Research Article

Cancer Prevention Research

Dietary Patterns after Prostate Cancer Diagnosis in Relation to Disease-Specific and Total Mortality

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Abstract

Men diagnosed with nonmetastatic prostate cancer have a long life expectancy, and many die of unrelated causes. It is therefore important to know to what extent post-diagnostic diet may affect disease-specific and overall mortality. A total of 926 men participating in the Physicians' Health Study diagnosed with nonmetastatic prostate cancer completed diet questionnaires for a median of 5.1 years after diagnosis, and were followed thereafter to assess mortality for a median of 9.9 years since questionnaire completion. Two post-diagnostic dietary patterns were identified: a Prudent pattern, characterized by higher intake of vegetables, fruits, fish, legumes, and whole grains; and a Western pattern, characterized by higher intake of processed and red meats, high-fat dairy and refined grains. Cox regression was used to estimate multivariable-adjusted hazard ratios (HR) and 95% confidence intervals (CI). During 8,093 person-years of follow-up, 333 men died, 56 (17%) of prostate cancer. The Western pattern was significantly related to a higher risk of prostate cancer–specific and all-cause mortality. Comparing men in the highest versus the lowest quartile of the Western pattern, the HRs were 2.53 (95% CI, 1.00–6.42; P_{trend} = 0.02) for prostate cancer–specific mortality and 1.67 (95% CI, 1.16–2.42; P_{trend} = 0.01) for all-cause mortality. The Prudent pattern was associated with a significantly lower all-cause mortality ($HR_{Quartile\ 4\ vs.\ Quartile\ 1}$: 0.64; 95% CI, 0.44–0.93; P_{trend} = 0.02); the relationship with prostate cancer–specific mortality was inverse but not statistically significant. A post-diagnostic Western dietary pattern was associated with higher prostate cancer–specific and all-cause mortality, whereas a Prudent dietary pattern was related to lower all-cause mortality after prostate cancer diagnosis. *Cancer Prev Res; 8(6); 545–51. ©2015 AACR.*

Introduction

Prostate cancer is the most commonly diagnosed and second most lethal cancer for men in the United States (1), resulting in nearly 3 million U.S. men currently living with prostate cancer (1, 2). Age and tumor characteristics such as grade and stage are well-established risk factors for prostate cancer–specific mortality (2, 3) but are unmodifiable. Increasing evidence suggests that some dietary factors, such as dairy products or fat intake, may have an impact on disease progression, as reflected by associations with biochemical recurrence or disease-specific mortality (4–6). Yet, most studies evaluating prostate cancer survival have focused on a single or a group of nutrients or foods without considering dietary patterns. In addition, research is sparse regarding post-diagnostic diet as a whole (7).

Dietary patterns can provide further insights into the role of nutrition in prostate cancer progression, as they account for interactive or synergistic effects of multiple foods and nutrients (8), and have the advantage of being more readily translatable into clinical and public health recommendations (9). To date, only one study has evaluated the potential role of dietary patterns after prostate cancer diagnosis, concluding that adherence to a Mediterranean dietary pattern was not related to disease-specific mortality (7). The aim of the present study was to prospectively evaluate the relation of data-derived post-diagnostic dietary patterns, with prostate cancer–specific and all-cause mortality among men diagnosed with nonmetastatic prostate cancer.

Materials and Methods

Study population

Men participating in the Physicians' Health Study (PHS) I or II who were diagnosed with nonmetastatic prostate cancer and had completed a dietary assessment after prostate cancer diagnosis were included in this study. The PHS I, initiated in 1982, was a randomized trial of aspirin and β-carotene for the primary prevention of cardiovascular disease (CVD) and cancer among 22,071 U.S. male physicians ages 40 to 84 years (10, 11). The aspirin and β-carotene arms were terminated in 1988 and 1995, respectively (10, 11). The PHS II, initiated in 1997, was a randomized trial of vitamin E, vitamin C, and a multivitamin supplement for the primary prevention of CVD, cancer, and age-related eye disease among 14,641 male U.S. physicians,

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7,641 of whom had participated in PHS I. The vitamin C and vitamin E arms ended in 2007 and the multivitamin arm ended in 2011. Men who participated in both trials continue to be followed with mailed annual questionnaires to update risk factors and ascertain study endpoints. Follow-up for nonfatal outcomes in PHS is over 97% complete, and for mortality, over 98%. The Institutional Review Boards of Partners HealthCare and the Harvard School of Public Health approved this study.

