

## RESEARCH ARTICLE

# Healthy Plant Foods Intake Could Protect Against Prostate Cancer Risk: A Case-Control Study

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### Abstract

**Background:** Several studies have investigated the association between healthy plant foods intake and prostate cancer risk with inconsistent results. So this study was conducted to examine the existence of any possible association between healthy plant foods and prostate cancer risk. **Materials and Methods:** Sixty newly diagnosed prostate cancer cases and 60 controls engaged in a hospital-based case-control study. A validated 160-items semi-quantitative FFQ was used to assess usual dietary intakes. Energy-adjusted amounts of healthy plant foods intake were calculated using the residual method. Logistic regression model was also used to derive beta estimates and odds ratios. **Results:** Cases were older and more likely to be inactive. In crude model, individuals in the highest tertile vs lowest tertile of total healthy plant foods (OR= 0.12; 95 % CI 0.04, 0.34), total fruits (OR= 0.11; 95 % CI 0.04, 0.30), total vegetables (OR= 0.08; 95 % CI 0.03, 0.24), fresh fruits (OR= 0.11; 95 % CI 0.04, 0.30), and raw vegetables (OR= 0.06; 95 % CI 0.02, 0.18) had significantly lower risk of prostate cancer. After controlling for potential confounders (age, BMI, total energy intake, job, education, smoking, physical activity, some drug usage, and also dietary intakes), just total healthy plant foods (OR= 0.12; 95 % CI 0.02, 0.55), total vegetables (OR=0.03; 95 % CI 0.00, 0.25), and raw vegetables (OR= 0.01; 95 % CI 0.00, 0.12) were associated with lower prostate cancer risk. **Conclusions:** The results of this study suggest that a diet rich in healthy plant foods and especially total or raw vegetable may protect against prostate cancer.

**Keywords:** Healthy plant foods- case-control study- prostate cancer

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### Introduction

Prostate cancer is the second most common cancer and the fifth leading cause of cancer death among men with an estimated 1.1 million new cases diagnosed and 307,000 deaths in 2012, globally (Ferley et al., 2013). It is estimated that there will be 1.7 million new cases all over the world, by 2030 (Ferlay et al., 2010). In Iranian population, its incidence rate is 9.6 per 100,000, ranging from 3.2 to 16.0 per 100,000 based on various geographical regions (Farahmand et al., 2010; Talaiezhadeh et al., 2013), which is approximately similar to Asia-Pacific region (9.9 per 100,000) and lower than the world (32.8 per 100,000) (Baade et al., 2009). Age, ethnicity and positive family history of the disease are some well-known risk factors in the etiology of prostate cancer (Bloom et al., 2006). The findings that the incidence of prostate cancer is rising in Iran (Pakzad et al., 2016) demonstrate that environmental factors including diet may involve in its etiology. Plant-based foods such as fruits, vegetables, legumes, whole grains, and nuts-olive are most important constituents of traditional regimens in Mediterranean and Asian regions (Kushi et al., 1995). Based on clinical studies, certain bioactive compounds in plant foods, such as vitamin C, vitamin E, lycopene,  $\beta$ -carotene, different phytoestrogens,

vitamin A also retinoids, may significantly reduce the risk of prostate cancer/ or prostate cancer cell growth (Willis and Wians, 2003). Several observational studies have investigated the relationships between fruits and vegetable intake on prostate cancer incidence, but the findings were inconsistent. One meta-analysis including 16 cohort studies did not find any protective effects of total vegetables or fruits on the risk of prostate cancer (Meng et al., 2014). On the other hand some case-control studies reveal that total vegetables (Deneo-Pellegrini et al., 1999; Cohen et al., 2000; Kolonel et al., 2000; McCann et al., 2005; Hardin et al., 2011; Askari et al., 2014; Bashir and Malik, 2015) or fruits (Askari et al., 2014; Bashir and Malik, 2015) intake may lower the risk of prostate cancer, while other studies found no association with total vegetables (Jain et al., 1999) or total fruits (Cohen et al., 2000; Kolonel et al., 2000; Darlington et al., 2007; Hardin et al., 2011). Besides, most case-control (Key et al., 1997; Jain et al., 1999; Cohen et al., 2000; Kolonel et al., 2000) and cohort studies (Mills et al., 1989; Schuurman et al., 1998; Park et al., 2008) demonstrated a significant or non-significant inverse relationships between legumes intake and prostate cancer risk. Furthermore, the results of one systematic review and meta-analysis including 18 case-control and 9 cohort studies have indicated that

