Dietary fiber, whole grains, carbohydrate, glycemic index, and glycemic load in relation to risk of prostate cancer

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Background: The relationships between dietary fiber, whole grains, carbohydrate, glycemic index (GI), glycemic load (GL), and prostate cancer risk are unclear. We conducted a systematic review and meta-analysis to investigate these associations.

Methods: Relevant studies were identified by a search of PubMed database and EMBASE database up to April 2015. A random effects model was used to calculate the summary relative risks (RRs) and their corresponding 95% confidence intervals (CIs).

Results: Twenty-seven epidemiological studies (18 case-control studies and nine cohort studies) were included in the final analysis. The pooled RRs of prostate cancer were 0.94 (95% CI 0.85–1.05, $P=0.285$), 1.13 (95% CI 0.98–1.30, $P=0.095$), 0.96 (95% CI 0.81–1.14, $P=0.672$), 1.06 (95% CI 0.96–1.18, $P=0.254$), and 1.04 (95% CI 0.91–1.18, $P=0.590$) for dietary fiber, whole grains, carbohydrate, GI, and GL, respectively. There was no evidence of significant publication bias based on the Begg's test and Egger's test.

Conclusion: The findings of this meta-analysis indicate that, based on available information, dietary fiber, whole grains, carbohydrate, GI, and GL are not associated with the risk of prostate cancer.

Keywords: prostate cancer, fiber, whole grains, carbohydrate, glycemic index, glycemic load

Introduction

Prostate cancer has the second highest incidence of all cancers in men after lung cancer worldwide, and it was estimated that prostate cancer alone accounted for ~14% of all newly diagnosed cancers in the world.¹ Well-established risk factors for prostate cancer include age, race/ethnicity, and family history.² In addition, physical activity, body mass index, hormones, and diet have been suggested to be associated with prostate cancer risk.

In various epidemiological studies, including case-control and cohort studies, the potential relationship between dietary fiber, whole grains, carbohydrate, glycemic index (GI), glycemic load (GL), and prostate cancer risk has been investigated with inconsistent findings. For example, Walker et al,³ Lewis et al,⁴ and Deschasaux et al⁵ reported an inverse association between fiber intake and prostate cancer risk. Augustin et al⁶ and Hu et al⁷ suggested a positive association between GI and prostate cancer risk. However, many other studies did not find such correlations.

To address the issues described earlier, we performed a systematic review and meta-analysis on dietary fiber, whole grains, carbohydrate, GI, GL, and risk of prostate cancer. Subgroup analyses were also carried out to identify possible variables or features moderating the results obtained.

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Materials and methods

Search strategy

We searched PubMed database and EMBASE database up to April 2015 for all relevant studies with the following key words: fiber, fibre, grains, grain, carbohydrate, carbohydrates, GI, GL, glycaemic index, or glycaemic load combined with prostate cancer or prostate neoplasm. We also manually reviewed reference lists of retrieved articles and related reviews for additional pertinent studies. No language limitations were imposed.

Study selection

Studies included in this meta-analysis had to fulfill all the following criteria: 1) they had a cohort or case-control design; 2) the exposure of interest was dietary fiber, whole grains, carbohydrate, GI, or GL; 3) the outcome of interest was primary prostate cancer; and 4) studies provided the risk estimates with their 95% confidence intervals (CIs) or data to calculate them. If more than one publication from the same study population was available, the most recent and detailed study was included in this meta-analysis.

Quality assessment

The quality of included studies was evaluated by two authors with the Newcastle-Ottawa Scale (NOS) (http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). NOS is a nine-star instrument designed to assess the selection of study population, study comparability, and ascertainment of either the exposure or the outcome of interest for case-control or cohort studies, respectively. The possible scores vary from 0 to 9. We used these scores to differentiate higher (7–9) from lower (0–6) quality studies.

Data extraction

The following data were extracted independently by two authors from each study: the first author's last name, year of

publication, study country, study design, sample size, age, types of exposure, the risk estimates with their corresponding 95% CIs, and matched or adjusted variables. From each study, we extracted the risk estimate that was most fully adjusted for potential confounders.