Diet assessment

One food-frequency questionnaire (FFQ) was sent to all PHS participants to collect information on usual diet between 1999 and 2002. The FFQ was modeled after the one used in the Health Professional Follow-up Study (HPFS), which has been previously validated (12). Dietary patterns were derived from FFQs as previously described (9, 13). Briefly, men were asked to report their usual intake over the previous year of foods and beverages included in the FFQ. Food items were classified into 39 predefined food groups to minimize within-person variation in intakes of individual foods (Supplementary Table S1; ref. 9). Dietary patterns were subsequently derived from these food groups through principal component analysis. Specifically, orthogonal transformations were used to obtain uncorrelated factors (dietary patterns) with simpler structures and greater interpretability (13). Eigenvalues (>1; the amount of variance explained by the factor), the Scree plot (a plot of all the eigenvalues for the derived factors in descending order), and the substantive meanings of the rotated factors and consistency with prior literature (9) were considered to determine the number of factors retained. Individual scores were calculated for each factor as the sum of the frequency of consumption multiplied by factor loadings across all food items. Thus, each participant was given a score for the "Prudent" and "Western" patterns.

Disease confirmation and death ascertainment

Participants were asked to report newly diagnosed prostate cancer in the yearly follow-up questionnaires. We obtained medical records and pathology reports to confirm the diagnosis and abstract information on date of diagnosis, tumor clinical stage (TNM staging system; ref. 14), grade (Gleason), prostate-specific antigen (PSA) values, initial treatments, and clinical presentation (PSA screening, abnormal digital rectal examination, clinical symptoms, or other). Among 1,002 men diagnosed with prostate cancer and complete diet information, we excluded men with metastatic disease (T4/N1/M1; $n = 23$) or missing data on clinical stage ($n = 53$), thus restricting the study to men with confirmed nonmetastatic disease. Deaths were identified by reports from family members and postal authorities, and systematic searches of the National Death Index. Deaths were confirmed through review of death certificates and medical records to determine cause of death, assigned by the Endpoints Committee of three physicians. When medical records cannot be obtained, cause of death is assigned upon reviews of all other available data by the Endpoints Committee. A death was attributed to prostate cancer if prostate cancer metastases were present and no more plausible cause of death was mentioned.

Statistical analysis

Men were classified into quartiles of the "Prudent" and "Western" dietary patterns. A χ^2 test and analysis of variance were used to test the associations of baseline characteristics across quartiles of dietary patterns. Cox proportional hazards regression models were used to examine post-diagnostic dietary patterns in relation to prostate cancer–specific and all-cause mortality, using the lowest quartile of dietary pattern as the reference group. For analyses of prostate cancer–specific mortality, men were followed from the date of FFQ completion until death due to prostate cancer, death due to other cause, or end of follow-up, whichever came first. For all-cause mortality, men were followed from the date of FFQ completion until death or end of follow-up. We initially fit models adjusted for age at diagnosis (years; continuous) and total energy intake (kcal; continuous). The multivariable models included additional terms for body mass index (BMI; kg/m^2; <25, 25–30, >30), smoking status (never, past, current), vigorous exercise (days/week, continuous), time interval between diagnosis and FFQ completion (years, continuous), Gleason score (<7, 7, >7), clinical stage (T1/T2, T3), PSA levels (ng/mL; <4, 4–9.9, 10–19.9, 20+), initial treatment (radiation, prostatectomy, others, unspecified or missing), and family history of prostate cancer (yes, no). Adjustment for randomization arm modified Charlson comorbidity index (15, 16), aspirin use, cholesterol medication, and personal history of diabetes did not change the results, and, therefore, these variables were not included in the main analysis. In addition, we utilized multivariable competing-risk regression model (17) to obtain subdistribution estimates, taking into account non–prostate cancer mortality risk.

To test the robustness of our results, we conducted sensitivity analyses excluding men who died within 2 years of completing the FFQ ($n = 35$), men with prostate cancer death classified as "unrefuted" ($n = 6$), and men who developed distant metastases between diagnosis and completion of FFQ ($n = 9$). P values for trend were calculated by the Wald statistics of a score variable that contained median values of each quartile of the dietary pattern. The proportional hazards assumption was assessed by creating an interaction term of pattern and follow-up time, and no violation was observed. Effect modification by age at diagnosis and BMI was evaluated by including cross-product terms to the multivariable model. All the statistical analyses were two-sided and carried out using SAS 9.2 (SAS Institute, Inc.). P values < 0.05 were considered statistically significant.