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there is no association between whole grains and prostate cancer risk (Wang et al., 2015). As mentioned above the association of healthy plant foods and prostate cancer risk is still unclear, and most of these studies were conducted in western regions, however, the eating habits of the Iranian population are greatly different from those in these regions (Esmailzadeh and Azadbakht, 2008). To further address this issue, and because of inconsistencies among epidemiological studies in relation to healthy plant foods and prostate cancer risk, we explored the association between A) total healthy plant foods; B) total fruits, vegetables, legumes, whole grains, and nuts-olive; and C) fruits and vegetables subgroups intakes and risk of prostate cancer in a hospital-based case-control study in Iranian subjects.

## Materials and Methods

### Study population

This hospital-based case-control study was conducted in Shiraz, Iran. From April to September 2015, 62 cases and 63 hospital-based controls were recruited from two main hospitals that are referral centers of urology disorders. Participants' demographic and dietary intake characteristics were assessed through face to face interview also anthropometric indices were measured. Cases were newly diagnosed prostate cancer patients (maximum 1 month after diagnosis), who did not have any history of dietary regimens for chronic diseases, diabetes or cancers of other sites. At the same time, controls were selected randomly from patients that admitted the same hospitals due to non-neoplastic, non-diabetes conditions. They were admitted to hospital due to eye (n=21), ENT (ear, nose, throat) (n=20), kidney (n=8), nerve (n=5) and gastrointestinal (n=9) problems. Controls also did not follow any dietary regimens for chronic diseases. Cases and controls were matched for body mass index (<19, 19-24.99, 25-29.99, 30≤) and age (5-year groups). Total energy intake of <800 or >4,200 kcal/day or poor response to food frequency questionnaire (FFQ) (do not respond to >70 items) were considered as exclusion criteria (Esmailzadeh and Azadbakht, 2008).

### Dietary intake assessment

A valid and reliable FFQ was used to assess dietary intakes of participants over the previous year (Mosallaei et al., 2015). Briefly, it included 160 food items, which its average food items were determined according to common average portion sizes within the Iranian population. In order to obtaining the frequency of each food item consumption, nine categories: "never or less than once a month", "1 to 3 times a month", "once a week", "2 to 4 times a week", "5 to 6 times a week", "once a day", "2 to 3 times a day", "4 to 5 times a day", and "6 times or more a day", and for classifying portions, three sizes: small (half of the defined average use or less), medium (equal to the defined average use), and large (one half of the defined average use or more), were considered. Then, all FFQs were analyzed using a software (Borland Delphi Professional, version 7.0), and selected choices delivered as an external file in TXT format. Using another software

(programmed by Visual Basic 2008 (VB 9.0)), the extracted data were analyzed and delivered as a SPSS file in which food items (grams of them) and daily intakes of energy, macronutrients, fiber, and some micronutrients (vitamin A, vitamin E, folate, and potassium) were included. Based on nutrient and culinary similarities, all food items were categorized into 18 food groups, within larger categories of animal foods (total red meats, poultry, fish, dairy products, egg, and Solid fats), healthy (vegetables, fruits, legumes, whole grains, nuts-olive) and less healthy (sweets and desserts, soft drinks, syrups, natural and artificial fruit juices, canned fruits, potato, refined grains) plant foods. We differentiated between healthy and less healthy plant foods using existing knowledge on the relationships of the foods and type 2 diabetes, cardiovascular disease, certain cancers, and intermediate conditions (obesity, hypertension, lipids, and inflammation).

