

Null Results in Brief

Dietary Patterns and Prostate Cancer Risk

David C. Muller,^{1,2} Gianluca Severi,^{1,2} Laura Baglietto,^{1,2} Kavitha Krishnan,¹ Dallas R. English,^{1,2} John L. Hopper,² and Graham G. Giles^{1,2}

¹Cancer Epidemiology Centre, The Cancer Council of Victoria and ²Centre for Molecular, Environmental, Genetic and Analytic Epidemiology, The University of Melbourne, Melbourne, Australia

Abstract

Recent studies report that certain dietary patterns, especially those high in red and processed meats, are associated with prostate cancer risk. We prospectively investigated associations between empirically derived dietary patterns and prostate cancer risk using the Melbourne Collaborative Cohort Study. We followed 14,627 men of ages 34 to 75 years for an average of 13.6 years, and identified 1,018 incident prostate cancers. Factor analysis of the 121-item food frequency questionnaire identified four factors with eigenvalues

>2 that explained 67% of the total variance. Using Cox proportional hazard models, we found no association between any dietary pattern and prostate cancer risk overall (all $P_{\text{trend}} \geq 0.2$). The hazard ratios for quartiles of the dietary pattern scores ranged from 0.87 to 1.14 and all 95% confidence intervals included 1. The analyses by aggressiveness, Gleason score groups, and age at diagnosis did not show any association (all $P_{\text{trend}} > 0.07$). (Cancer Epidemiol Biomarkers Prev 2009;18(11):3126-9)

Introduction

It has been suggested that diet is one factor that might be modified to reduce prostate cancer risk (1). Examining dietary patterns rather than individual foods or nutrients has the advantage of studying the effect of the whole diet, capturing patterns of consumption that may modify risk (2). Four studies to date have used cluster or factor analytic methods to examine dietary patterns and prostate cancer risk, two of which have been prospective (3-6). Two of these studies have suggested that diets characterized by high intakes of red and processed meats may be important in the development of prostate cancer (4, 6), whereas another study found that a "Southern" (cornbread, sweet potatoes, etc.) dietary pattern was associated with decreased prostate cancer risk (3). Our objective was to assess possible associations between dietary patterns and prostate cancer risk using an ethnically diverse Australian cohort.

Materials and Methods

The Melbourne Collaborative Cohort Study (MCCS) is a prospective study of 41,514 people (17,045 men) recruited between 1990 and 1994, ages between 27 and 81 y at baseline (99.3% of whom were ages 40-69 y). Details of the MCCS have been published previously (7, 8). Dietary information was obtained by means of a 121-item food fre-

quency questionnaire specifically developed for the MCCS (9).

Men with a confirmed diagnosis before baseline of invasive prostate cancer ($n = 105$) or unknown primary cancer ($n = 2$) were excluded from the analysis. We also excluded men who reported extreme values of total energy intake (<1st percentile or >99th percentile) or had a previous diagnosis of angina, myocardial infarction, or diabetes ($n = 2,267$) because their diets were not representative of the whole cohort, and we could not exclude the possibility that they had changed their diet after a recent diagnosis. In addition, 34 men did not complete the diet section of the questionnaire and 10 men had missing values on potential confounders, leaving 14,627 men available for analysis. End of follow-up was set at the end of 2007, death, the date the participant left Australia, or the date of diagnosis of an unknown primary tumor, whichever occurred first. During an average follow-up of 13.6 y, 1,018 incident prostate cancer cases were identified via linkage to the Victorian Cancer Registry.

Principal factor analysis was done on the 121 items from the food frequency questionnaire plus the consumption of olive and vegetable oils and alcohol from wine. The methods of factor analysis we used have been described previously (10) and factors with eigenvalues >2 were selected for further analysis. Cox regression models, with age as the time metric, were used to estimate hazard ratios (HR) and 95% confidence intervals (95% CI). All analyses were adjusted for total energy intake and ethnicity. Further adjustment for body mass index, physical activity, smoking, alcohol intake, and education did not change estimated HRs or 95% CIs materially. Tests for linear trend were based on pseudo-continuous variables under the assumption that subjects within each quartile had the same values, equal to the within-quartile median.

