RESEARCH ARTICLE

Fruit and Vegetable Intake in Relation to Prostate Cancer in Iranian Men: A Case-Control Study

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Abstract

Background: Findings of epidemiologic studies on the relationship between fruit and vegetable consumption and prostate cancer (PCa) risk have been inconclusive. We therefore examined the association between intake of fruits and vegetables and PCa risk in Iran. Materials and Methods: In this hospital based, case-control study, a total of 50 patients with PCa and 100 controls underwent face-to-face interviews. Regression analysis was used to examine the relation between fruit and vegetable intake and PCa risk. Results: A protective independent effect was observed for the highest tertile of total fruit and vegetable (OR: 0.33, CI: 0.04-0.30, p value<0.001), total fruit (OR: 0.30, CI: 0.06-0.4, p value=0.03) and total vegetable (OR: 0.31, CI: 0.02-0.21, p value<0.001) consumption. Within the group of fruits, a significant inverse association was observed for apple and pomegranate (p trends were 0.01 and 0.016, respectively). In the vegetable group, a significant inverse association was observed for tomatoes (p trend<0.001) and cabbage (p trend=0.021). Conclusions: The results of the present study suggested that fruits and vegetable intake might be negatively associated with PCa risk.

Keywords: Prostate cancer - fruits - vegetable - risk - case-control study

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Introduction

Prostate cancer (PCa) is the most common cancer among men in United States. It is also one of the leading causes of cancer death among men of all races (XIE and HE, 2013). Literature reviews of PCa epidemiol¬ogy have reported high incidence in Western countries, with lower but typically increasing incidence in less developed countries (Baade et al., 2009; Mohagheghi et al, 2010; Zhang et al., 2011; Center et al., 2012). In Iran, PCa has an incidence of 9.6 per 100,000 (ranging from 3.2 to 16.0 per 100,000 according to different geographical setting) (Farahmand et al., 2010; Talaiezadeh et al, 2013). This is similar to Asia-Pacific region (9.9 per 100,000) but much lower than the world (32.8 per 100,000) (Baade et al., 2013). This Wide variation exists internationally for PCa rates is due to differences in screening methods, genetic factors, treatments and lifestyle (Baade et al., 2009; Zhang et al., 2011). Diet (as a part of lifestyle) may play a major etiological role and might explain this variation in PCa incidence and mortality. There are many biologically plausible explanations why fruits and vegetables consumption might prevent or slow the development of cancer. These include the presence in plant foods of such potentially anti carcinogenic substances as vitamin E, carotenoids, dithiolthiones, isoflavones, isothiocyanates and vitamin C. Recent reports have examined the effect of fruits and vegetable intake on the risk of PCa, but the results are inconsistent (Meng et al., 2013). Before any firm conclusion can be drawn, more results from developing countries studies are needed. There is a lack of published data in developing countries on this issue. Epidemiological studies in these countries could not only substantiate the existing evidence, but they could also provide valuable new information. Furthermore most of the reports relate to consumption of specific subtypes of fruits and vegetables, while information about total fruits and vegetables for PCa risk remains sparse. To verify the biologically plausible hypothesis about the protective role of fruits and vegetables against PCa, we used data from a hospital-based case-control study in Tehran (capital city of Iran) with high prevalence of this cancer.

Materials and Methods

Study population

The present study was done in Tehran Province in Iran. Cases were patients aged 40-78 years who were admitted to 'Labbafi-NejadHospital' with incident, histologically confirmed cancers of the prostate within the past 6 month and did not have a history of cancers of other sites. Controls were patients (43-71years) who were sampled

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randomly from patients admitted to the same hospital as cases during the same time period (for acute, non-neoplastic conditions and not afflicted with diet related chronic diseases). They were admitted to the hospitals for various medical issues (eye or nose disorders, skin diseases, fractures and sprains, for trauma and injuries, and for other illnesses e.g.; removal of plates, pins, screws and wires) (Askari et al., 2014).

Cases and controls were frequency matched according to body mass index (<19, 19-25, 25-30, 30<) and age (5-year groups). Participation rate was 85%. In total, 52 patients with PCa and 104 controls underwent face-to-face inter-views by specifically trained professional interviewers. We excluded one patients from the analysis because their log scales of total energy intake were either>3or<3 SD from the mean, indicating errors in their responses to the dietary questions. We further excluded 5 subjects due to poor responses with regard to dietary questions. After exclusions, the data included 50 cases with PCa and 100 controls remained for analysis.