### Non-dietary variables assessment

Lifestyle and demographic characteristics were assessed using a questionnaire, including information on smoking (smokers/non-smokers), ethnicity (Fars/Non Fars), job (Employed/Unemployed), education (Illiterate & primary/ Diploma & academic), physical activity (less or never/moderate/high), and some drug usage (antihyperlipidemic drugs, antihypertensive drugs, and aspirin) (Yes/No). Also, weight and height were measured then body mass index (BMI) was calculated. Weight was measured by a digital scale in light clothing to the nearest 0.1 kg (Glamor BS-801, Hitachi, China), and height was measured using a non-stretchable tape measure without shoes to the nearest 0.1 cm.

### Statistical analysis

Kolmogorov-Smirnov test was used for testing the normal distribution of variables. Independent sample T-test or Mann-Whitney test were applied for assessing the relationship between quantitative variables and study groups (cases and controls). Comparing the distribution of participants between groups in terms of qualitative variables chi-square test or Fisher's exact test was done. Energy-adjusted amounts of healthy plant foods intakes were calculated using the residual method and its tertile cut-off points were used for categorizing participants. General characteristics of participants across tertiles of total healthy plant foods intakes were compared using ANOVA and the chi-square test, where appropriate. Using general linear models with age and total energy intake as covariates, all dietary intakes were derived. Then, the association between healthy plant foods consumption and prostate cancer risk were evaluated through multiple logistic regression with adjustments for potential confounders in different models. When the analyses were performed across tertiles of healthy plant foods intake, the first tertile was considered as the reference. The overall trend of odds ratios across tertiles of healthy plant foods consumption was assessed using tertile categories as an ordinal variable in the model. Data were analyzed using SPSS software version 22, and statistical significance was considered at P<0.05.

## Results

Two cases and three controls were excluded from the study due to poor respond to FFQ, so data of 60 cases and 60 controls were included in final analysis.

Demographic, anthropometric and energy intakes of participant's based on case and control groups as well as across tertiles of energy-adjusted total healthy plant foods intake are summarized in Table 1. As it is shown age was significantly higher in cases compared to the controls (p=0.01), but physical activity level was significantly (p=0.02) and education not significantly (p=0.09) higher

in controls than cases. Also higher consumption of total healthy plant foods was associated with higher BMI and lower total energy intake. Participants in highest category had higher education status and smoking usage, too.

As illustrated in Table 2, dietary intakes of participants based on case and control groups as well as across tertiles of energy-adjusted total healthy plant foods intake were compared, respectively. Cases had significantly more red meats and less healthy plant foods intakes. They also had significantly lower total healthy plant foods, total fruits, and total vegetable intakes. The results also showed higher consumption of total healthy plant foods was associated

Table 1. General Characteristics of the Study Participants Based on Case and Control Groups as Well as Across Tertiles of Energy-Adjusted Total Healthy Plant Foods Intake