Results

We identified 333 deaths, 56 (17%) due to prostate cancer, during 8,093 person-years of follow-up among 926 men with nonmetastatic prostate cancer. Two dietary patterns were identified. The Prudent pattern was characterized by higher intake of legumes, vegetables, fruits, whole grains, garlic, soy products, fish, and oil and vinegar dressing. The Western pattern was characterized by higher intake of processed and red meats, eggs, potatoes, high-fat dairy products, butter, refined grains, snacks, sweets, and desserts (Table 1). Men with higher Prudent pattern score were more likely to be never smokers and consume less fat from animal sources and alcohol (Table 2). Men with higher Western pattern scores were older at prostate cancer diagnosis and more likely to be Caucasian and smokers. They had higher intake of animal fats and lower intake of calcium and vitamin D.

The post-diagnostic Prudent pattern score was associated with lower prostate cancer–specific mortality, but this association did not reach statistical significance (Table 3). On the other hand, we found a positive association between adherence to the Western dietary pattern and disease-specific mortality. Men in the highest

Table 1. Factor-loading matrix for two dietary patterns identified from post-diagnostic FFQ among men with prostate cancer ($n = 926$) in the PHS[a]

Food group	Prudent dietary pattern	Western dietary pattern
Legumes	0.55	—
Dark-yellow vegetables	0.55	—
Green, leafy vegetables	0.54	—
Other vegetables	0.54	—
Fruit	0.51	—
Cruciferous vegetables	0.51	—
Tomatoes	0.49	—
Whole grains	0.44	—
Garlic	0.40	—
Soy products	0.36	—
Fish	0.32	—
Oil and vinegar dressing	0.31	—
Processed meats	—	0.66
Red meats	—	0.60
Eggs	—	0.48
Snacks	—	0.46
High-fat dairy products	—	0.45
Potatoes	—	0.44
French fries	—	0.42
Butter	—	0.39
Sweets and desserts	—	0.35
Refined grains	—	0.33

[a]Food groups with loading factors less than 0.3 for both dietary patterns were not listed in the table, and included fruit juice, poultry, condiments, nuts, tea, low-fat dairy products, pizza, organ, cold breakfast cereal, wine, margarine, mayonnaise, low-energy drink, beer, coffee, high-energy drink, and liquor.

quartile of the Western pattern had a 2.5-fold higher risk of prostate cancer–specific death compared with men in the lowest quartile [hazard ratio (HR) $_{\text{Quartile 4 vs. Quartile 1}}$: 2.53; 95% confidence interval (95% CI), 1.00–6.42; $P_{\text{linear-trend}} = 0.02$; Table 3]. Results were similar using competing-risk regression models (Supplementary Table S2).

The Prudent pattern score was inversely associated with all-cause mortality. Men in the highest quartile of this pattern had a 36% lower risk (95% CI, 7%–56%) of death compared with men in the lowest quartile (Table 4). Conversely, greater adherence to the Western pattern was associated with a 67% higher risk of overall mortality (95% CI, 16%–142%) after full adjustment of potential confounders.

The relation of the Western pattern with prostate cancer–specific mortality appeared to be predominantly driven by intake of processed meats. In the adjusted model, the HR for prostate cancer death was 1.32 (95% CI, 1.06–1.64; $P = 0.01$) for each one-ounce increase in the daily intake of processed meats (Supplementary Table S3). In addition, the inverse relation of the Prudent pattern with all-cause mortality appeared to be driven by oil and vinegar-dressing intake ($HR_{1\ \text{SD increase}} = 0.84$; 95% CI, 0.74–0.95; $P = 0.005$), whereas the positive relation between the Western pattern and total deaths was driven by processed meat ($HR_{1\ \text{SD increase}} = 1.17$; 95% CI, 1.06–1.30; $P = 0.003$) and high-fat dairy intake ($HR_{1\ \text{SD increase}} = 1.18$; 95% CI, 1.07–1.30; $P = 0.001$; Supplementary Table S3).

