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Fruit and Vegetable Intake in Relation to Lower Urinary Tract Symptoms and Erectile Dysfunction Among Southern Chinese Elderly Men

A 4-Year Prospective Study of Mr OS Hong Kong

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Abstract: The role of fruit and vegetable (FV) intake in relation to prostate health remains inconclusive. This 4-year longitudinal study aims to explore the association of FV intake and the development of lower urinary tract symptoms (LUTS), a cluster of chronic urinary symptoms occurring in bladder, prostate and urethra, incidence of symptomatic benign prostatic hyperplasia (BPH) and erectile dysfunction (ED) in Chinese elderly men.

Data were obtained from a 4 years longitudinal study (Mr OS Hong Kong, the largest prospective study on bone health in Chinese elderly). Two thousand Chinese men aged 65 years and older were recruited from the local community, of whom 1998 (99.9%) at baseline and 1564 (78.2%) at 4-year follow-up reported data on LUTS, which were evaluated by a validated International Prostate Symptoms Scale (IPSS). Erectile function was evaluated by the International Index of Erectile Dysfunction-5 (IIEF-5) questionnaires at 2- (n=386) and 4-year (n=475) follow-ups. Dietary intake was assessed using a validated food frequency questionnaire at baseline. Analysis was conducted using multivariate linear and logistic regression.

For total FV and most of their subclasses, moderate consumption had the lowest mean changes of LUTS; we thus applied the moderate levels as the reference in the regression models. The high levels of total

FV intake (>350 g/1000 kcal/day) were significantly associated with reduced IPSS by scores of -1.174 ± 0.459 (or -17.3% of basal IPSS, $P = 0.011$) relative to the moderate groups (250–350 g/1000 kcal/day). FV consumption had no significant association with the score change of ED or the odds of sexual activities at 4-year (all $P > 0.05$). High intake of dark and leafy vegetables (>50 g/1000 kcal/day) significantly reduced the risk of LUTS progression by 37.2% [odds ratio (OR) (95% confidence interval, 95% CI): 0.628 (0.466~0.848), $P = 0.002$] or risk of symptomatic BPH by 34.3% [OR (95% CI): 0.657 (0.442-0.976), $P = 0.038$] after 4 years compared with the moderate group (25–50 g/1000 kcal/day).

Adequate FV intakes, especially dark and leafy vegetables, were associated with improved LUTS among Chinese elderly men, but lack an association with ED and sexuality.

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Abbreviations: BPH = Benign prostatic hyperplasia, ED = Erectile dysfunction, FFQ = Food frequency questionnaire, FV = Fruit and vegetable, GLM = General Linear Model, IIEF-5 = International Index of Erectile Function, IPSS = International Prostatic Symptoms Scale, LUTS = Lower urinary tract symptoms, OR = Odds ratio, PASE = Physical Activity Scale of the Elderly.

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INTRODUCTION

Lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH) are highly prevalent conditions among elderly men associated with an impaired quality of life and an increased risk of sexual dysfunction and mortality.¹ LUTS represents a cluster of chronic urinary problems occurring in more than half of men in their 60s and increase with age.² BPH is the principal underlying cause of LUTS.³ An estimated 612 million men will have BPH globally by 2018.⁴ Studies have shown a strong correlation between sexual dysfunction and the severity of LUTS.⁵ Pharmacological treatments are available for management of symptoms but can be expensive and may be associated with adverse events⁶; lifestyle modifications therefore become the primary treatment strategies for improvement of prostate health due to its noninvasive and modifiable properties.⁷

Fruits and vegetable (FV) contain high levels of antioxidants, polyphenols, vitamins, minerals, and fibers, and are essential components of a healthy diet and beneficial for a range of chronic conditions. Evidence from basic studies suggested that FV intake may beneficially influence the disorders underlying BPH via inhibiting inflammation and oxidative damage, altering the hormonal or growth-regulatory factors to inhibit cellular proliferation,⁸ or modulating sympathetic nervous system and subsequently affect prostate

smooth muscle tone.⁹ Thus, FV consumption may offer feasible therapeutic targets to delay the disease onset, prevent the progression, or attenuate the severity of LUTS.

Although LUTS/BPH is a common condition in elderly men, dietary factors especially FV intake on prostate health, remain largely undefined and inconsistent. Most of previous studies were conducted among Caucasian populations and majority of reports have been based on cross-sectional or hospital-based case-control studies. Evidence from prospective cohort studies was limited. It is unclear whether various subclasses of FV may have a different impact on prostate health.

In this study, we used data from study by Mr OS,¹⁰ a longitudinal study among Chinese elderly men to examine whether dietary FV intake and its subclasses affect the development and progression of LUTS, risk of BPH, and erectile function. The potential mechanisms related to dietary vitamin C, fiber, and isoflavones were also examined. We hypothesize that dietary FV intakes improve prostate health of Chinese elderly men.

METHODS

Participants

This was a 4-year prospective cohort study (Mr Os Hong Kong) among 2000 Chinese men aged 65 years and older. The details of subjects' recruitment have been described previously.¹⁰ In brief, participants who were able to walk independently were recruited on voluntary basis from local community of Hong Kong (South China) in a health survey between 2001 and 2003. Stratified sampling was adopted in order to have around 33% of subjects in each of the following age groups: 65 to 69; 70 to 74; and ≥ 75 years. Recruitment notices were placed in housing estates and community centers for the elderly. Subjects were invited to the research center for interviews and physical examination. The present study was conducted according to the guidelines of the Declaration of Helsinki, and all procedures involving human subjects were approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong. Written informed consent was obtained from all subjects.