Received 8/5/09; accepted 8/14/09; published OnlineFirst 10/27/09.

Requests for reprints: David C. Muller, Cancer Epidemiology Centre, The Cancer Council Victoria, 100 Drummond Street, Carlton, Victoria 3053, Australia.

Phone: 61-3-9635-5293; Fax: 61-3-9635-5330. E-mail: David.Muller@cancervic.org.au

Copyright © 2009 American Association for Cancer Research.

doi:10.1158/1055-9965.EPI-09-0780

Table 1. Rotated factor loadings for food items with loadings having absolute values of ≥ 0.2 for any factor

Variable	Rotated factor loadings			
	Mediterranean	Vegetable	Meat & Potatoes	Fruit & Salad
Wine	0.23			
Olive oil	0.41			
Other cereal	-0.26			
Boiled rice		0.20		
Fried rice	0.22			
Mixed rice dish	0.21			
White bread			0.27	
Wholemeal bread		0.27		
Sweet biscuit	-0.32			
Cakes/sweet pastries	-0.31			
Pudding	-0.25			
Pasta or noodle dish	0.29			
Savory pastries			0.31	
Ricotta cheese	0.25			
Feta cheese	0.29			
Hard cheese	0.22			
Ice cream	-0.25			
Cream/sour cream	-0.20			
Yogurt		0.21		
Fried egg			0.35	
Egg dish			0.28	
Margarine	-0.36			
Beef/veal schnitzel	0.28		0.32	
Beef/veal roast			0.37	
Beef steak			0.31	
Beef rissole			0.39	
Beef dish			0.27	
Roast/fried chicken			0.27	
Boiled chicken	0.23			
Chicken dish				
Lamb roast/chops			0.32	
Lamb dish			0.37	
Pork roast			0.32	
Game	0.23			
Sausage/frankfurter	-0.22		0.28	
Bacon			0.32	
Corned beef			0.22	
Steamed fish	0.26			
Fried fish			0.26	
Legume soup	0.33			
Pickled vegetables	0.21			
Tomato	0.31	0.23		0.22
Capsicum	0.37	0.31		
Salad greens	0.38	0.29		0.24
Cucumber	0.42	0.26		0.26
Celery/fennel	0.30	0.40		0.23
Beetroot		0.43		
Coleslaw		0.30		
Potato cooked in fat			0.34	
Potato cooked without fat	-0.22	0.49		
Carrot		0.59		
Cabbage/brussels sprouts		0.58		
Cauliflower		0.60		
Broccoli		0.62		
Leafy greens	0.25	0.47		
Green beans/peas		0.52		
Cooked dried legumes	0.34	0.28		
Pumpkin		0.57		
Onion/leek	0.28	0.30		
Mushroom		0.26		
Sweet corn		0.25		
Zucchini/squash/eggplant	0.20	0.35		
Vegetable dish		0.24		
Fruit salad		0.24		
Orange/mandarin				0.44
Apple				0.42
Banana		0.27		0.30
Peach/nectarine				0.70
Pear				0.58
Cantaloupe/honeydew	0.21			0.58
Watermelon	0.24			0.60

(Continued on the following page)

Table 1. Rotated factor loadings for food items with loadings having absolute values of ≥ 0.2 for any factor (Cont'd)

Variable	Rotated factor loadings			
	Mediterranean	Vegetable	Meat & Potatoes	Fruit & Salad
Strawberry				0.43
Plum				0.63
Apricot				0.71
Grapefruit				0.21
Pineapple		0.24		0.35
Olive	0.27			0.35
Fig				0.50
Grape				0.62
Tea	-0.36	0.23		
Chocolate	-0.23			
Jam/honey	-0.28	0.24		

We estimated HRs for each dietary pattern overall, by three Gleason score groups (2-4, 5-7, and 8-10) and by tumor aggressiveness classified according to Gleason score, tumor stage, and prostate cancer cause-specific death; aggressive tumors were those with Gleason score >7 or stage IV or having prostate cancer as cause of death. To test for heterogeneity in the HRs by Gleason score and aggressiveness, we fitted Cox models using the data duplication method (11). We also estimated separate HRs for two follow-up age groups (≤ 68 and >68 y, 68 y being the median age at diagnosis of cases) by splitting the data into the specific groups and fitting Cox model with the inclusion of a term for the interaction between factor scores and groups.