Statistical analysis

Considering that the absolute risk of prostate cancer is low, the odds ratio (OR) was assumed approximately the same as relative risk (RR), and the RR was used as the study outcome. Summary RR estimates with their corresponding 95% CIs for the highest versus the lowest level of fiber, whole grains, carbohydrate, GI, and GL were calculated with the DerSimonian and Laird random effect model,⁸ which take into account both within-study and between-study variation. Subgroup analyses were performed by study design and geographic region. Heterogeneity between studies was assessed by Q statistic (significance level at $P < 0.10$) and I^2 ($I^2 < 25\%$, no heterogeneity; $I^2 = 25\%–50\%$, low heterogeneity; $I^2 = 50\%–75\%$, moderate heterogeneity; $I^2 > 75\%$, large or extreme heterogeneity).⁹ A sensitivity analysis was carried out whereby each study was removed in turn and the combined estimate recalculated to determine the influence of each study. Publication bias was tested by Begg's test¹⁰ and Egger's test.¹¹ A two-tailed $P < 0.05$ was considered to be representative of a significant statistical publication bias. All the statistical analyses were conducted with STATA 12.0 (StataCorp LP, College Station, TX, USA).

Results

Study selection

Figure 1 shows a flow diagram of the procedure used to identify potentially relevant studies. Searches of the electronic databases yielded 3,369 articles. After carefully reading the titles and abstracts, 3,344 studies that were

Figure 1 Flow diagram of identification of relevant studies.

obviously unrelated to our topic were excluded. Then, we reviewed the full text of the remaining 25 articles and six articles were excluded with the following reasons: duplicate population ($n=2$), lacking control group ($n=1$), and lacking sufficient data ($n=3$). Eight studies were identified through checking reference lists of retrieved studies. Finally, the present study included 27 epidemiological studies.^{3–7,12–33}

Characteristics of the included studies

The main clinical features of these 27 eligible studies are summarized in Table 1. These studies were published between 1988 and 2015, including 18 case–control and nine cohort studies. Thirteen articles evaluated patients from North America, ten from Europe, two from Asia, one from Africa, and one from South America. The total number of prostate cancer patients was 39,352. Fiber was reported in 16 studies, whole grains reported in eight studies, carbohydrate reported in 13 studies, GI reported in six studies, and GL reported in five studies. Although the number of studies included in GI and GL was limited, the sample sizes were large with a total of 26,656 and 26,500 prostate cancer patients for GI and GL, respectively. In addition, these studies had high quality (mean NOS =6.8 and 7 for GI and GL, respectively) and adjusted major confounding.

Quantitative synthesis

The pooled RRs of prostate cancer were 0.94 (95% CI 0.85–1.05, $P=0.285$), 1.13 (95% CI 0.98–1.30, $P=0.095$), 0.96 (95% CI 0.81–1.14, $P=0.672$), 1.06 (95% CI 0.96–1.18, $P=0.254$), and 1.04 (95% CI 0.91–1.18, $P=0.590$) for dietary fiber (Figure 2), whole grains (Figure 3), carbohydrate (Figure 4), GI (Figure 5A), and GL (Figure 5B), respectively.

In the stratified analysis by study design and region, significant associations were observed for whole grains intake in cohort studies (RR =1.10, 95% CI 1.02–1.19, $P=0.014$), GI in case–control studies (RR =1.34, 95% CI 1.10–1.62, $P=0.004$), and GL in case–control studies (RR =1.36, 95% CI 1.08–1.70, $P=0.008$) (Table 2). For dietary fiber, we further conducted stratified analysis by the types of fiber. The pooled RRs of prostate cancer were 0.86 (95% CI 0.59–1.26, $P=0.452$), 0.93 (95% CI 0.83–1.04, $P=0.213$), 0.92 (95% CI 0.76–1.10, $P=0.353$), and 0.82 (95% CI 0.57–1.16, $P=0.258$) for vegetable fiber, fruit fiber, soluble fiber, and insoluble fiber, respectively.

Low-to-moderate between-study heterogeneity was observed for dietary fiber ($I^2=39.5\%$), whole grains ($I^2=52.5\%$), carbohydrate ($I^2=51.2\%$), GI ($I^2=69.5\%$),

and GL ($I^2=67.0\%$). There was no evidence of significant publication bias based on the Begg's test and Egger's test (fiber, $P_{\text{Begg}}=0.558$, $P_{\text{Egger}}=0.545$; whole grains, $P_{\text{Begg}}=1.000$, $P_{\text{Egger}}=0.475$; carbohydrate, $P_{\text{Begg}}=0.428$, $P_{\text{Egger}}=0.598$; GI, $P_{\text{Begg}}=0.260$, $P_{\text{Egger}}=0.299$; GL, $P_{\text{Begg}}=0.221$, $P_{\text{Egger}}=0.247$) (Figure 6). Sensitivity analysis was carried out by removing each study sequentially. As shown in Figure 7, for dietary fiber, carbohydrate, GI, and GL, all the pooled estimates were stable and not influenced by any included single study. However, for whole grains, the pooled estimate became statistically significant after removing the study by Jain et al.²⁸

Discussion

This systematic review of epidemiological studies evaluated the potential association between dietary fiber, whole grains, carbohydrate, GI, GL, and prostate cancer risk based on nine prospective and 18 case–control studies. Overall, the summary RRs indicated that there was no clear relationship between the above factors and prostate cancer incidence, although a few results of stratified analysis were statistically significant.