Assessment of dietary intake

Participants' dietary intake during the past year was evaluated using a valid and reliable semi-quantitative food frequency questionnaire (FFQ) (Esfahani et al., 2010). This FFQ consists of 168 food items with standard serving sizes, and subjects were asked to report their consumption frequency for each food item on a daily, weekly, monthly or yearly basis. These reported consumptions were then converted to daily frequencies and the manual for household measures was used to convert intake frequencies to daily grams of food intake (Ghaffarpour et al., 1999). Food energy value was based on the Nutrients Composition of Iranian Foods (NCIF) and the USDA Food Composition Data (Safari et al., 2013). The latter was used for foods or food ingredients that were not available in NCIF. For data reduction, we grouped the food items based on similarity of their nutrients or culinary usage of the foods. Fruits and vegetable intake were among these groups that we aimed to consider their relation with risk of PCa.

Salad vegetables include lettuce and cucumber, root vegetables include carrot and beet, citrus fruits include orange, grapefruit and citrus.

The consumption of alcohol was not answered by our participants due to their cultural beliefs and was not included in the analysis

Assessment of non-dietary exposures

We administered general questionnaires to gathered participants' socio demographic and lifestyle information, including age (years), family history of cancer (yes/no), smoking (yes/no), ethnicity (fars, not fars) and having diabetes (yes/no).

Weight and height were assessed while participants were wearing only light clothing without shoes. Height was evaluated using a stadiometer (Seca 214 portable stadiometer) and was recorded to the nearest 0.1 cm. Weight was measured by using digital scales (Seca 881, Germany) and it was recorded to the nearest 0.1 kilograms. Body mass index (BMI) was then calculated dividing the weight in kg by square of height in meters. Waist circumference was measured at the slimmest part, using a tape and was recorded to the nearest 0.1 cm.

Statistical analysis

The cumulative monthly intake of fruits and vegetable was obtained by summing the consumption frequency of individual food items in the same group, which was then distributed in to approximate marginal tertiles. We used Chi-square test to evaluate the differences in distribution of categorical variables (e.g. and smoking), and analysis of variance tests to check the differences in distribution of continuous variables (e.g. BMI) across fruits and vegetable score categories. Odds ratios (OR) of PCa and the corresponding 95% confidence intervals (CI) for a tertile increment of intake of the respective food groups were estimated using multiple logistic regression models including terms for age (5-yr groups), having diabetes (yes/no), smoking (yes/no) and total energy intake, where appropriate. Tests for trends were performed by treating the categorical variables as continuous predictors in the logistic regression models.

Results

Table 1 shows the association between total fruits and vegetable intake and risk of PCa. A protective independent effect was observed for the highest tertile of total fruits and vegetable (OR: 0.33, CI: 0.04-0.30, P value<0.001), total fruit (OR: 0.30, CI: 0.06-0.4, P value=0.03) and total vegetable (OR: 0.31, CI: 0.02-0.21, P value<0.001) consumption.

To further investigate the protective effects of fruits and vegetable, their subgroups were analyzed in association with PCa separately.

Within the group of fruits (Table 2), a significant inverse association was observed for apple and pomegranate (p trends were 0.01 and 0.016, respectively).

In vegetable group (Table 3), a significant inverse association was observed for tomato (p trend<0.001) and cabbage (p trend=0.021).

Table 1. Characteristics of the Subjects in a Case-Control Study of Prostate Cancer, Iran

	Controls	Prostate cancer	p-value
Number	100	50	
Age (median, yr)	56.9 (6.0)*	57.4 (5.9)*	0.816a
BMI (median, kg/m)	27.1 (4.6)*	27.8 (4.5)*	0.103a
Waist circumference (mean, cm)	102.9 (9.1)*	105.7 (8.3)*	0.247a
Ethnicity			0.071b
Fars (n, %)	89 (89)	41 (82)	
Not Fars	11 (11)	9 (18)	
Smoking (n, %)			0.010b
Yes	5 (5)	23 (46)	
No	95 (95)	27 (54)	
Family history of cancer (n, %)			0.621b
Yes	13 (13)	14 (28)	
No	87 (87)	36 (72)	
Diabetes (n, %)			0.031b
Yes	7 (7)	13 (26)	
No	93 (93)	37 (74)	

*indicates mean (SD); otherwise data are presented as n (%); [a]Student t-test; [b]Chi-square

Table 2. Adjusted Odds Ratios and 95% Confidence Interval by Intake Tertiles of Total Fruit and Vegetable, in a Case-Control Study of Prostate Cancer, Iran