Data Collection

The cohort study initially collected information related to risk factors associated with osteoporosis (bone mineral density and fracture incidence) and later expanded to include measurements of LUTS and sexuality (the details please see the following information on Erectile Function and Sexual Activity). Subjects were interviewed using structured and standardized questionnaires or examination form covering the following aspects: socio-demographic characteristics (such as age, education, income, marital status, etc.), medical history [such as fracture, depression, cardiovascular diseases (CVDs), and cancers, etc.] and medications, lifestyle factors including cigarette smoking, alcohol consumption, dietary intake, and physical activity (for details please see the following paragraph of "Other covariates").

Fruit and Vegetable Consumption

Dietary intake at baseline was assessed using a 289-item validated semi-quantitative food frequency questionnaire (FFQ).¹¹ The food consumption and nutrients intake were calculated on the basis of food composition database from McCance and Widdowson¹² and the Chinese Food Composition

Table.¹³ Each subject was asked by a trained interviewer to report the frequency and the usual amount of consumption of each food item over the past year. A series of food photographs with individual food portions were provided to participants for estimation of portion sizes. The participants were asked to indicate how often, on average, they consumed each food, with 9 possible response categories ranging from "never" to "every day." The FFQ consisted of 8 categories: bread/pasta/rice; vegetables; fruits; meat/fish/eggs; beverages; dimsum/snacks; soups; and oil/salt/sauces.

Fruit intake was assessed by the inclusion of fresh fruit, cooked or canned fruit, dried fruit and fruit juices based on 28 fruit items, such as apple, apricot, banana, cherry, grape, raisins, lemon, lychee, logan, mango, melon, papaya, pear, plum, peach, pineapple, prunes, orange, persimmon, watermelon, kiwi, pomelo, strawberry, carambola. Citrus fruit intake in our study included intake of grape fruit, lemon, orange, and pomelo.

Total vegetable intakes were assessed by the inclusion of green vegetables, root vegetables, pulses, salad vegetables, and mixed-vegetable dishes based on 64 vegetable items, such as green leafy vegetables, corn, onion, cucumber, pepper, asparagus, egg-plant, bamboo shoot, Chinese radish and chives, Chinese water chestnut, lotus root, celery, leeks, peppers, lily, pumpkin, taro, tomatoes, and legumes. Subclasses of vegetable were further assessed for cruciferous, dark and leafy vegetables, legumes, soy, and tomatoes. Cruciferous group in our study included broccoli, sauerkraut, coleslaw, cooked cabbage, cauliflower, Brussels sprouts, and kale.

Lower Urinary Tract Symptoms (LUTS) and Symptomatic BPH

The presence and severity of LUTS were assessed using a validated Chinese version of the International Prostatic Symptoms Scale (IPSS)^{14,15} at baseline and at the end of 4-year follow-up by an interviewer-administered mode. The IPSS is an 8-item questionnaire including 7 symptom questions (nocturia, frequency, urgency, intermittency, weak stream, incomplete emptying, and straining) and 1 global quality of life question. For the 7 symptoms during the last month, each has a score from 1 to 5 for a total of maximum 35 points. According to the IPSS,¹⁴ men were defined as severe LUTS if they scored ≥ 20 ; moderate LUTS if they scored 8~19, and mild LUTS with a score ≤ 7 . The overall and 2 components (voiding and storage symptoms) of the IPSS were reported separately as outcomes. Voiding symptoms included 4 items such as incomplete bladder emptying, intermittency, weak urinary stream, and hesitancy, while storage symptoms included 3 questions on urinary frequency, urgency, and nocturia.

The analyses of progression of LUTS were based on the absolute score change of IPSS at 4-year follow-up from baseline. The progression of overall LUTS was defined as IPSS increase ≥ 3 .¹⁶ For voiding and storage symptoms, the increase of score ≥ 2 indicated progression over time.¹⁷ Symptomatic BPH incidence was assessed over 4 years and was defined as either the new self-report of BPH or receiving pharmaceutical or surgical treatment on prostate or the second report of an IPSS of 15 or higher.¹⁸

Erectile Function and Sexual Activity

Erectile dysfunction (ED) was measured by an abridged 5-item version of the International Index of Erectile Function (IIEF-5) questionnaire.¹⁹ This is a validated and sensitive indicator of changes in ED and treatment outcomes and was

use to evaluate symptoms at 2- and 4-year follow-up. The total IIEF-5 score was calculated by totaling the response to all 5 questions. For the assessment of sexual activity at 4 years, all subjects were asked whether they had sexual intercourse in the previous 6 months.

Other Covariates

Cigarette smoking and alcohol consumption were investigated on the basis of self-report using validated methods.²⁰ Information on the duration and level of past and current use of cigarettes, cigars, and pipes was obtained. For current smokers, the number of cigarettes smoked per day over the previous 12 months was collected. For alcohol consumption, subjects were asked to report their daily frequency of intake of alcohol and other beverages in portion sizes. One standard drink was defined as 1 unit of alcohol, which is equal to 10 g of alcohol. For beer, 1 standard drink equals to 1 can of beer (330 mL), 1 glass of wine (100 mL), or 1 shot of spirit or liquor (30 mL).

Anthropometric measures were conducted at the baseline and 4-year follow-ups by standardized protocol. Body weight and height were measured using the Physician Balance Beam Scale (Healthometer, Alsip, IL, with an accuracy of 0.1 kg) and the Holtain Harpenden stadiometer (Holtain, Crosswell, UK, with an accuracy of 0.1 cm), respectively. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2).

A validated 12-item Physical Activity Scale of the Elderly (PASE)²¹ was used to assess the level of physical activity. The PASE is composed of self-reported occupational, household, and leisure items over a 1-week period. It uses frequency, duration, and intensity level of activity to determine the score, with higher scores indicating greater physical activity level. Depressive symptoms were assessed using a validated 15-item Chinese version of the Geriatric Depression Scale (GDS),²² with depression being defined as a score of 8 or more.