In the pooled analysis, low-to-moderate between-study heterogeneity was observed, I^2 ranging from 39.5% for dietary fiber to 69.5% for GI. Significant heterogeneity may be attributed to the study population, study design, sample size, method of exposure measurement, and adjustment for confounders. The presence of heterogeneity somewhat limited the interpretation of the results.

Up to now, the only fully established risk factors of prostate cancer are age, African–American ethnicity, and family history of prostate cancer.² No lifestyle factors (eg, diet and exercise) have been conclusively confirmed as prostate cancer risk or protective factors, although many have been considered with supporting evidence. For example, physical activity in both occupational and recreational time has been associated with a decreased risk of prostate cancer.³⁴ Another recent meta-analysis of cohort studies has indicated that high intakes of dairy products and dairy calcium may increase total prostate cancer risk.³⁵ Conversely, consumption of dietary carrot³⁶ and cruciferous vegetables³⁷ might be inversely associated with prostate cancer risk.

As for dietary fiber, whole grains, and carbohydrate, several clinical and animal studies have indicated that they may play a role in prostate cancer development. Landberg et al³⁸ reported that whole grains and bran from rye led to significantly lower plasma prostate specific antigen. Bylund et al³⁹ suggested that factors in rye bran could inhibit prostate cancer growth. Mavropoulos et al⁴⁰ and Freedland et al⁴¹

Table 1 Main characteristics of the studies included in this meta-analysis

Study	Year	Country	Cases	Controls or cohort	Age (years)	Quality score	Type of exposure	Matched or adjusted variables
Sawada et al ¹³	2015	Japan	825	43,435	45–74	8	Fiber	Age, public health center area, smoking status, drinking frequency, marital status, BMI, and intake of green tea, genistein, SFAs, and carbohydrate
Vidal et al ¹²	2015	USA	156	274	63 (SD 6.0)	6	Fiber, carbohydrate, GI	Age, race, family history, caloric intake, carbohydrate/fiber intake, BMI, diabetes, physical activity, alcohol, and smoking status
Deschasaux et al ⁵	2014	France	139	3,313	63	8	Fiber	Age, energy intake without alcohol, intervention group, number of 24-h dietary records, smoking, educational level, physical activity, height, BMI, alcohol intake, family history, PSA, calcium intake, processed meat intake, tomato product intake, vitamin E intake, and blood selenium
Hu et al ⁷	2013	Canada	1,799	5,039	67	7	GI, GL	10-year age group, province, education, BMI, alcohol consumption, pack-year smoking, and energy intake (noncarbohydrate and alcohol)
Drake et al ¹⁴	2012	Sweden	817	8,128	45–73	7	Fiber, carbohydrate, whole grains	Age, year of study entry, season of data collection, energy intake, height, waist, physical activity, smoking, educational level, birth in Sweden, alcohol, calcium, and selenium
Egeberg et al ¹⁸	2011	Denmark	1,081	26,691	50–64	7	Whole grains	Height, weight, school education, intake of red meat, processed meat and dairy products, and smoking status
Hardin et al ¹⁷	2011	USA	470	512	65.8 (SD 8.3)	6	Whole grains	Age, race, institution, energy intake, and history of first-degree relative with prostate cancer
Nimptsch et al ¹⁶	2011	USA	5,112	49,934	40–75	7	Fiber, whole grains, GI, GL	Age, BMI, height, history of diabetes, family history, race/ethnicity, smoking, vigorous physical activity, energy intake, alcohol intake, calcium intake, alpha-linolenic acid, and tomato sauce
Shikany et al ¹⁵	2011	USA	2,436	30,482	55–74	8	Carbohydrate, GI, GL	Age, year of entry, race, center, compliant for baseline screen, marital status, BMI, vigorous physical activity, smoking, history of diabetes, history of cancer, aspirin use, family history, any prostate problems, prior PSA test, prostate biopsy prior to entry, and dietary factors
Hu et al ¹⁹	2010	Canada	1,797	2,547	20–76	7	Carbohydrate	Age, province, education, family income, BMI, total alcohol intake, and total energy intake
Lewis et al ⁴	2009	USA	478	382	63.3 (SD 8.2) 66.9 (SD 8.1)	6	Fiber, carbohydrate, whole grains	Age, education, BMI, smoking history, family history of prostate cancer in first-degree relatives, and total caloric intake
Suzuki et al ²⁰	2009	Multicenter	2,747	142,590	52	8	Fiber	Study center, age, energy intake, height, weight, smoking, education, and marital status
George et al ²¹	2009	USA	15,949	262,642	50–71	7	GI, GL	Age, race/ethnicity, education, marital status, BMI, family history of any cancer, physical activity, smoking, alcohol consumption, and energy intake
McCann et al ²³	2005	USA	433	538	NA	6	Fiber, carbohydrate	Age, county of residence, education, BMI, cigarette smoking status, total energy, and vegetable intake
Walker et al ²²	2005	Canada	80	334	65.0 (SD 6.0)	5	Fiber, carbohydrate	Age, alcohol intake, carbohydrate/fiber, total energy, protein, fat, cholesterol, and calcium