We further mutually adjusted for dietary patterns in multivariable models. The linear trends remained similar, although the associations were slightly attenuated. Specifically, the HRs (95% CI) comparing top with bottom quartiles of Western pattern scores were 2.18 (0.81–5.89) for disease-specific mortality and 1.50 (1.01–2.24) for all-cause mortality. In sensitivity analyses, excluding deaths within 2 years of the diet assessment (35 deaths; 8 due to prostate cancer) attenuated the association of the Western pattern with prostate cancer–specific mortality ($HR_{\text{Quartile 4 vs. Quartile 1}} = 1.66$; 95% CI, 0.61–4.52), whereas the relationship with all-cause mortality remained similar ($HR_{\text{Quartile 4 vs. Quartile 1}} = 1.69$; 95% CI, 1.15–2.49). Excluding unrefuted deaths or men who reported distant metastases between diagnosis and diet assessment did not appreciatively alter the results. In addition, the associations of the Western and Prudent patterns with disease-specific mortality were not modified by age at diagnosis (<65 years vs. ≥65 years) and BMI (<25 kg/m^2 vs. ≥25 kg/m^2).

Discussion

In a cohort of men diagnosed with nonmetastatic prostate cancer, greater post-diagnostic adherence to a Western dietary pattern was associated with higher risk of disease-specific and all-cause mortality, whereas a Prudent dietary pattern was inversely related to mortality risks. The associations of the Western pattern appeared to be driven by intake of processed meats, whereas the Prudent pattern association with all-cause mortality appeared to be driven by intake of oil and vinegar dressing. These findings add to the growing literature suggesting that dietary choices after prostate cancer diagnosis may have an impact on disease progression and survivorship.

Prospective studies investigating the relation of dietary pattern and prostate cancer incidence have reported inconsistent results (8, 18–21). Three cohorts evaluating dietary patterns using principal component analysis (as we did in this study) found no association between the data-derived patterns and prostate cancer risk (8, 19, 20). Using index-based methods, studies indicated that alternate or modified Mediterranean diet score was not appreciatively associated with risk of prostate cancer (18, 21), whereas the Healthy Eating Index-2005 and Alternate Healthy Eating Index-2000 were significantly associated with lower risk of developing incident prostate cancer (18, 21). However, studies on risk of total prostate cancer are expected to differ from those that focus on disease-specific mortality, due to the high incidence of indolent prostate cancer in populations with PSA screening.

Data on post-diagnostic dietary patterns in relation to disease-specific and overall survival are scarce. In the HPFS, greater post-diagnostic adherence to a Mediterranean diet, which overlapped considerably with our Prudent dietary pattern, was completely unrelated to disease-specific survival (7). Although we did not find a statistically significant association between the Prudent pattern and disease-specific mortality, our results suggest an inverse relation with this outcome. Despite similarity between two studies, reasons for the divergent findings may include different cutoffs of dietary patterns (Mediterranean diet score of 0–3, 4–5, and 6–9 in HPFS vs. quartiles of Prudent diet in PHS), differences in follow-up time after diagnosis (a median 7.6 years in HPFS vs. a median of 13.8 years in this report), calendar year of disease diagnosis (diagnosis date of 1986 to 2006 in HPFS vs. diagnosis date of 1982 to 2000 in PHS), and lower statistical power in the current study relative to the previous report. The positive association between the Western pattern and greater risk of prostate cancer–specific mortality in our study is consistent with previous studies that indicated that higher intake of saturated fat, primarily from animal sources, may be related to disease progression. Strom and colleagues (22) documented a 2-fold greater risk of biochemical failure with high saturated fat intake in a cohort of 390 Caucasian men with localized prostate cancer

Table 2 . Demographic and post-diagnostic dietary characteristics according to quartiles of dietary pattern scores among 926 men with nonmetastatic prostate cancer in PHS ($n = 926$)

