.83-1.43)	1.02 (0.77-1.36)	1.16 (0.88-1.53)	0.20
Multivariate RR*	1.00	0.90 (0.68-1.19)	1.07 (0.81-1.41)	1.01 (0.76-1.35)	1.14 (0.85-1.53)	0.28

NOTE: Numbers in parentheses are 95% CIs.
*Models adjusted for age, height, smoking, family history of prostate cancer, race, history of vasectomy, vigorous exercise, body mass index, alcohol intake, and total energy intake.

the prudent pattern and risk of prostate cancer, an inverse association between vegetable intake and risk of organ-confined prostate cancer was suggested (highest versus lowest quintile [RR, 0.87; 95% confidence intervals (CI). 0.73-1.03]), but CIs included one. Vegetable intake was not associated with advanced prostate cancer. Fruit intake was neither associated with organ-confined nor advanced prostate cancer (data not shown).

Discussion

Our results do not support associations between either prudent or western pattern dietary patterns and risk of total prostate cancer. We found a suggestion that higher western pattern scores may be associated with a slightly greater risk of advanced prostate cancer among older men. However, this association was largely attributable to higher intake of processed meat. One small prospective study, which used data from the National Health and Nutrition Examination Survey Epidemiological Follow-up Study Cohort, investigated the association between dietary patterns and risk of prostate cancer (5). Three dietary patterns were described: ''vegetable-fruit,'' ''red meat-starch,'' and a ''Southern'' pattern, which was characterized by higher intakes of foods such as okra, cornbread, or sweet potatoes. The ''Southern pattern'' had a suggestive inverse association with prostate cancer risk (highest versus lowest tertile: RR, 0.6; 95% CI, 0.4-1.1; $P_{trend} = 0.08$). The authors speculated that the observed association was due to living in the South, which may be related to lower risk of prostate cancer due to higher sunlight (vitamin D) exposure. In that study, statistical power was limited (136 cases). In a small case-control study from Canada (80 cases) a ''processed diet'' was significantly associated with an increased risk of prostate cancer (4).

In addition, we found no evidence for a protective association of a higher prudent pattern score. Epidemiologic studies do not support a substantial effect of fruits on prostate cancer risk. However, some, albeit inconsistent, evidence indicated that higher intake of vegetables such as tomatoes, legumes, and beans may reduce prostate cancer risk (17). In previous analysis in this cohort, we found that higher intake of tomato products, primarily tomato sauce, was associated with lower risk of total and advanced prostate cancer (18). Tomato sauce intake was only weakly correlated with prudent pattern in our cohort (Spearman $r = 0.14$)

Results from a recent prospective study and a randomized clinical trial also do not support a protective effect of vegetables and fruit intake against prostate cancer risk. In the large European Investigation into Cancer and Nutrition cohort total fruit and vegetable intake was not associated with prostate cancer risk (19). In participants from the Polyp Prevention Trial, a randomized clinical trial, consumption of a low-fat, high-fruit, vegetable, and fiber diet over a period of 4 years did not lower PSA levels over that time period (20).

Red and processed meats are two main contributors to the western pattern. Higher consumption of fat and meat has been associated with higher risk of prostate cancers in some but not all epidemiologic studies (21). In this analysis, the slightly increased risk of advanced prostate cancer with a western pattern among older men did not change considerably after controlling for red meat intake. On the other hand, controlling for processed meat, another major contributor to western pattern, eliminated the suggestive positive associations between western pattern and risk of advanced prostate cancer. The positive associations between intake of processed meat and risk of advanced prostate cancer in older men remained basically unchanged after adjusting for western pattern. Although the rationale of controlling for major components of a specific dietary pattern may be questioned, one of the goals of dietary pattern analysis is to capture associations due to a combination of food items and nutrients, including complex interactions among them, which may be missed by

Table 3. Multivariate RR of advanced prostate cancer according to quintiles of western pattern and meat intake by age (Health Professionals Follow-up Study, 1986-2000)