Statistical analyses were done using Stata 10.1 (Stata Corporation, College Station, TX).

Results

Four factors with eigenvalues >2.35 and explaining 67% of the variance in all the food and beverage items were

identified. The male dietary factors identified here are similar to those identified for both men and women by a study on type 2 diabetes in the MCCS, details of which have been published previously (10). The four factors were characterized by (a) some meats, vegetables, and fruits, and avoidance of cakes and sweet biscuits; (b) high intake of vegetables; (c) high intake of meats and potato cooked in fat; and (d) high intake of salad greens and fruit. We have labeled the factors Mediterranean, Vegetable, Meat & Potatoes, and Fruit & Salad, respectively. The correlations with all the food items are presented in Table 1.

We found no associations between any of the dietary factors and prostate cancer risk, either overall or for aggressive and nonaggressive cancers separately (Table 2). Splitting at the median age at diagnosis (≤ 68 , >68 y) did not change the results materially, with HRs for all four dietary factors remaining near unity. Specifically, we found no association between the Meat & Potatoes dietary pattern and prostate cancer risk in the older cases (HR for highest versus lowest quartile, 0.90; 95% CI,

Table 2. Multivariate adjusted HRs and 95% CIs for the association between dietary pattern scores (quartiles) and prostate cancer risk

	Overall			Nonaggressive			Aggressive*			$P_{\text{interaction}}$
	<i>n</i> cases	HR (95% CI)	P_{trend}	<i>n</i> cases	HR (95% CI)	P_{trend}	<i>n</i> cases	HR (95% CI)	P_{trend}	
Mediterranean										
1	337	Reference		276	Reference		61	Reference		
2	247	0.93 (0.79-1.11)		213	0.98 (0.81-1.18)		34	0.72 (0.47-1.10)		
3	241	1.14 (0.95-1.37)		208	1.19 (0.98-1.45)		33	0.93 (0.59-1.46)		
4	193	0.93 (0.74-1.18)	0.9	155	0.91 (0.71-1.16)	0.7	38	1.05 (0.68-1.63)	0.5	0.4
Vegetable										
1	200	Reference		164	Reference		36	Reference		
2	254	1.11 (0.90-1.36)		211	1.12 (0.90-1.41)		43	1.02 (0.64-1.62)		
3	257	1.02 (0.83-1.27)		226	1.10 (0.87-1.39)		31	0.67 (0.41-1.10)		
4	307	1.12 (0.90-1.40)	0.5	251	1.12 (0.88-1.44)	0.5	56	1.11 (0.71-1.73)	0.8	>0.9
Meat & Potatoes										
1	258	Reference		213	Reference		45	Reference		
2	257	1.00 (0.84-1.20)		226	1.07 (0.89-1.30)		31	0.68 (0.43-1.08)		
3	272	1.04 (0.87-1.24)		224	1.04 (0.85-1.27)		48	1.03 (0.68-1.57)		
4	231	0.87 (0.71-1.08)	0.2	189	0.87 (0.69-1.10)	0.1	42	0.89 (0.57-1.37)	0.9	0.4
Fruit & Salad										
1	234	Reference		190	Reference		44	Reference		
2	277	1.14 (0.96-1.36)		231	1.19 (0.98-1.44)		46	0.94 (0.62-1.43)		
3	278	1.10 (0.92-1.32)		240	1.20 (0.98-1.46)		38	0.72 (0.46-1.12)		
4	229	1.00 (0.81-1.23)	0.6	191	1.07 (0.85-1.33)	0.8	38	0.74 (0.47-1.15)	0.4	0.5

NOTE: HRs were estimated from Cox regression models with age as the time metric. Models were adjusted for total energy intake and ethnicity.

*Aggressive cases are those with total Gleason score >7 and/or tumor stage IV. Prostate cancer cause-specific deaths have also been included as aggressive cases.