		Prudent dietary pattern			Western dietary pattern		
	Total population	Quartile 1	Quartile 4	P^a	Quartile 1	Quartile 4	P^a
n	926	231	231		231	231	
Subject characteristics							
Age at diagnosis, y, mean (SD)	68.6 (6.9)	69.4 (7.2)	67.8 (6.5)	0.08	68.2 (7.1)	69.9 (6.5)	0.01
Caucasian, %	95.68	95.7	96.1	0.98	93.5	97	0.01
BMI, kg/m^2, %				0.04			0.24
<25	46.7	39.4	48.9		52.8	40.7	
25–30	47.3	56.7	42.9		42.9	52	
>30	6.1	3.9	8.2		4.3	7.4	
Smoking status, %				0.009			<0.001
Never	47.1	42.4	54.1		48.1	37.7	
Past	50.4	53.3	43.7		51.2	57.6	
Current	2.5	4.3	2.2		0.4	4.8	
Days per week of vigorous exercise[b]				0.04			0.04
None	33.7	37.2	29.0		27.3	28.5	
<1 day/week	2.5	3.0	1.7		2.6	2.6	
1–2 day/week	17.7	16.0	14.3		20.4	13.0	
3–4 day/week	29.5	26.8	36.8		30.3	24.7	
5–7 day/week	16.6	16.9	18.2		19.5	21.2	
Family history of prostate cancer, %[c]	16.9	11.7	19.1	0.07	20.4	15.2	0.35
Clinical stage, %				0.97			0.97
T1/T2	95.1	94.8	95.2		95.7	95.2	
T3	4.9	5.2	4.8		4.3	4.8	
Gleason score, %				0.86			0.54
<7	69.1	71.9	69.3		73.6	64.9	
7	21.5	19.1	20.8		17.3	24.2	
>7	6.9	5.6	7.8		6.9	7.4	
Missing	2.5	3.5	2.2		2.2	3.5	
PSA at diagnosis, ng/mL, %				0.19			0.007
<4	10.5	10.8	13		11.7	13.4	
4–9.9	46.0	41.9	48.5		50.7	39.4	
10–19.9	19.7	21.2	18.2		17.3	20.4	
≥20	10.8	7.4	9.5		10.8	8.2	
Missing	13.1	17.8	10.8		9.5	18.6	
Primary treatment,%[d]				0.60			0.72
Radiation	10.4	12.6	7.4		10.0	10.8	
Prostatectomy	43.7	44.2	46.8		48.5	39.8	
Chemo- or hormone therapy	7.1	5.19	7.36		6.9	7.8	
Others	1.8	2.16	1.73		0.9	3.0	
Unspecified or missing	36.9	35.9	36.8		33.8	38.5	
Daily dietary nutrients (energy adjusted)							
Carbohydrate, g, mean (SD)	217.4 (40.9)	203.3 (43.8)	232.4 (36.0)	<0.001	242.7 (38.9)	192.7 (32.7)	<0.001
Protein, g, mean (SD)	76.9 (13.6)	74.3 (15.6)	78.7 (12.6)	<0.001	76.9 (14.0)	78.4 (12.7)	0.28
Fat, g, mean (SD)	50.5 (11.9)	55.3 (12.8)	45.6 (10.8)	<0.001	41.3 (9.4)	59.1 (9.8)	<0.001
Vegetable fat, g, mean (SD)	20.2 (7.3)	19.5 (7.9)	20.5 (7.3)	0.27	19.2 (7.2)	20.5 (7.3)	0.08
Animal fat, g, mean (SD)	30.3 (11.6)	35.7 (12.6)	25.1 (10.4)	<0.001	22.1 (8.9)	38.6 (10.5)	<0.001
Cholesterol, mg, mean (SD)	211 (95)	238 (119)	187 (85)	<0.001	162 (68)	269 (110)	<0.001
Caffeine, mg, mean (SD)	165 (135)	180 (149)	159 (124)	0.21	150 (135)	185 (142)	0.05
Alcohol, g, mean (SD)	13.2 (15.3)	17.6 (20.1)	9.5 (10.1)	<0.001	13.8 (17.0)	12.2 (12.6)	0.64
Calcium, mg, mean (SD)	989 (559)	917 (576)	1,023 (527)	0.12	1,162 (670)	841 (376)	<0.001
Vitamin D, IU, mean (SD)	379 (283)	363 (300)	363 (219)	0.32	459 (320)	321 (220)	<0.001

Abbreviation: IU, international unit.

[a]The χ^2 test was used for categorical variables, and analysis of variance was used for continuous variables. All statistical tests were two-sided.

[b]If a patient reported to engage in a regular program of exercise vigorous enough to work up a sweat, additional information on the frequency of engagement was collected.

[c]If a patient reported he had a brother or father was ever diagnosed with prostate cancer without including half siblings.