Posteriori Sample Size Estimation

The posteriori sample size is estimated on the basis of the primary outcome of our analysis—the 4-year score change of IPSS. With a conservative IPSS change of 1.0 (the current change of standard deviation of 6.25), assuming 80% power and a convention assumption of α level 0.05, the posteriori sample size in our study is 1228.

Statistical Analysis

Statistical analyses were performed using the statistical package SPSS 19.0 (SPSS Inc., Chicago, IL). α level of 5% was used as the level of significance. We evaluated the associations of FV intakes and their subcategories in relation to the score change of IPSS and ED, the progression of LUTS, and the incidence of symptomatic BPH after 4 years by either General Linear Models (GLMs) or logistic regression models. Adjusted variables were age, education, cigarette smoking (no, current, ever), coffee (mL/day), alcohol (g/day), use of anti-hypertensive medication (yes or no), BMI, GDS score, medical history of fracture, hypertension, stroke, diabetes, heart attack and any kinds of cancers (yes or no), PASE total score, and dietary energy (kcal/day). Dietary fruit and/or vegetable intakes and subclasses were adjusted for total energy using multivariate nutrient density model²³ and then categorized as low, moderate, and high levels on the basis of conventional cut-points,^{24–26} which were further confirmed by the curve estimation of polynomial regression models (data not shown). For total FV

intakes and their subclasses, there were no significant differences between low and moderate consumption in the changes of IPSS or other outcomes. In addition, several comparisons indicated that compared with moderate group (not low consumption group), the high consumption group had a significant reduction of IPSS or reduced risk of progression of LUTS or incidence of symptomatic BPH. We thus applied the moderate level as the reference in regression models. The moderate levels (g/1000 kcal/day) of various FV were defined as 250 to 350 for total FV; 100 to 150 for total vegetables; 25 to 50 for dark and leafy vegetables; 15 to 30 for soy foods; 7.5 to 15 for crucifers, 2.5 to 10 for tomatoes; 100 to 150 for total fruits; and 15 to 30 for citrus fruits.

GLMs were used to compare the adjusted mean changes in scores of PSS and ED at 4-year follow-up across low, moderate, and high intakes of FV groups. Separate models were created for voiding and storage symptoms of LUTS, respectively. Subjects with bladder or prostate cancers, or any medical or surgical treatment for prostate were excluded for the analyses. A total of 1667 men at baseline and 1301 at 4-year follow-up were included in the analysis.

Binary logistic regression was performed to calculate odds ratios (ORs) and 95% confidence interval (95% CI) for dichotomous outcomes of progression of LUTS and incidence of symptomatic BPH across low, moderate, and high FV intakes after controlling for above confounders within 4 years. Subjects with bladder or prostate cancers, LUTS >15 at baseline, or no self-reported BPH were excluded for the analysis. Thus, 1388 and 1275 men were included in the analysis for LUTS progression and incidence of symptomatic BPH, respectively.

To investigate the possible mechanisms of dietary vitamin C, fiber, and isoflavones relating to the associations of FV and LUTS, we conducted exploratory analysis to test whether the association of score changes of LUTS and FV was modified by dietary levels of vitamin C, fiber, and isoflavones intake in univariate models.

RESULTS

Among the 2000 recruited elderly men, 1998 (99.9%) at baseline and 1564 (78.2%) at 4-year follow-up reported data on LUTS. Baseline characteristics are described in Table 1. The mean age of participants was 72.4 ± 5.0 years. Their daily FV intakes were 132.2 ± 87.9 and 118.4 ± 74.8 g/1000 kcal, respectively. Of 1998 men, 41.0% suffered from moderate to severe LUTS. The progression of LUTS occurred in 485 (31.0%) participants after 4 years. Among the subjects who attended the 4-year follow-up ($n = 1564$), 69.4% ($n = 1086$) had no sexual intercourse over the past 6 months and 475 men answered questions on IIEF-5.

The adjusted mean changes in scores of overall, voiding, and storage symptoms by low, moderate, and high fruits or vegetables intake are indicated in Table 2 and Supplemental Figures 1 to 3, <http://links.lww.com/MD/A646> (see figures, Supplemental Figure 1–3, <http://links.lww.com/MD/A646>, which demonstrates the adjusted mean changes in scores of overall, voiding, and storage symptoms by low, moderate, and high FV intakes). Compared with the moderate group, high levels of total FV intake (>350 g/1000 kcal/day) significantly reduced overall, storage, and voiding symptoms by scores of -1.174 ± 0.459 (-17.3% of basal PSS, $P = 0.011$), -0.448 ± 0.230 ($P = 0.039$), and -0.312 ± 0.190 ($P = 0.042$), respectively. High intake of fruit (>150 g/1000 kcal/day) and total vegetable (>150 g/1000 kcal/day), especially dark and leafy vegetable