Pelucchi et al ²⁴	2004	Italy	1,294	1,451	66 (46–74)	6	Fiber	Age, study center, education, family history, smoking, alcohol consumption, and energy intake
Augustin et al ⁶	2004	Italy	1,204	1,352	66 (46–74)	6	GI, GL	Age, study center, education, family history, energy intake, alcohol consumption, smoking, BMI, occupational physical activity at 50 years, intake of fiber, and intake of lycopene
Lu et al ²⁵	2001	USA	65	132	59.98	5	Fiber	Age, race, education, alcohol drinking, smoking, family history, and total dietary caloric intake
Ramon et al ²⁶	2000	Spain	217	434	≤80	6	Fiber, carbohydrate	Age, residence, calories, family history, and BMI; carbohydrate further adjusted for total protein and total fat intake
Chan et al ²⁷	2000	Finland	184	27,062	50–69	7	Carbohydrate	Supplementation group, education, age, BMI, energy, and number of years as a smoker
Deneo-Pellegrini et al ²⁹	1999	Uruguay	175	233	40–89	6	Fiber, carbohydrate, whole grains	Age, residence, urban/rural status, education, family history, BMI, and total energy intake
Jain et al ²⁸	1999	Canada	617	636	69.8	7	Whole grains	Total energy, vasectomy, age, ever-smoked, marital status, study area, BMI, education, ever-used multivitamin supplements, area of study, and log-converted amounts for grains, fruit, vegetables, total plants, total carotenoids, folic acid, dietary fiber, conjugated linoleic acid, vitamin E, vitamin C, retinol, total fat, and linoleic acid
Chatenoud et al ³⁰	1998	Italy	127	7,990	<75	6	Whole grains	Age, sex, education, smoking, alcohol, and BMI
Andersson et al ³¹	1996	Sweden	526	536	70.7 (SD 5.9)	6	Fiber, carbohydrate	Age and energy
Walker et al ³	1992	South Africa	166	166	69.2 (SD 8.9)	5	Fiber	Age and residence
West et al ³²	1991	USA	358	679	45–74	6	Carbohydrate	Since interaction and confounding did not exist, crude ORs are presented
Oishi et al ³³	1988	Japan	100	100	50–79	5	Fiber, carbohydrate	Age, date of admission

Abbreviations: BMI, body mass index; SD, standard deviation; GI, glycemic index; h, hours; PSA, prostate specific antigen; GL, glycemic load; ORs, odds ratios; SFAs, saturated fatty acids; NA, not available.

Figure 2 Summary RR of fiber intake and prostate cancer risk.

Note: Weights are from random effects analysis.

Abbreviations: RR, relative risk; CI, confidence interval.

Figure 3 Summary RR of whole grains intake and prostate cancer risk.

Note: Weights are from random effects analysis.

Abbreviations: RR, relative risk; CI, confidence interval.

Figure 4 Summary RR of carbohydrate intake and prostate cancer risk.

Note: Weights are from random effects analysis.

Abbreviations: RR, relative risk; CI, confidence interval.

Figure 5 Summary RRs of GI (A), GL (B), and prostate cancer risk.

Note: Weights are from random effects analysis.

Abbreviations: RRs, relative risks; GI, glycemic index; GL, glycemic load; CI, confidence interval.