[d]Others include orchiectomy, watchful waiting, and other treatments.

treated with prostatectomy. Meyer and colleagues (23) found a 3-fold greater risk of prostate cancer–specific death among Canadian men in the upper tertile of saturated fat intake than those in the lowest tertile (HR, 3.13; 95% CI, 1.28–7.67), and Epstein and colleagues (24) reported that Swedish men in the highest quartile of myristic acid and short-chain saturated fatty acids had more than 2-fold higher risk of disease-specific death than those in the lowest quartile (HR for myristic acid: 2.39; 95% CI, 1.06, 5.38; HR for short-chain saturated fat: 2.88; 95% CI, 1.24–6.67). Nevertheless, these relations of saturated fat with prostate cancer-specific mortality were not replicated in HPFS (6). Clearly, whether diet after prostate cancer diagnosis influences disease progression deserves further investigation.

We also documented significant relations of the Prudent and Western patterns after prostate cancer diagnosis with all-cause mortality. Specifically, the Prudent diet was related to a lower risk,

Table 3. Relative risk of prostate cancer–specific mortality among 926 men diagnosed with nonmetastatic prostate cancer by post-diagnostic dietary patterns

	1	2	3	4	P_{trend}[a]
Quartile of prudent dietary pattern					
Number	231	232	232	231	
Events	16	16	14	10	
Follow-up time, py	1,923	2,014	2,079	2,077	
Incidence rate, #/10,000 py	83	79	67	48	
Model 1, HR (95% CI)[b]	1.00 (ref.)	0.91 (0.45–1.83)	0.72 (0.34–1.53)	0.48 (0.19–1.18)	0.09
Model 2, HR (95% CI)[c]	1.00 (ref.)	0.87 (0.41–1.82)	0.73 (0.33–1.63)	0.46 (0.17–1.24)	0.11
Quartile of Western dietary pattern					
Number	231	232	232	231	
Events	9	11	15	21	
Follow-up time, py	2,096	2,035	2,065	1,897	
Incidence rate, #/10,000 py	43	54	73	111	
Model 1, HR (95% CI)[b]	1.00 (ref.)	1.31 (0.54–3.18)	1.92 (0.82–4.49)	3.20 (1.32–7.75)	0.005
Model 2, HR (95% CI)[c]	1.00 (ref.)	0.95 (0.38–2.34)	1.81 (0.76–4.33)	2.53 (1.00–6.42)	0.02

Abbreviation: py, person years.

[a]P_{trend} calculated by modeling the median of each category as a continuous term. All statistical tests were two-sided.

[b]Cox proportional hazards regression model adjusted for age at diagnosis (years, continuous) and total energy intake (kcal, continuous).

[c]Cox proportional hazards regression model adjusted for variables in model 1 plus BMI (kg/m^2, <25, 25–30, >30), smoking status (never, past, current), vigorous exercise (days/week, continuous), Gleason score (<7, 7, >7), clinical stage (T1/T2, T3), prostate-specific antigen level (ng/mL, <4, 4–9.9, 10–19.9, ≥20), time interval between diagnosis and FFQ completion (years, continuous), initial treatment after diagnosis (radiation, prostatectomy, others, unspecified or missing), and family history of prostate cancer (yes, no).

whereas the Western diet was related to a higher risk of all-cause mortality. These findings are consistent with results from the HPFS where a greater adherence to Mediterranean diet after diagnosis of prostate cancer was associated with 22% reduction in overall mortality (7). Moreover, because CVD was the leading cause of death among men with localized prostate cancer in this cohort (21% of deaths), the results of this study can also be interpreted in light of the wider literature on the relation between diet patterns and CVD mortality (7, 25–29). Interestingly, oil and vinegar dressing, processed meats, and high-fat dairy appeared to be the main drivers of the associations of all-cause mortality with Prudent and Western diets, respectively. The oil and vinegar-dressing result is in agreement with previous findings of an inverse relation between vegetable oil intake with all-cause mortality among men with localized prostate cancer (6), and with results of the PREDIMED trial, where individuals randomized to a Mediterranean diet supplemented with olive oil had significantly lower risk of CVD than the control group (29). Furthermore, in a recent meta-analysis composed of nine prospective studies, the highest consumption of processed meat increased the risk of all-cause mortality by 23%, compared with lowest consumption (30). High-fat dairy was reported to be associated with increased CVD mortality (31), although not in all studies (32). Although these food groups were identified as major drivers, admittedly, the highly correlated matrix obtained by principal component analysis indicated a collective effect on mortality risks from grouped food items in Prudent or Western pattern. Our findings suggest that adherence to a heart-healthy diet could increase survival among men with nonmetastatic prostate cancer—a highly relevant finding given that most men with nonmetastatic prostate cancer die of unrelated causes.