Variables	Case		control		p-value ^		
	Mean or N	SD or %	Mean or N	SD or %			
Age (year)	66	9.71	61.38	9.44	0.01		
BMI(kg/m <sup>2</sup> )	24.84	3.64	25.85	3.46	0.12		
Total energy intake (kcal/d)	2712.24	593.48	2596.1	712.77	0.33		
Ethnicity (%)					0.65		
Fars	48	80	46	77			
Non Fars	12	20	14	23			
Job (%)					0.57		
Employed	34	57	37	62			
Unemployed *	26	43	23	38			
Smokers (%)	14	23	16	27	0.67		
Education (%)					0.09		
Illiterate & primary	41	68	32	53			
Diploma & academic	19	32	28	47			
Physical activity (%)					0.02		
never or low	23	38	12	20			
moderate	25	42	24	40			
high	12	20	24	40			
Antihyperlipidemic drug user (%)	6	11	6	11	1		
Antihypertensive drug user (%)	19	32	13	22	0.21		
Aspirin user (%)	10	17	15	25	0.26		
Tertile of energy-adjusted total healthy plant foods intake							
	Tertile 1 (lowest)		Tertile 2		Tertile 3 (highest)		
	Mean or N	SE or %	Mean or N	SE or %	Mean or N	SE or %	P‡
Age (year)	63.8	11.74	65.85	8.96	61.42	8.09	0.13
BMI(kg/m <sup>2</sup> )	24.57	3.43	24.57	3.42	26.9	3.43	0.003
Total energy intake (kcal/d)	2,900.98	625.76	2,263.28	536.42	2,798.26	626.08	<0.001
Unemployed (%)	13	26.5	14	28.6	22	44.9	0.08
Smokers (%)	12	40.0	4	13.3	14	44.7	0.02
Smokers (%)	12	40.0	4	13.3	14	44.7	0.02
Illiterate & primary (%)	29	39.7	28	38.4	16	21.9	0.004
Physical activity (never or low) (%)	16	45.7	10	28.6	9	25.7	0.12
Antihyperlipidemic drug user(%)	1	8.3	5	41.7	6	50	0.14
Antihypertensive drug user(%)	11	34.4	10	31.3	11	34.4	0.95
Aspirin user (%)	5	20.0	9	36	11	44	0.24

Data are presented as mean ± standard deviation or standard error and Number (%); \*, Unemployed participants were retired or jobless individuals; ^, Independent sample t-test or Mann-Whitney U-test were used for comparison of quantitative variables; Chi-square test or Fisher's exact test were used for comparison of qualitative variables; ‡, Obtained by the use of ANOVA or the  $\chi^2$  test, where appropriate; P<0.05 was considered as statistically significant.

Table 2. Dietary Intakes of Study Participants Based on Case and Control Groups as Well as Across Tertiles of Energy-Adjusted Total Healthy Plant Foods Intake\*

Food group	Cases (n=60)		Controls (n=60)		P†
	Mean	SD	Mean	SD	
Total energy intake (kcal/d)	2712.24	593.48	2596.1	712.77	0.2
Total healthy plant foods (g/d)	737.28	273.17	1078.51	564.69	<0.001
Less healthy plant foods (g/d)	642.74	199.91	551.03	175.38	0.009
Total fruits (g/d)	324.02	161.38	514.12	380.4	<0.001
Total vegetables (g/d)	352.5	155.35	501.86	255.66	<0.001
Whole grains (g/d)	4.31	14.77	6.39	19.87	0.34
Legumes (g/d)	47.71	17.18	45.05	16.25	0.59
Red meats (g/d)	114.05	86.4	77.38	44.2	0.01
White meats (g/d)	122.83	72.15	119.6	84.6	0.84
Dairy products (g/d)	463.7	235.05	458.95	315.2	0.77
Egg (g/d)	40.73	29.06	36.86	26.93	0.87
Solid fats (g/d)	2.45	4.05	1.7	2.61	0.41
Nuts-olive (g/d)	8.71	8.4	11.07	11.26	0.17

  

	Tertile of energy-adjusted total healthy plant foods intake						
	Tertile 1 (lowest)		Tertile 2		Tertile 3 (highest)		P‡
	Mean	SD	Mean	SD	Mean	SD	
Total energy intake (kcal/d)	2900.98	625.76	2263.28	536.42	2798.26	626.08	<0.001
Total healthy plant foods (g/d)	599.47	174.79	698.4	160.94	1425.8	459.03	<0.001
Less healthy plant foods (g/d)	691.26	191.11	539.87	170.24	559.52	184.53	<0.001
Red meats (g/d)	125.09	93.49	71.9	45.37	90.16	54.65	0.12
Total fruits (g/d)	238.12	106.04	315.24	103.36	703.86	369.27	<0.001
Total vegetables (g/d)	303.61	109.25	328.49	97.13	649.45	234.23	<0.001
Whole grains (g/d)	1.7	5.32	2.15	3.65	12.21	28.58	0.01
Legumes (g/d)	49.67	18.18	44.5	16.33	44.97	15.41	0.43
White meats (g/d)	135.29	83.15	95.58	50.82	132.78	90.55	0.62
Dairy products (g/d)	515.05	280.6	335.71	182.27	533.21	312.24	0.38
Egg (g/d)	54.82	37.49	33.33	15.32	28.24	18.36	<0.001
Solid fats (g/d)	3.4	4.47	0.71	2.09	2.12	2.74	0.03
Nuts-olive (g/d)	6.35	7.21	8.01	8.89	15.3	11.19	<0.001