TABLE 1. Baseline and Follow-up Characteristics of Participants

Baseline Characteristics	Mean \pm SD or n (%)
n	1998
Age (yrs)	72.4 \pm 5.0
Education (university or above %)	271 (13.6)
Married or living together (%)	1760 (88.0)
BMI (kg/m ²)	23.4 \pm 3.1
PASE score at baseline	97.3 \pm 50.3
Comorbidities (%)	
Diabetes	293 (14.7)
Stroke	109 (5.5)
Hypertension	836 (41.8)
Bladder cancer	13 (0.7)
Prostate cancer	16 (0.8)
Dietary intake	
Total energy (kcal/d)	2099 \pm 587
Total fruits and vegetables (g/1000 kcal/d)	272.7 \pm 131.7
Fruits (g/1000 kcal/d)	132.2 \pm 87.9
Vegetables (g/1000 kcal/d)	118.4 \pm 74.8
Dark green vegetables (g/1000 kcal/d)	44.1 \pm 35.7
Soy (g/1000 kcal/d)	23.3 \pm 33.2
Tomatoes (g/1000 kcal/d)	9.9 \pm 15.4
Coffee (mL/d)	30.5 \pm 78.0
Alcohol intake (%)	576 (28.9)
Fiber (g/d)	9.66 \pm 5.23
Vitamin C (mg/d)	160.0 \pm 112.7
Isoflavones (mg/d)	15.6 \pm 23.1
IPSS at baseline	
Overall IPSS score	7.8 \pm 6.9
IPSS score 8–19 (moderate LUTS, %)	666 (33.3)
IPSS score \geq 20 (severe LUTS, %)	154 (7.7)
Prostate medication at baseline (%)	305 (15.3)
Self-reported BPH incidence at 4 yrs (%)	681 (34.1)
LUTS progression at 4 yrs (IPSS change \geq 3, %, n = 1563) (%)	485 (31.0)
Sexuality and erectile dysfunction	
ED score at 2 yrs (n = 372)	17.0 \pm 4.2
Sexuality in past 6 mths at 2 yrs (n = 1174) (%)	386 (32.9)

According to the IPSS, men were defined as severe LUTS if they scored \geq 20; moderate LUTS if they scored 8–19, and mild LUTS with a score \leq 7. The analyses of progression of LUTS were based on the absolute score change of IPSS at 4-year follow-up from baseline. The progression of overall LUTS was defined as IPSS increase \geq 3. ED was measured by an abridged 5-item version of the International Index of Erectile Function (IIEF-5) questionnaire.

BMI = body mass index, BPH = Benign Prostatic Hyperplasia, ED = erectile dysfunction, IPSS = International Prostate Symptoms Scale, LUTS = lower urinary tract symptoms, PASE = Physical Activity Scale for the Elderly.

(>50 g/1000 kcal/day) and tomatoes (>10 g/1000 kcal/day), were significantly associated with decreased symptoms relative to moderate groups, with mean score changes for overall IPSS by -1.039 ± 0.451 ($P = 0.021$), -1.0 ± 0.479 ($P = 0.037$), -1.041 ± 0.375 ($P = 0.006$), and -0.944 ± 0.391 ($P = 0.016$), respectively. However, soy foods, cruciferous vegetables, and citrus fruits intake were not significantly associated with the changes of LUTS. Among 475 men who had sex in previous 6

months at 4-year follow-up, FV consumption and their botanical subgroups had no significant association with the score change of ED, as well as the odds of sexuality at 4 years (Table 3).

For the associations of FV intake and progression of LUTS, the multivariate logistic regression models (Table 4) indicated that compared with the moderate group, high intake of dark and leafy vegetables (>50 g/1000 kcal/day) significantly reduced the risk of LUTS progression by 37.2% [OR (95% CI): 0.628 (0.466–0.848), $P = 0.002$] over 4 years. Total FV consumption was not significantly associated with the overall LUTS progression, but marginal significance was observed in storage symptoms with high FV intake ($P = 0.051$) after adjusting for potential covariates.

Table 5 summarizes the odds and 95% CI of incidence of symptomatic BPH at 4-year follow-up. After adjusting for potential covariates, the risk of BPH significantly decreased by 34.3% [OR (95% CI): 0.657 (0.442–0.976), $P = 0.038$] with high consumption of dark and leafy vegetables, respectively, compared with moderate group.

We further examined whether the associations of FV intake and the changes of LUTS or the odds of LUTS progression could be modified by dietary vitamin C, isoflavones, or fiber intakes. No statistically significant effect modification by these micronutrients was observed ($P = 0.085$ – 0.527) in regression models (data not shown).

DISCUSSION

Summary and Implications

In this prospective cohort study, men who consumed adequate FV (>350 g/1000 kcal/day), especially dark and leafy vegetables (>50 g/1000 kcal/day), were more likely to have reduced symptoms or progression of LUTS over 4-year follow-up. To our knowledge, this is the first longitudinal study undertaken in Chinese elderly men to temporally assess the role of FV intake on prostate health. Because LUTS/BPH represents the most common urologic disease among elderly men, even the modest improvement of symptoms (-1.76 points or -17.3% basal score reduction of LUTS) may have important relevance on a public health level.

Age is the primary risk factor for LUTS and BPH. The Olmsted county study, which followed for 12 years in 2115 men aged 40 to 79 years, observed an average increase of IPSS by 0.18 point per year.²⁷ Another 15-year longitudinal community-based study in Japanese men reported an annual change (standard deviation) of IPSS by 0.11 (0.40).²⁸ Our findings in Chinese elderly men with FV intake above 350 g/1000 kcal/day reported an annual score reduction of 0.44 point (1.76/4), implying that adequate FV intake may overtly counteract the aging-exacerbated LUTS with effect size of 2 to 4-folds than age-related score increase.

The Chinese Dietary Guideline 2007 recommended daily consumption of 300 to 500 g vegetables and 200 to 400 g fruits.²⁹ Our findings in Chinese elderly indicated that quite a portion of men (39.5%) had fruit intake less than 200 g/day, and around two-thirds (62.6%) had vegetable intake less than 300 g/day. FV are important components of a healthy diet. Our data suggested a room for improvement of FV consumption in Chinese elderly.