0.68-1.19). The results did not differ when analyzing cases with low (2-4), moderate (5-7), or high (8-10) Gleason score separately (data not shown).

Discussion

None of the dietary patterns identified was associated with prostate cancer risk overall, by aggressiveness, by Gleason score group, or by age at diagnosis. Our results do not support the two case-control studies that have reported statistically significant associations between prostate cancer risk and dietary patterns characterized by high consumption of red and processed meats (4, 6). Our results are broadly consistent with those from the Health Professionals Follow-up Study, which found no overall association between either "prudent" or "western" (the latter characterized by high intake of red meats, refined grains, and high-fat dairy) dietary patterns and prostate cancer risk (5). There was suggestive evidence from the Health Professionals Follow-up Study analysis that higher western pattern scores might be associated with a slightly greater risk of prostate cancer for men 65 years or older, although the authors attributed this to higher intake of processed meat. The results of our age-stratified analysis do not support this hypothesis.

The major strengths of our study are its prospective design and its ability to assess subgroups of prostate cancer by aggressiveness and age of onset. Its limitation is that it has inadequate statistical power to detect very small associations. Also, whereas analyzing empirically derived dietary patterns has the advantage of taking into account the whole diet, a key disadvantage of this approach is the difficulty in making direct comparisons between studies. However, all four studies of dietary factors and prostate cancer to date have identified a factor strongly characterized by high intake of red and processed meat, indicating some degree of comparability between studies.

In conclusion, we found no evidence for association between any dietary pattern and prostate cancer risk. In particular, the meat dietary pattern that has been associated

with an increased risk of type 2 diabetes in this cohort as well as in others (10, 12) does not seem to be associated with prostate cancer risk.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Acknowledgments

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

References

- Clinton SK, Giovannucci E. Diet, nutrition, and prostate cancer. *Annu Rev Nutr* 1998;18:413-40.
- Jacques PF, Tucker KL. Are dietary patterns useful for understanding the role of diet in chronic disease? *Am J Clin Nutr* 2001;73:1-2.
- Tseng M, Breslow RA, DeVellis RF, Ziegler RG. Dietary patterns and prostate cancer risk in the National Health and Nutrition Examination Survey Epidemiological Follow-up Study cohort. *Cancer Epidemiol Biomarkers Prev* 2004;13:71-7.
- Walker M, Aronson KJ, King W, et al. Dietary patterns and risk of prostate cancer in Ontario, Canada. *Int J Cancer* 2005;116:592-8.
- Wu K, Hu FB, Willett WC, Giovannucci E. Dietary patterns and risk of prostate cancer in U.S. men. *Cancer Epidemiol Biomarkers Prev* 2006;15:167-71.
- Ambrosini GL, Fritschi L, de Klerk NH, Mackerras D, Leavy J. Dietary patterns identified using factor analysis and prostate cancer risk: a case control study in Western Australia. *Ann Epidemiol* 2007;18:364-70.
- Giles GG, English DR. The Melbourne Collaborative Cohort Study. *IARC Sci Publ* 2002;156:69-70.
- MacInnis RJ, English DR, Gertig DM, Hopper JL, Giles GG. Body size and composition and prostate cancer risk. *Cancer Epidemiol Biomarkers Prev* 2003;12:1417-21.
- Ireland P, Jolley D, Giles G, et al. Development of the Melbourne FFQ: a food frequency questionnaire for use in an Australian prospective study involving an ethnically diverse cohort. *Asia Pac J Clin Nutr* 1994;3:19-31.
- Hodge AM, English DR, O'Dea K, Giles GG. Dietary patterns and diabetes incidence in the Melbourne Collaborative Cohort Study. *Am J Epidemiol* 2007;165:603-10.
- Lunn M, McNeil D. Applying Cox regression to competing risks. *Biometrics* 1995;51:524-32.
- van Dam RM, Rimm EB, Willett WC, Stampfer MJ, Hu FB. Dietary patterns and risk for type 2 diabetes mellitus in U.S. men. *Ann Intern Med* 2002;136:201-9.