\* energy intake is adjusted for age, other dietary variables are adjusted for age and total energy intake; Data are presented as mean ± standard deviation; P<0.05 was considered as statistically significant; ‡, Obtained by ANCOVA.

with higher intakes of total fruits, total vegetables, whole grains, nuts-olive and lower intakes of total energy, less healthy plant foods, egg and solid fats. Statistical differences for other dietary variables across tertiles of total healthy plant foods were not significant.

Crude and multivariable-adjusted odds ratios for prostate cancer risk across tertiles of energy-adjusted healthy plant foods intake are shown in Table 3. In the crude model, individuals in the highest tertile of total healthy plant foods (OR= 0.12; 95 % CI 0.04, 0.34), total fruits (OR= 0.11; 95 % CI 0.04, 0.30), total vegetables (OR= 0.08; 95 % CI 0.03, 0.24), fresh fruits (OR= 0.11; 95 % CI 0.04, 0.30), and raw vegetables (OR= 0.06; 95 % CI 0.02, 0.18) intake had lower risk of prostate cancer compared with those in the lowest tertile. After controlling for potential confounders in different models, being in the highest category compared with lowest category of total healthy plant foods (OR= 0.12; 95 % CI 0.02, 0.55), total vegetables (OR=0.03; 95 % CI 0.00, 0.25),

and raw vegetables (OR= 0.01; 95 % CI 0.00, 0.12) were associated with lower prostate cancer risk.

## Discussion

In this hospital-based case-control study, we examined the associations of healthy plant foods intake and prostate cancer risk in newly diagnosed prostate cancer patients. Our results showed that higher intake of total healthy plant foods (fruits, vegetables, whole grains, legumes, and nuts-olive) was independently associated with less risk of prostate cancer.

Studies in which investigating the association between total healthy plant foods intake and prostate cancer risk are limited. These foods are the most important constituents of traditional regimens in Mediterranean and Asian regions (Kushi et al., 1995). Several epidemiological studies investigated the association between Mediterranean diet (MD) and prostate cancer risk, with inconsistent



Table 3. Multivariate-Adjusted Odds Ratios for Prostate Cancer Risk Across Tertiles of Energy-Adjusted Healthy Plant Foods Intakes