Comparison With Other Studies

We observed that men who consumed high amounts of FV, especially dark and leafy vegetables, were more likely to be

TABLE 2. Adjusted Mean of Absolute Changes of IPSS (Including Overall, Storage, and Voiding Symptoms) at 4-year Follow-up by Low, Moderate, and High Fruit and/or Vegetable Intake

	Overall LUTS Symptoms Change			Storage Symptoms Change			Voiding Symptoms Change		
	No	Adjusted Mean ± SE	P	Adjusted Mean ± SE	Mean Difference ± SE	P	Adjusted Mean ± SE	Mean Difference ± SE	P
Total fruits and vegetables (g/1000 kcal/d)			0.034			0.113			0.114
<250	576	1.026 ± 0.245	0.655	0.123 ± 0.150	0.103 ± 0.243	0.671	0.534 ± 0.124	-0.275 ± 0.201	0.172
250–350	333	0.844 ± 0.320	Ref.	0.020 ± 0.188	-0.572 ± 0.277	Ref.	0.809 ± 0.155	-0.497 ± 0.244	Ref.
>350	233	-0.147 ± 0.382	0.011	-0.448 ± 0.230		0.039	0.312 ± 0.190		0.042
Vegetables (g/1000 kcal/d)									
Total vegetables									
<100	551	0.783 ± 0.249	0.348	-0.017 ± 0.154	0.181	0.346	0.500 ± 0.127	0.165	0.161
100–150	303	1.175 ± 0.333	Ref.	0.219 ± 0.196	-0.236 ± 0.251	Ref.	0.790 ± 0.162	-0.290 ± 0.207	Ref.
>150	288	0.175 ± 0.345	0.037	-0.306 ± 0.206	-0.524 ± 0.284	0.065	0.471 ± 0.170	-0.320 ± 0.234	0.173
Dark and leafy vegetables			0.009						0.093
<25	508	0.320 ± 0.227	0.440	0.406 ± 0.138	-0.362 ± 0.196	0.066	-0.144 ± 0.168	-0.382 ± 0.238	0.109
25–50	500	1.069 ± 0.227	Ref.	0.827 ± 0.138	-0.480 ± 0.229	Ref.	0.237 ± 0.167	-0.556 ± 0.277	Ref.
>50	293	0.027 ± 0.299	0.006	0.347 ± 0.183		0.036	-0.319 ± 0.221		0.045
Soy foods			0.698			0.328			0.523
<15	632	0.418 ± 0.203	0.460	0.508 ± 0.124	-0.268 ± 0.204	0.191	-0.090 ± 0.150	0.021 ± 0.247	0.933
15–30	370	0.665 ± 0.265	Ref.	0.776 ± 0.162	-0.314 ± 0.241	Ref.	-0.110 ± 0.196		Ref.
>30	307	0.652 ± 0.293	0.975	0.462 ± 0.178		0.192	0.183 ± 0.215	0.293 ± 0.291	0.314
Crucifers			0.324			0.693			0.181
<7.5	622	0.677 ± 0.204	0.102	0.605 ± 0.125	0.145 ± 0.204	0.477	0.073 ± 0.151	0.407 ± 0.246	0.099
7.5–15	374	0.130 ± 0.264	Ref.	0.495 ± 0.161	0.187 ± 0.238	Ref.	-0.334 ± 0.194		Ref.
>15	313	0.768 ± 0.288	0.103	0.646 ± 0.176		0.433	0.123 ± 0.212	0.456 ± 0.288	0.113
Tomatoes			0.089			0.836			0.072
<2.5	368	0.816 ± 0.285	0.280	0.480 ± 0.179	0.108 ± 0.217	0.618	0.367 ± 0.217	-0.430 ± 0.262	0.101
2.5–10	749	0.441 ± 0.197	Ref.	0.588 ± 0.122	0.032 ± 0.207	Ref.	-0.064 ± 0.148		Ref.
>10	445	-0.128 ± 0.260	0.016	0.612 ± 0.166		0.876	-0.314 ± 0.201	-0.681 ± 0.299	0.023
Fruits (g/1000 kcal/d)									
Total fruits			0.048			0.177			0.077
≤100	469	0.838 ± 0.273	0.490	-0.018 ± 0.167	-0.207 ± 0.250	0.407	0.512 ± 0.138	-0.322 ± 0.206	0.119
100–150	368	1.125 ± 0.304	Ref.	0.189 ± 0.182	-0.500 ± 0.269	Ref.	0.834 ± 0.150	-0.486 ± 0.222	Ref.
>150	303	0.085 ± 0.336	0.021	-0.310 ± 0.200		0.063	0.348 ± 0.165		0.029
Citrus fruits			0.856			0.790			0.838
<15	628	0.806 ± 0.234	0.756	0.558 ± 0.116	0.034 ± 0.201	0.864	0.004 ± 0.141	0.019 ± 0.243	0.937
15–30	324	0.681 ± 0.325	Ref.	0.524 ± 0.163	0.178 ± 0.269	Ref.	-0.016 ± 0.196		Ref.
>30	191	0.544 ± 0.429	0.799	0.702 ± 0.213		0.507	-0.170 ± 0.257	-0.155 ± 0.325	0.634

Data were analyzed by General Linear Models and results were expressed as mean ± SE standard error; Subjects with no bladder or prostate cancer, no medical treatment on prostate were included in the analyses. The adjusted variables include age, educational level, cigarette smoking (no, current, ever), coffee (mL/d), alcohol (g/d), use of anti-hypertensive medication (yes or no), body mass index, Geriatric Depression Scale score, history of fracture, hypertension, stroke, diabetes, heart attack and any kinds of cancers (yes or no), PASE (Physical Activity Scale for the Elderly) total score, and dietary energy (kcal/d). Citrus fruit intake in our study included intake of grape fruit, lemon, orange, and pomelo. Cruciferous vegetables included broccoli, sauerkraut, coleslaw, cooked cabbage, cauliflower, Brussels sprouts, and kale. FV = fruits and vegetables; IPSS = International Prostate Symptoms Scale; LUTS = lower urinary track symptoms; Ref. = Reference; SE = standard error.