Table 2 Pooled and subgroup analyses stratified by study design and area

	Fiber intake				Whole grains intake				Carbohydrate intake				GI				GL			
	N ^a	RR (95% CI)	I ² (%)	N ^a	RR (95% CI)	I ² (%)	N ^a	RR (95% CI)	I ² (%)	N ^a	RR (95% CI)	I ² (%)	N ^a	RR (95% CI)	I ² (%)	N ^a	RR (95% CI)	I ² (%)		
Overall	16	0.94 (0.85–1.05)	39.5	8	1.13 (0.98–1.30)	52.5	13	0.96 (0.81–1.14)	51.2	6	1.06 (0.96–1.18)	69.5	5	1.04 (0.91–1.18)	67.0					
Study design																				
Cohort	5	0.99 (0.87–1.14)	52.6	3	1.10 (1.02–1.19)	0.0	3	0.98 (0.83–1.17)	1.9	3	0.98 (0.94–1.02)	0.0	3	0.96 (0.87–1.06)	43.9					
Case-control	11	0.89 (0.75–1.06)	27.6	5	1.27 (0.87–1.86)	69.4	10	0.94 (0.73–1.20)	60.1	3	1.34 (1.10–1.62)	22.1	2	1.36 (1.08–1.70)	0.0					
Area																				
Asia	2	0.96 (0.76–1.21)	0.0	0	–	–	1	1.33 (0.76–2.32)	–	0	–	–	0	–	–					
Europe	6	0.94 (0.79–1.11)	48.9	3	1.03 (0.90–1.18)	0.0	4	0.96 (0.75–1.22)	44.5	1	1.57 (1.19–2.07)	–	1	1.41 (1.05–1.90)	–					
North America	6	0.95 (0.75–1.21)	35.8	4	1.22 (0.93–1.61)	72.5	7	1.00 (0.78–1.29)	54.5	5	1.00 (0.94–1.07)	33.8	4	0.98 (0.88–1.10)	53.0					

Note: ^aThe number of studies included.

Abbreviations: GI, glycemic index; GL, glycemic load; RR, relative risk; CI, confidence interval.

indicated that increased carbohydrate consumption may promote tumor growth and inhibit apoptosis of prostate cancer cells. However, our meta-analysis, based on all available epidemiologic studies, indicated no statistically significant relationships between dietary fiber, whole grains, carbohydrate, and prostate cancer risk.

Emerging studies also have evaluated the relationship between dietary fiber, whole grains, carbohydrate, GI, GL, and various types of other human diseases. Aune et al⁴² reported that there was an inverse association between dietary fiber intake and breast cancer risk. Yang et al⁴³ suggested that fiber intake was associated with a reduced risk of all-cause mortality. Consumption of whole grains has been reported to be inversely associated with the risk of colorectal cancer⁴⁴ and type 2 diabetes.⁴⁵ GI and GL have been suggested to be related with the risk of breast cancer⁴⁶ and digestive tract neoplasms.⁴⁷ Therefore, dietary fiber, whole grains, carbohydrate, GI, and GL may only play a role in specific diseases.

Our study has several strengths. This meta-analysis included a large number of studies and more than 39,000 cases, which enhanced the statistical power. All included studies ascertained outcomes according to histologic findings. A recent meta-analysis reported that there was no clear association between carbohydrate intake and the risk of prostate cancer,⁴⁸ which was in accordance with our study. However, we evaluated as many as five factors, including dietary fiber, whole grains, carbohydrate, GI, and GL.

Some limitations of this meta-analysis should be acknowledged. First, measurement errors in the assessment of exposure may bias the overall effect estimates. Second, residual confounding (ie, uncontrolled confounding) are always a concern in observational studies. Third, as discussed earlier, significant heterogeneity was observed among several analyses. Fourth, sensitivity analysis indicated that the summary estimate for whole grains was not stable and influenced by a single study. Finally, publication bias could not be ruled out as small studies with null results tend not to be reported.

Conclusion

Overall, the findings of this meta-analysis indicate that, based on available information, dietary fiber, whole grains, carbohydrate, GI, and GL are not associated with the risk of prostate cancer. To provide a more definitive conclusion, further prospective cohort studies with larger sample size, better exposure assessment, and longer follow-up are warranted in this area.

Figure 6 Begg's funnel plots of dietary fiber, whole grains, carbohydrate, GI, GL, and prostate cancer risk.
Abbreviations: GI, glycemic index; GL, glycemic load; RR, relative risk.

Figure 7 Sensitivity analyses of dietary fiber, whole grains, carbohydrate, GI, GL, and prostate cancer risk.

Abbreviations: GI, glycemic index; GL, glycemic load; CI, confidence interval.

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Disclosure

The authors report no conflicts of interest in this work.

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