Variables	Tertile 1 (lowest)		Tertile 2		Tertile 3 (highest)		P trend
	OR	OR	95% CI	OR	95% CI		
<b>Total healthy plant foods</b>							
Crude	1.0	0.3	0.11 - 0.77	0.12	0.04 - 0.34		<0.001
Model 1	1.0	0.29	0.09 - 0.85	0.12	0.04 - 0.37		0.001
Model 2	1.0	0.34	0.10 - 1.12	0.13	0.04 - 0.48		0.007
Model 3	1.0	0.25	0.06 - 0.98	0.12	0.02 - 0.55		0.02
<b>Total fruits</b>							
Crude	1.0	0.23	0.09 - 0.62	0.11	0.04 - 0.30		<0.001
Model 1	1.0	0.23	0.08 - 0.66	0.12	0.04 - 0.36		0.001
Model 2	1.0	0.23	0.07 - 0.73	0.14	0.03 - 0.52		0.007
Model 4	1.0	0.22	0.05 - 0.90	0.73	0.11 - 4.79		0.07
<b>Total vegetables</b>							
Crude	1.0	0.29	0.11 - 0.76	0.08	0.03 - 0.24		<0.001
Model 1	1.0	0.28	0.10 - 0.80	0.08	0.02 - 0.26		<0.001
Model 2	1.0	0.23	0.07 - 0.74	0.05	0.01 - 0.21		<0.001
Model 5	1.0	0.18	0.04 - 0.73	0.03	0.00 - 0.25		0.003
<b>Whole grains</b>							
Crude	1.0	0.54	0.22 - 1.32	0.4	0.16 - 0.98		0.12
Model 1	1.0	0.47	0.16 - 1.38	0.31	0.10 - 0.93		0.11
Model 2	1.0	0.6	0.18 - 2.00	0.35	0.08 - 1.36		0.31
Model 6	1.0	0.8	0.16 - 4.03	0.88	0.13 - 5.95		0.96
<b>Legumes</b>							
Crude	1.0	0.9	0.37 - 2.17	1.49	0.61 - 3.61		0.49
Model 1	1.0	0.9	0.36 - 2.26	1.24	0.49 - 3.15		0.79
Model 2	1.0	0.65	0.23 - 1.81	1.16	0.39 - 3.44		0.54
Model 7	1.0	0.68	0.18 - 2.59	1.2	0.29 - 4.96		0.72
<b>Nuts-olive</b>							
Crude	1.0	1.1	0.45 - 2.66	0.66	0.27 - 1.61		0.49
Model 1	1.0	1.28	0.50 - 3.25	0.73	0.29 - 1.83		0.48
Model 2	1.0	1.38	0.49 - 3.86	1	0.35 - 2.87		0.78
Model 8	1.0	2.49	0.65 - 9.50	1.62	0.37 - 6.94		0.4
<b>Fresh fruits</b>							
Crude	1.0	0.23	0.09 - 0.62	0.11	0.04 - 0.30		<0.001
Model 1	1.0	0.24	0.08 - 0.70	0.12	0.04 - 0.37		0.001
Model 2	1.0	0.24	0.07 - 0.75	0.14	0.04 - 0.52		0.008
Model 9	1.0	0.25	0.6 - 1.11	0.85	0.13 - 5.64		0.11
<b>Dried fruits</b>							
Crude	1.0	0.44	0.18 - 1.08	0.49	0.20 - 1.19		0.15
Model 1	1.0	0.44	0.14 - 1.40	0.53	0.20 - 1.41		0.32
Model 2	1.0	0.36	0.10 - 1.28	0.52	0.17 - 1.55		0.27
Model 10	1.0	0.95	0.18 - 5.03	2.22	0.48 - 0.15		0.45
<b>Raw vegetables</b>							
Crude	1.0	0.25	0.09 - 0.67	0.06	0.02 - 0.18		<0.001
Model 1	1.0	0.23	0.08 - 0.70	0.05	0.01 - 0.19		<0.001
Model 2	1.0	0.17	0.05 - 0.61	0.02	0.00 - 0.13		<0.001
Model 11	1.0	0.13	0.03 - 0.62	0.01	0.00 - 0.12		0.001

results. One meta-analysis including 56 observational studies, showed that higher adherence to this diet was significantly associated with lower risk of prostate cancer (Schwingshackl and Hoffmann, 2015). Among the studies on the association between different MD scores

Table 3. Continued

Variables	Tertile 1 (lowest)		Tertile 2		Tertile 3 (highest)		P trend
	OR	OR	95% CI	OR	95% CI		
<b>Cooked vegetables</b>							
Crude	1.0	1.1	0.45 - 2.66	1.65	0.68 - 4.00		0.49
Model 1	1.0	1.19	0.47 - 2.99	1.41	0.55 - 3.59		0.76
Model 2	1.0	2.04	0.68 - 6.04	1.76	0.61 - 5.08		0.39
Model 12	1.0	3.76	0.83 - 17.04	2.52	0.52 - 12.18		0.21