TABLE 3. Adjusted Means of Score Change of Erectile Dysfunction and Odds Ratio (OR) of Sexuality at 4-year Follow-up by Low, Moderate, and High Levels of Fruit and/or Vegetable Intakes

	Erectile Dysfunction Score Change				Sexuality at 4-yr Follow-up		
	n	Adjusted Mean \pm SE	Mean Difference \pm SE	P	n	Adjusted OR (95% CI)	P
Total fruits and vegetables (g/1000 kcal/d)				0.862			
<250	98	-0.239 \pm 0.381	0.008 \pm 0.769	0.992	635	1.166 (0.856~1.586)	0.330
250-350	59	-0.895 \pm 0.483		Ref.	403	1	Ref.
>350	38	-0.888 \pm 0.610	0.656 \pm 0.635	0.303	268	0.906 (0.620~1.323)	0.609
Vegetables (g/1000 kcal/d)							
Total vegetables				0.517			
<100	95	-0.642 \pm 0.389	-0.408 \pm 0.650	0.532	604	0.961 (0.716~1.291)	0.793
100-150	56	-0.235 \pm 0.497		Ref.	364	1	Ref.
>150	44	0.814 \pm 0.571	-0.579 \pm 0.749	0.441	338	0.858 (0.612-1.201)	0.372
Dark and leafy vegetables				0.495			
<25	82	-0.966 \pm 0.423	-0.793 \pm 0.631	0.211	506	0.832 (0.629~1.100)	0.197
25-50	72	-0.172 \pm 0.437		Ref.	500	1	Ref.
>50	40	-0.586 \pm 0.592	-0.413 \pm 0.726	0.570	293	0.803 (0.577-1.118)	0.194
Soy foods				0.877			
<15	79	-0.729 \pm 0.413	-0.274 \pm 0.655	0.676	632	0.753 (0.563~1.006)	0.055
15-30	56	-0.455 \pm 0.495		Ref.	368	1	Ref.
>30	60	-0.448 \pm 0.473	0.007 \pm 0.691	0.992	307	0.776 (0.551~1.093)	0.146
Crucififers				0.345			Ref.
<7.5	82	-1.006 \pm 0.410	0.621 \pm 0.624	0.624	619	0.898 (0.673~1.199)	0.466
7.5-15	68	-0.385 \pm 0.450		Ref.	375	1	Ref.
>15	45	-0.030 \pm 0.555	0.345 \pm 0.722	0.284	313	0.794 (0.565~1.114)	0.182
Tomatoes				0.614			
<2.5	49	0.155 \pm 0.523	1.001 \pm 0.642	0.121	306	0.964 (0.707~1.314)	0.815
2.5-10	100	-0.845 \pm 0.346		Ref.	641	1	Ref.
>10	46	-0.719 \pm 0.545	0.127 \pm 0.665	0.849	359	0.948 (0.665~1.352)	0.769
Total fruits (g/1000 kcal/d)				0.178			
\leq 100	78	-0.541 \pm 0.426	-0.495 \pm 0.642	0.441	518	0.813 (0.606-1.089)	0.165
100-150	68	-0.045 \pm 0.449		Ref.	430	1	Ref.
>150	49	-1.321 \pm 0.520	-1.276 \pm 0.684	0.064	356	0.882 (0.644-1.208)	0.434

Data were analyzed by general linear models for the changes of erectile dysfunction scores and logistic regression models for sexuality at 4-yr follow-up. Subjects who had sexuality in previous 6 months were included in data analysis. Erectile dysfunction (ED) was measured by an abridged 5-item version of the International Index of Erectile Function (IIEF-5) questionnaire. Adjusted variables included age, education, smoking status; intakes of coffee (mL/day), tea (mL/week) and alcohol (g/day), GDS (Geriatric Depression Scale) Score, comorbidities (yes or no) including fracture, diabetes, history of cardiovascular diseases (yes or no) including stroke, heart attack, angina, and coronary heart failure; total energy; dietary fat intake, PASE (Physical activity scale for the elderly) total score; marriage status (yes or no).

Citrus fruit intake in our study included intake of grape fruit, lemon, orange, and pomelo. Cruciferous vegetables included broccoli, sauerkraut, coleslaw, cooked cabbage, cauliflower, Brussels sprouts, and kale.

IPSS = International Prostate Symptoms Scale; LUTS = lower urinary track symptoms; Ref. = Reference; SE = standard error.

associated with reduced symptoms or LUTS progression. Previous epidemiological studies examined the relationship of FV consumption and the risk of BPH reported conflicting findings and limited studies investigated the association with the changes of LUTS. Several small case-control studies³⁰⁻³² and a cross-sectional study³³ found that fruit or/and vegetable consumption was inversely associated with the risk of BPH. However, findings from prospective studies were inconsistent. An early cohort study³⁴ among 6581 Japanese-American men in Hawaii reported no association of FV consumption and the incidence of BPH. A US cohort study reported an 11% reduction (OR = 0.89, 95% CI 0.80-0.99) in BPH prevalence when comparing the lowest and highest quintiles of vegetable intake,¹⁸ whereas fruit intake was not. The Prostate Cancer

Prevention Trial that included 4770 placebo-arm participants reported a significantly lower risk (hazard ratio = 0.68) of BPH over 7 years among men who consumed at least 4 servings of vegetables daily.³⁵ The discrepancies might be attributed to the differences in ethnicity of participants, study design, definition of BPH endpoints, duration of follow-up, dietary assessment methods, or unadjusted confounding factors.

Results Explanation

Our study indicated that a high intake of dark and leafy vegetables was associated with both reduced symptoms, risk of LUTS progression, and incidence of BPH. Dark and leafy vegetables are rich in beta-carotene, lutein, or vitamin C relative to general vegetables that may be beneficial to prostate health.