Strengths and limitations of this study are worth careful weighing. On one hand, the study had high follow-up rates and a long follow-up time, which allowed us to study mortality rather than surrogate outcomes such as biochemical recurrence. Nevertheless, the study had a small number of disease-specific deaths,

Table 4. Relative risk of all-cause mortality among 926 men diagnosed with nonmetastatic prostate cancer by post-diagnostic dietary patterns

	1	2	3	4	P_{trend}[a]
Quartile of prudent dietary pattern					
Number	231	232	232	231	
Events	97	86	82	68	
Follow-up time, py	1,923	2,014	2,079	2,077	
Incidence rate, #/10,000 py	504	427	394	327	
Model 1, HR (95% CI)[b]	1.00 (ref.)	0.84 (0.62–1.13)	0.72 (0.53–0.99)	0.59 (0.41–0.84)	0.003
Model 2, HR (95% CI)[c]	1.00 (ref.)	0.88 (0.64–1.20)	0.83 (0.60–1.14)	0.64 (0.44–0.93)	0.02
Quartile of Western dietary pattern					
Number	231	232	232	231	
Events	59	88	76	110	
Follow-up time, py	2,096	2,035	2,065	1,897	
Incidence rate, #/10,000 py	281	432	368	580	
Model 1, HR (95% CI)[b]	1.00 (ref.)	1.65 (1.18–2.30)	1.43 (1.01–2.02)	2.06 (1.44–2.95)	<0.001
Model 2, HR (95% CI)[c]	1.00 (ref.)	1.40 (0.99–1.97)	1.33 (0.93–1.90)	1.67 (1.16–2.42)	0.01

Abbreviation: py, person years.

[a]P_{trend} calculated by modeling the median of each category as a continuous term. All statistical tests were two-sided.

[b]Cox proportional hazards regression model adjusted for age at diagnosis (years, continuous) and total energy intake (kcal, continuous).

[c]Cox proportional hazards regression model adjusted for variables in model 1 plus BMI (kg/m^2, <25, 25–30, >30), smoking status (never, past, current), vigorous exercise (days/week, continuous), Gleason score (<7, 7, >7), clinical stage (T1/T2, T3), prostate-specific antigen level (ng/mL, <4, 4–9.9, 10–19.9, ≥20), time interval between diagnosis and FFQ completion (years, continuous), initial treatment after diagnosis (radiation, prostatectomy, others, unspecified or missing), and family history of prostate cancer (yes, no).

resulting in wide confidence intervals and unstable estimates in some sensitivity analyses, and suggesting caution in the interpretation of the results. In addition, because we did not collect data on pre-diagnostic diet, we cannot evaluate its potential confounding effects on post-diagnostic diet. However, studies where both pre- and post-diagnostic diets were assessed have found that adjustment for pre-diagnostic diet had little influence on post-diagnostic diet effect estimates (7). In addition, we relied on a single prospective measure of post-diagnostic diet and lacked detail on certain potential confounders such as physical activity (e.g., time in nonvigorous activity), history of PSA screening, and treatment combinations. Furthermore, most men in the cohort are Caucasian physicians, which may limit the generalizability of the results to men with different socioeconomic backgrounds or from racial or ethnic minorities. Although the study setting may potentially minimize residual confounding by socioeconomic status, our results need to be replicated in independent populations with a larger number of disease-specific endpoints, pre-diagnostic exposure data, repeated dietary assessments, more detailed covariate assessment, and more diverse socioeconomic and racial/ethnic backgrounds.

In conclusion, among men diagnosed with nonmetastatic prostate cancer, greater post-diagnostic adherence to a Western dietary pattern may increase risks of prostate cancer-specific and all-cause mortality, whereas a Prudent dietary pattern may lower mortality risks after prostate cancer diagnosis. These findings suggest that modifications to diet after prostate cancer diagnosis may influence survival and have a direct clinical translation. These diet choices are informative to clinicians and prostate cancer survivors who are highly motivated to seek informing treatment and lifestyle decisions in order to reduce the suffering and improve the overall survival of men living with prostate cancer. Nevertheless, given the scarcity of literature on the relation between post-diagnostic diet and prostate cancer progression, and the small number of disease-specific deaths in the current study, these associations, particularly those for disease-specific mortality, merit caution in their interpretation as well as further evaluation.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: M. Yang, S.A. Kenfield, J.E. Chavarro
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