P<0.05 was considered as statistically significant; Model 1, Adjusted for age, BMI and energy intake; Model 2, model 1 plus job, education, smoking and physical activity and some drug usage (antihyperlipidemic drugs, antihypertensive drugs, and aspirin); Model 3, model 2 plus less healthy plant foods, and animal foods; Model 4, model 2 plus less healthy plant foods, animal foods, total vegetables, legumes, whole grains, and nuts-olive; Model 5, model 2 plus less healthy plant foods, animal foods, total fruits, legumes, whole grains, and nuts-olive; Model 6, model 2 plus less healthy plant foods, animal foods, total vegetables, total fruits, legumes, and nuts-olive; Model 7, model 2 plus less healthy plant foods, animal foods, total vegetables, total fruits, whole grains, and nuts-olive; Model 8, model 2 plus less healthy plant foods, animal foods, total vegetables, total fruits, legumes, and whole grains; Model 9, model 2 plus less healthy plant foods, animal foods, dried fruits, total vegetables, legumes, whole grains, and nuts-olive; Model 10, model 2 plus less healthy plant foods, animal foods, fresh fruits, total vegetables, legumes, whole grains, and nuts-olive; Model 11, model 2 plus less healthy plant foods, animal foods, cooked vegetables, total fruits, legumes, whole grains, and nuts-olive; Model 12, model 2 plus less healthy plant foods, animal foods, raw vegetables, total fruits, legumes, whole grains, and nuts-olive.

and risk of prostate cancer, some showed no relationship (Bosire et al., 2013; Möller et al., 2013; Ax et al., 2014; Kenfield et al., 2014) and one found inverse (Askari et al., 2016) association. Also, Muller (2009) concluded that Mediterranean dietary pattern was not associated with prostate cancer.

Based on clinical studies, certain bioactive compounds in plant foods, such as vitamin C, vitamin E, lycopene, β-carotene, different phytoestrogens, vitamin A also retinoids may significantly reduce the risk of prostate cancer/ or prostate cancer cell growth (Willis and Wians, 2003). Further, antioxidants compounds such as flavonoids, naringenin, and apigenin in plant foods have been reported to reduce oxidative stress in prostate epithelial cells (Sharma et al., 2014) and to promote DNA repair in prostate cancer cells (Gao et al., 2006).

Our findings indicated that total vegetable intake was also independently associated with less risk of prostate cancer. Several studies have been examined the associations of total vegetable intake on prostate cancer risk, but the findings are inconsistent. Based on cohort studies, total vegetables intake may not exert a protective effect on prostate cancer risk (Meng et al., 2014), but in some case-control studies inverse association (Deneo-Pellegrini et al., 1999; Cohen et al., 2000; Kolonel et al., 2000; McCann et al., 2005; Hardin et al., 2011, Askari et al., 2014; Bashir and Malik, 2015) and in one study no association (Jain et al., 1999) were found.

Our findings on the association of total fruits intake and risk of prostate cancer are in line with cohort studies (Meng et al., 2014), however, case-control studies showed positive (Jain et al., 1999), inverse (Askari et al., 2014;

Bashir and Malik, 2015) or no association (Cohen et al., 2000; Kolonel et al., 2000; Darlington et al., 2007; Hardin et al., 2011). Studies on the association between legumes intake and prostate cancer risk also showed inconsistent results in which some showed preventive (Mills et al., 1989; Schuurman et al., 1998; Jain et al., 1999; Kolonel et al., 2000; Park et al., 2008) and some no effects (Ewings and Bowie, 1996; Key et al., 1997; Deneo-Pellegrini et al., 1999; Cohen et al., 2000; Darlington et al., 2007; Kirsh et al., 2007; Smit et al., 2007; Aune et al., 2009). Besides, in line with our results preventive effect of whole grains on prostate cancer risk was not approved in previous studies, too (Wang et al., 2015).