TABLE 4. Odds Ratio (OR) and 95% Confidence Interval (CI) of Consumption of Fruits and/or Vegetables With Progression of Overall Lower Urinary Track Symptoms, Voiding, and Storage Symptoms at 4-yr Follow-up by Multivariable Logistic Regression

	Overall LUTS			Voiding Symptoms			Storage Symptoms		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Total fruits and vegetables (g/1000 kcal/d)									
<250	1.031	0.802~1.327	0.811	1.040	0.796~1.359	0.773	0.958	0.742~1.238	0.744
250–350	1		Ref.	1		Ref.	1		Ref.
>350	0.835	0.608~1.1456	0.262	0.925	0.663~1.291	0.647	0.723	0.522~1.001	0.051
Vegetables (g/1000 kcal/d)									
Total vegetables									
<100	0.942	0.726~1.233	0.654	0.875	0.666~1.149	0.336	0.876	0.673~1.141	0.327
100–150	1		Ref.	1		Ref.	1		Ref.
>150	0.823	0.610~1.111	0.204	0.782	0.571~1.073	0.127	0.757	0.559~1.027	0.074
Dark and leafy vegetables									
<25	0.684	0.534~1.278	0.203	0.698	0.510~1.255	0.085	0.847	0.679~1.124	0.294
25–50	1		Ref.	1		Ref.	1		Ref.
>50	0.628	0.466~0.848	0.002	0.647	0.497~0.842	0.001	0.666	0.488~0.907	0.010
Soy foods									
<15	1.153	0.888~1.498	0.285	1.073	0.814~1.416	0.616	0.942	0.724~1.226	0.656
15–30	1		Ref.	1		Ref.	1		Ref.
>30	1.159	0.851~1.579	0.350	1.218	0.881~1.684	0.232	0.944	0.690~1.290	0.716
Crucififers									
<7.5	1.245	0.956~1.621	0.104	1.228	0.928~1.626	0.151	1.262	0.967~1.647	0.187
7.5–15	1		Ref.	1		Ref.	1		Ref.
>15	1.443	1.065~1.955	0.018	1.478	1.073~2.036	0.017	1.035	0.755~1.419	0.829
Tomatoes									
<2.5	0.917	0.698~1.204	0.534	0.707	0.534~0.936	0.015	1.017	0.806~1.423	0.636
2.5–10	1		Ref.	1		Ref.	1		Ref.
>10	0.878	0.644~1.198	0.412	0.638	0.461~0.884	0.007	1.127	0.819~1.550	0.462
Fruits (g/1000 kcal/d)									
Total fruits									
≤100	0.916	0.706~1.187	0.505	1.068	0.811~1.407	0.639	1.092	0.836~1.425	0.518
100–160	1		Ref.	1		Ref.	1		Ref.
>160	0.813	0.611~1.083	0.157	0.958	0.707~1.298	0.782	0.952	0.710~1.275	0.739
Citrus fruits									
<15	0.869	0.669~1.127	0.290	0.849	0.646~1.116	0.241	0.978	0.753~1.270	0.866
15–30	1		Ref.	1		Ref.	1		Ref.
>30	1.060	0.775~1.449	0.716	1.021	0.735~1.418	0.901	0.978	0.710~1.347	0.893

Data were analyzed by multivariate logistic regression models. The progression of overall LUTS was defined as IPSS (International Prostate Symptoms Score) =3 from baseline. For voiding and storage symptoms, the increase of score =2 indicated progression over time. Adjusted variables included age, education, smoking status; intakes of coffee (mL/day), tea (mL/week) and alcohol (g/day), GDS (Geriatric Depression Scale) Score, comorbidities (yes or no) including fracture, diabetes, history of cardiovascular diseases (yes or no) including stroke, heart attack, angina, and coronary heart failure; total energy; dietary fat intake, PASE (Physical activity scale for the elderly) total score, etc. Citrus fruit intake in our study included intake of grape fruit, lemon, orange, and pomelo. Cruciferous vegetables included broccoli, sauerkraut, coleslaw, cooked cabbage, cauliflower, Brussels sprouts, and kale. 95% CI = 95% confidence interval; BPH = benign prostatic hyperplasia; OR = odds ratio.

However, the exploratory analysis in our results suggested that antioxidants or micronutrients such as vitamin C, isoflavones, and dietary fiber were not significantly associated with the absolute change or progression of LUTS or incidence of BPH. Our findings are consistent with previously reports^{18,31,36} and do not support an association of dietary antioxidant intake with BPH risk. It is possible that the observed favorable associations between FV intake and LUTS were not attributable to single micronutrients itself, but to some other food components in FV or the interactions of nutrients available in FV foods. In addition, as FV intakes are considered to be part of a healthy diet that improves general health and well-being, when

adjusting for these factors in multivariate models, the associations with antioxidant nutrients may become nonsignificant.

We used the score change of LUTS to evaluate the temporal association of FV on LUTS in our study; the continuous outcome measures may increase the study power to find more significant associations than those of categorized outcomes (the progression of LUTS or incidence of BPH). The variations in our results when using different outcomes measures may also reflect a different constellation of underlying biologic factors. Our results suggested a nonlinear association between FV intake with LUTS and only adequate FV consumption (>350 g/1000 kcal/day) could significantly improve LUTS relative to those of low to

TABLE 5. Odds Ratio (OR) and 95% Confidence Interval (CI) for Incidence of Symptomatic Benign Prostatic Hyperplasia (BPH) by Low, Moderate, and High Fruit and Vegetable Intakes Using Multivariable Logistic Models Among Chinese Elderly Men