	Tertiles of intake (g/day)			P trend
	1	2	3	
Total fruit and vegetable				
Cases, n (%)	<75.16	75.16-207.02	>207.02	<0.001
OR (95%CI)	31(62)	11(22)	8 (16)	
Age- adjusted	1.0 (ref)	0.37(0.07-0.53)	0.33(0.04-0.39)	
Multivariate- adjusted	1.0 (ref)	0.37(0.07-0.41)	0.33(0.04-0.30)	
Total fruit				
Cases, n (%)	<63.01	63.01-105.13	>105.13	0.03
OR (95%CI)	29(58)	12(24)	9 (18)	
Age- adjusted	1.0 (ref)	0.30(0.08-0.50)	0.30(0.06-0.39)	
Multivariate- adjusted	1.0 (ref)	0.31(0.09-0.54)	0.30(0.06-0.40)	
Total vegetable				
Cases, n (%)	<12.14	12.14-103.01	>103.01	<0.001
OR (95%CI)	28(56)	18(36)	4 (8)	
Age- adjusted	1.0 (ref)	0.44(0.11-0.10)	0.31(0.02-0.31)	
Multivariate- adjusted	1.0 (ref)	0.44(0.11-0.98)	0.31(0.06-1.01)	

[a]Abbreviations are as follows: CI, confidence interval; [b]having diabetes (yes/no) , smoking (yes/no) and total energy intake were also included in the regression models as covariates

Table 3. Adjusted Odds Ratios and 95% Confidence Interval by intake Tertiles of Fruits, in a Case-Control Study of Prostate Cancer, Iran

	Tertiles of intake (g/day)			P trend
	1	2	3	
Apple				
Cases, n (%)	<7.59	7.59-56.41	>56.41	0.01
OR (95%CI)	23(46)	15(30)	12 (24)	
Age- adjusted	1.0 (ref)	0.89(-0.01-0.8)	0.60(0.04-1.00)	
Multivariate- adjusted	1.0 (ref)	0.91(-0.21-1.40)	0.60(0.02-1.03)	
Citrus fruit				
Cases, n (%)	<1.19	1.19-3.97	>3.97	0.07
OR (95%CI)	18(36)	18(36)	14 (28)	
Age- adjusted	1.0 (ref)	0.60(-1.0-0.30)	0.53(0.06-0.91)	
Multivariate- adjusted	1.0 (ref)	0.60(-1.3-0.54)	0.53(1.0-1.40)	
banana				
Cases, n (%)	<8.05	8.05-14.50	>14.50	0.1
OR (95%CI)	20(40)	13(26)	17 (8)	
Age- adjusted	1.0 (ref)	0.91(-6.0-2.15)	0.96(-0.02-0.31)	
Multivariate- adjusted	1.0 (ref)	0.91(-3.18-0.98)	0.98(-0.41-1.01)	
pomegranate				
Cases, n (%)	<3.78	3.78-9.07	>9.07	0.016
OR (95%CI)	26(52)	9(18)	5 (10)	
Age- adjusted	1.0 (ref)	0.41(0.21-1.0)	0.39(0.1-0.91)	
Multivariate- adjusted	1.0 (ref)	0.41(0.20-0.96)	0.39(0.1-2.13)	

[a]Abbreviations are as follows: CI, confidence interval; [b]having diabetes (yes/no) , smoking (yes/no) and total energy intake were also included in the regression models as covariates

Discussion

In the present study, we observed a protective independent effect for the highest tertile of total fruits and vegetable, total fruit and total vegetable consumption. Within the group of fruits, a significant inverse association was observed for apple and pomegranate and in vegetable group, a significant inverse association was observed for tomato and cabbage.

Studies in developing countries such as Iran, can provide great opportunities to assess the association between diet and chronic diseases (Willet, 1998).As economic resources are severely restricted in developing countries, small economic difference will increase between person variations in dietary variables. Thus link between these dietary variables and disease could be detected easily. One of the other strength of the present study is the high participation rate (85%). We collect our data from Labafi Nejad Hospital that is a referral hospital for PCa and to decrease the probability of recall bias, we registered incident cases. We also carefully selected controls from patients only with conditions that were not associated with diet or other major risk factors of PCa.

Before the implications of our findings, it is necessary to consider potential biases. First, although we used a validated food-frequency questionnaire (FFQ) for assessing the dietary intake, measurement errors that might led to underestimation or even over estimation of associations were inevitable. PCa is a slowly growing cancer. Even though diet in mid-life may be more important than the diet later in life, the long time passed from the patients' mid-life restricts our ability to evaluate that time period. In this study we measured diet during the past year to avoid the measurement errors and assumed that probability of changing diet was lower using this approach. Furthermore, the studies have suggested that if remote diet is of interest, focusing questions on the period of interest provides the most accurate information. However the use of current diet as a surrogate for past diet provides almost the similar information in some instances (Willet, 1998). We could not adjust our risk estimates for potentially confounding effects of physical activity, educational level and access to health care because information about these exposures was not gathered at baseline (residual confounding). Small sample size is also another limitation which might result unstable results and extreme relative risk estimates.