Few studies have investigated the relationship between nuts-olive consumption and prostate cancer risk. In agreement with our study, a cohort study by Mills (1989), did not find any protective effect of nuts on prostate cancer risk. In contrast, in a cross-sectional ecological study (Hebert et al., 1998), a negative correlation has been reported between prostate cancer mortality and a number of calories supplied by nuts and seed oils. Besides, in a population-based case-control study in Canadian men (Jain et al., 1999), a statistically significant reduction in the risk of prostate cancer have been reported for the group of nuts, legumes, and seeds.

Further analysis also performed on the associations of fruits and vegetable subgroups and prostate cancer risk. Based on our findings, just raw vegetables were associated with less prostate cancer risk, however, in other studies both cooked or raw vegetables were not associated with lower death from prostate cancer (Taborrelli et al., 2016) or lower risk of the disease (Schuurman et al., 1998). In contrast, a review article (Link and Potter, 2004) on the association between raw and cooked vegetables and cancer risk revealed that both raw and cooked vegetable consumption are inversely linked to epithelial cancers, particularly those of the upper gastrointestinal tract, and likely breast cancer; however, these associations seemed to be stronger for raw vegetables than cooked ones. The non-significant but higher risk of prostate cancer with increased consumption of cooked vegetables in our study could be due to inappropriate cooking methods. In most of the Iranian cuisines, vegetables are fried in oil using high temperature which could endanger consumers' health. Increasing of cooking time and temperature could lead to Maillard reaction through which some inflammatory mediators and/or mutagen factors are produced (Mauron, 1990; Vlassara et al., 2002). Besides, cooking vegetables causes an increase in the soluble dietary fiber content of vegetables and tubers and a decrease in insoluble fiber (Khanum et al., 2000). Insoluble fiber excretes carcinogen substances via decreasing fecal transit time and increasing binding capacity (Moore et al., 1998). Furthermore, certain enzymes which naturally exist in some food items such as cruciferous vegetables and garlic have a prominent role in the production of phytochemicals and are easily destroyed by heat (Song and Milner, 2001; Talalay and Fahey, 2001).

Several mechanisms may involve in protective effects of vegetables on prostate cancer. First, Vegetable components such as glucosinolates and isothiocyanates detoxify carcinogens through stimulating cancer cell

apoptosis and activating phase 2 enzyme (Hayes et al., 2008; Ho et al., 2009). Second, carotene content of vegetables reduces cancer cell generation via inhibition of systemic inflammation which is a well-established risk factor for prostate cancer (Sfanos and De Marzo, 2012). All in all, considering the potentially protective effect of total healthy plant foods in relation to prostate cancer need further comprehensive studies.

There are some Strengths for our study: First, to the best of our knowledge, this is the first study to investigate the relationship between healthy plant foods and prostate cancer risk in newly diagnosed prostate cancer patients (which minimize recall bias) on Middle Eastern men population. Second, results were adjusted for most of demographic, lifestyle and dietary confounders involved in prostate cancer pathogenesis, which reduced the residual confounding bias probability. Third, our data were collected from two main hospitals which are referral centers for urology disorders and data were analyzed without any missing.

Our study also had some limitations: Although we used a validated semi-quantitate FFQ to minimize measurement error, using FFQ is one of the problems associated with dietary pattern assessment. Small sample size which might affect our findings is another limitation. Besides, although we selected cases and controls from the same hospitals, at the same time and matched them for BMI and age, the selection bias in case-control studies should not be neglected.

In conclusion, findings of this study have shown that higher consumption of total healthy plant foods was independently associated with lower risk of prostate cancer. We also found that total vegetables also raw vegetable intakes were independently associated with lower prostate cancer risk. To evaluate the associations of other subgroups of healthy plant foods with prostate cancer risk, further studies are needed. Taken together, the results of this study suggest that a diet rich in total healthy plant foods and especially total or raw vegetable may protect against prostate cancer.

#### *Conflict of interest*

The authors declare no conflict of interest.

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