	Quintile western pattern/meat intake					*P* for trend
	1 (low)	2	3	4	5 (high)	
Age <65 y						
Western pattern						
Cases	28	23	30	27	25	
Multivariate RR*	1.00	0.84 (0.48-1.46)	1.05 (0.62-1.78)	0.88 (0.51-1.52)	0.76 (0.43-1.34)	0.39
Multivariate RR* + red meat	1.00	0.80 (0.46-1.41)	0.94 (0.54-1.62)	0.71 (0.40-1.28)	0.53 (0.28-0.98)	0.04
Multivariate RR* + processed meat	1.00	0.95 (0.54-1.68)	1.25 (0.72-2.19)	1.02 (0.56-1.87)	0.79 (0.40-1.55)	0.56
Age ≥ 65 y						
Western pattern						
Cases	80	70	71	61	69	
Multivariate RR*	1.00	0.91 (0.66-1.26)	1.07 (0.77-1.48)	1.05 (0.75-1.47)	1.34 (0.96-1.88)	0.07
Multivariate RR* + red meat	1.00	0.91 (0.66-1.26)	1.06 (0.76-1.48)	1.04 (0.73-1.49)	1.30 (0.90-1.88)	0.13
Multivariate RR* + processed meat	1.00	0.86 (0.62-1.19)	0.95 (0.68-1.33)	0.88 (0.61-1.28)	1.08 (0.73-1.58)	0.68
Age <65 y						
Total red meat						
Cases	22	21	20	29	41	
Multivariate RR*	1.00	0.89 (0.49-1.62)	0.79 (0.43-1.46)	1.23 (0.70-2.16)	1.68 (0.99-2.87)	0.003
Multivariate RR* + western pattern	1.00	0.94 (0.51-1.73)	0.88 (0.47-1.66)	1.44 (0.79-2.61)	2.12 (1.18-3.78)	0.0002
Processed meat						
Cases	30	28	19	22	34	
Multivariate RR*	1.00	0.62 (0.37-1.05)	0.46 (0.26-0.83)	0.55 (0.31-0.97)	0.78 (0.47-1.30)	0.94
Multivariate RR* + western pattern	1.00	0.61 (0.36-1.04)	0.46 (0.25-0.84)	0.56 (0.30-1.02)	0.85 (0.47-1.56)	0.55
Age ≥65 y						
Total red meat						
Cases	75	81	70	53	72	
Multivariate RR*	1.00	1.23 (0.89-1.68)	1.04 (0.75-1.44)	0.97 (0.68-1.39)	1.35 (0.97-1.87)	0.20
Multivariate RR* + western pattern	1.00	1.20 (0.87-1.66)	0.99 (0.71-1.40)	0.91 (0.63-1.32)	1.21 (0.85-1.74)	0.54
Processed meat						
Cases	54	72	72	74	79	
Multivariate RR*	1.00	1.04 (0.73-1.49)	1.35 (0.94-1.93)	1.41 (0.98-2.01)	1.55 (1.08-2.22)	0.004
Multivariate RR* + western pattern	1.00	1.06 (0.74-1.52)	1.38 (0.95-2.00)	1.42 (0.97-2.08)	1.51 (1.00-2.26)	0.03

NOTE: Numbers in parentheses are 95% CIs. Body mass index (in quintiles). Total red meat intake is defined as the sum of the following meat items on the FFQs: regular hamburger, lean hamburger, beef, lamb, and pork as main dish; beef, lamb, and pork as mixed dish, pork as main dish; processed meat intake is defined as sum of salami, bologna, or other processed meat sandwiches (1998 FFQ), other processed meats, e.g., sausage, kielbasa, etc. (1998 FFQ), processed meats, e.g., sausage, salami, bologna, etc. (1986-1994 FFQ), hotdogs (1986-1998 FFQ), and bacon (1986-1998 FFQ).

*Models adjusted for age, height, smoking, family history of prostate cancer, race, history of vasectomy, vigorous exercise, body mass index, alcohol intake, and total energy intake. Models with western pattern were adjusted for the same variables but not alcohol intake.

analyses focused on single nutrients, foods, or food groups (3, 22). The fact that the association with advanced prostate cancer was more robust for processed meats than for western pattern suggests either that the causative risk factor is related specifically to processed meats (e.g., through nitrates found in processed meats; ref. 23), or that processed meat captures a correlated dietary factor better than does western pattern with regard to prostate cancer.

To our knowledge, this is by far the largest study that has investigated the association between dietary patterns and prostate cancer risk. Besides the large number of cases, the use of multiple dietary assessments and the long follow-up period (14 years) were major strengths of this study. In addition, we were able to assess subgroups of prostate cancer by stage and age of onset. This study also has some limitations. Subjective decisions had to be made by the investigators with regard to the number of factors to be extracted, types of foods to be grouped together, and labeling of factors. However, results from previously published sensitivity analyses in this cohort showed high reproducibility of those two derived factors (9, 22).

In conclusion, we did not find any evidence for a protective association between prudent and western patterns as identified by factor analysis in our cohort and prostate cancer risk. The lack of association between a western dietary pattern and prostate cancer risk in this study suggests that dietary risk factors for prostate cancer are likely to differ from those for other conditions, such as cardiovascular disease and type 2 diabetes, that have been associated with a western dietary pattern in this cohort (9, 10).

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