The term 'the Mediterranean diet' was first popularized by Ancel Keys in his book "How to Eat Well and Stay Well: the Mediterranean Way", in 1975. This followed the publication of his studies which showed that Mediterranean countries have diets associated with low incidence of cancer and cardiovascular disease. There is now little doubt that the Mediterranean countries enjoy a low risk of many of the diet-related diseases of affluence (Hill and Giacosa, 1992, Hu, 2003). The Mediterranean is a large area with many different diet patterns, but they are all characterized by high consumption of fruits, vegetables, legumes and dietary fiber and low intakes of meat and saturated fats.

Several studies, asserts the protective effect of fruits and vegetable intake on PCa risk. Sunny probed PCa risk and a low fat diet rich in fruits and vegetable. The findings from this study support the hypothesis that a low fat diet rich in fruits and vegetable may reduce the risk of PCa. But they didn't specify that witch of the fruits and vegetables had a significant relation with the risk of PCa (Sunny, 2005). Kolonel et al investigated vegetables, fruits and legumes consumption with the risk of PCa. The results suggest that legumes (not limited to soy products) and certain categories of vegetables may protect against PCa (Kolonel et al., 2000).

Hardin et al, investigated the impact of consumption of vegetable, fruits, grain, and high glycemic index foods on aggressive PCa risk in a case control study. They founded that increasing intakes of leafy vegetables were inversely associated with risk of aggressive PCa, As was higher consumption of high carotenoid vegetables (Hardin et al., 2011).

Some of the studies although investigated the relation of certain types of fruits with PCa risk. Adhami et al investigated the effect of oral infusion of pomegranate fruit extract on the risk of PCa carcinogenesis, in the TRAMP model. They observed that supplementation resulted in simultaneous and significant inhibition of IGF-I/Akt/mTOR pathways in the prostate tissues and tumors (Adhami et al., 2012). Malik et al investigated PCa prevention through pomegranate fruit. They observed that pomegranate consumption may retard PCa progression, which may prolong the survival and quality of life in the PCa patients (Malik and Mukhtar, 2006). In our study consumption of pomegranate was inversely associated with PCa, too.

Furthermore vegetables and fruits that are among healthy diet foods, are rich in several micronutrients and other food compounds such as carotenoids, vitamins C and E, fibers, flavonoids and other plant sterols, which display both complementary and overlapping mechanisms of action, including antioxidant effects, binding and dilution of carcinogens, and alteration of hormone metabolism (Lucenteforte et al., 2008, Garg et al, 2014).

Umesawa etal, examined the associations of vegetables intake and carotenes with risk of PCa in Japanese in a cohort study. The results of their study showed that vegetable intake was not associated with the risk of prostate cancer, but Alpha-carotene intake is associated with lower risk of PCa among Japanese (Umesawa et al., 2014).

Zhou et al, evaluated the relationship between allium vegetables intake and risk of PCa, with a systematic literature search. They found a significantly decreased risk of PCa for intake of allium vegetables (OR=0.82, 95%CI 0.70, 0.97). In our study there was an inverse relation between onion group and risk of PCa too, but the relation was marginally significant (ptrend=0.060). (Zhou et al., 2014).

Unlike the results of our study, some of the studies didn't show a protective effect for fruits or vegetable intake against PCa risk. For example, in a recent meta-analysis by Meng et al. (2013), they didn't find a significant protective effect for fruits and vegetable against PCa risk. But according to the researcher statements, most enrolled studies in that meta-analysis, were from developed countries. Whether the non-significant relationship applies to low-income areas with a nutritional deficiency in vegetable and fruit intake is unknown. They also did not examine the effects of individual types of vegetables and fruit, such as cruciferous vegetables, pulses and citrus fruit, on PCa risk, while it has been reported that cruciferous vegetables and tomatoes, which are rich in isothiocyanates and the carotenoid lycopene, respectively, might reduce the risk for PCa (Etminan et al., 2004, Liu et al., 2012), as the results that we observed in our study (cabbage and tomato consumption were negatively associated with PCa).

Bae et al investigated Citrus fruits intake and PCa risk using a quantitative systematic review. They didn't observed an association between intake of citrus fruits and the risk of PCa (Bae et al., 2008). They didn't gather the information about the other types of fruits and vegetable or the relation between whole consumption of fruits and vegetable with PCa risk.

Rohani rasaf et al. investigated the correlations of the incidence of common cancers with food groups, total energy, smoking, and socio economic position. The results of this study showed that, the consumption of fruits adjusting for energy was positively correlated with PCa and consumption of vegetable adjusting for smoking, was inversely associated with PCa. But these correlations were not significant (Rohani rasaf et al., 2014).

In conclusion, the results of the present study suggested that fruits and vegetables intake might be negatively associated with the risk of PCa.

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