Incidence of Symptomatic BPH					
	N	Crude OR (95% CI)	P	Adjusted OR (95% CI)	P
Total fruits and vegetables (g/1000 kcal/d)					
<250	634	1.065 (0.772–1.469)	0.703	1.065 (0.765–1.478)	0.715
250–350	375	1	Ref.	1	Ref.
>350	253	0.886 (0.585–1.341)	0.567	0.875 (0.576–1.327)	0.529
Vegetables (g/1000 kcal/d)					
Total vegetables					
<100	621	0.994 (0.712–1.387)	0.973	0.994 (0.709–1.395)	0.974
100–150	338	1	Ref.	1	Ref.
>150	315	0.837 (0.563–1.242)	0.376	0.842 (0.564–1.257)	0.402
Dark and leafy vegetables					
<25	525	0.708 (0.520–1.146)	0.088	0.706 (0.515–1.168)	0.101
25–50	476	1	Ref.	1	Ref.
>50	267	0.631 (0.428–0.932)	0.021	0.657 (0.442–0.976)	0.038
Crucifera					
<7.5	618	0.981 (0.710–1.354)	0.905	0.968 (0.697–1.344)	0.845
7.5–15	366	1	Ref.	1	Ref.
>15	291	0.859 (0.579–1.273)	0.448	0.844 (0.565–1.260)	0.407
Tomatoes					
<2.5	307	0.682 (0.473–1.182)	0.240	0.677 (0.466, 1.082)	0.094
2.5–10	625	1	Ref.	1	Ref.
>10	342	0.970 (0.701–1.344)	0.857	0.958 (0.687–1.337)	0.802
Fruits (g/1000 kcal/d)					
Total fruits					
≤100	538	0.736 (0.532–1.018)	0.064	0.751 (0.536–1.051)	0.095
100–160	390	1	Ref.	1	Ref.
>160	343	0.802 (0.560–1.150)	0.230	0.830 (0.577–1.194)	0.316
Citrus					
<15	712	0.905 (0.614–1.334)	0.615	0.849 (0.567–1.271)	0.426
15–30	357	1	Ref.	1	Ref.
>30	206	1.004 (0.656–1.536)	0.986	0.934 (0.602–1.448)	0.761

Data were analyzed by multivariate logistic models. Adjusted variables included age, education, smoking status; intakes of coffee (mL/d), tea (mL/week), and alcohol (g/d), GDS (Geriatric Depression Scale) Score, comorbidities (yes or no) including fracture, diabetes, history of cardiovascular diseases (yes or no) including stroke, heart attack, angina and coronary heart failure; total energy; dietary fat intake, PASE (Physical activity scale for the elderly) total score; marriage status (yes or no). Citrus fruit intake in our study included intake of grape fruit, lemon, orange, and pomelo. Cruciferous vegetables included broccoli, sauerkraut, coleslaw, cooked cabbage, cauliflower, Brussels sprouts, and kale. 95% CI = 95% confidence interval; BPH = benign prostatic hyperplasia; OR = odds ratio.

moderate FV consumption. Epidemiological data reported that FV consumption is inversely associated with a range of chronic diseases, especially CVD risk; however, consistent with our findings, no evidence of a dose–response association was observed between increased FV intake and reduced risk of coronary heart disease,^{37,38} stroke,³⁹ or other CVD.⁴⁰

In this study, we observed that men with low FV intake had a trend of reduced LUTS over 4 years compared with men with moderate FV intake, although the mean differences were not statistically significant in most of the comparisons. It is possible that men with low FV intake at baseline may increase FV intake during follow-up due to increased health consciousness or regression to mean. Men with LUTS are likely to adopt healthy lifestyle that may increase FV intake or physical activity in order to reduce their symptoms. Although the prospective design of the study provides some confidence in the association being causal, we cannot dismiss the possibility that it may represent a partial reverse effect.

Studies assessing the role of diet on ED are limited. FV consumption may have a protective effect against ED.⁴¹ In this study, we did not observe a significant association of FV intakes with ED and sexuality. This could be due to the large proportion of men who were not sexually active in this cohort within the previous 6 months and the small sample size may have limited statistical power to conclude a significant association. In addition, ED is often associated with chronic conditions such as hypertension, dyslipidemia, and diabetes⁴²; thus, the adjustment for these comorbidities may attenuate the association of FV and ED.

MECHANISMS

It was hypothesized that oxidative damage might contribute to the disorder of BPH.⁴³ De De Nunzio et al⁴⁴ suggested that the prostate may be particularly vulnerable to oxidative stress, especially in the setting of chronic intraprostatic inflammation. FV contain high levels of antioxidants such as beta-carotene,

anthocyanins, flavonoids, lutein, lycopene, selenium, vitamin C, A, and E, etc that may play important roles in altering inflammatory pathways and influencing cell growth and differentiation associated with the pathogenesis of BPH. In addition, dietary factors can affect both steroid hormone concentrations and the sympathetic nervous system.^{45,46} It is possible that the physiologic effects of FV moderate both the hormonally regulated prostate growth and heightened smooth muscle tone that cause BPH.

STRENGTHS

The strengths of our study include its large, prospective design, use of validated instruments for measuring dietary intake and urinary symptoms, and availability of data on many potential confounding variables. Furthermore, the survey assessed symptoms rather than diagnosed conditions, thereby capturing the broader spectrum of the population who may suffer and diagnostic bias was avoided.

LIMITATIONS

The study has several limitations. First, as in all observational studies of diet and disease, reversal confounding effects could exist despite prospective design. Second, FV intake and other dietary factors were self-reported and not assessed by objective biomarkers. Potential biases due to the misclassification of dietary assessment, exposure categories, and the reference category cannot be excluded. However, any bias from the measurement errors would probably tend to attenuate the associations.

Third, in our study, assessment of diagnosed BPH was not conducted. The variability in the case definition of BPH (histological, radiological, symptomatic, or surgical BPH) renders it a problematic endpoint to compare across different study populations. The diagnostic instruments for BPH would be more time-consuming and invasive and impractical in a large cohort like ours. In addition, the measurement errors or misclassification on BPH can only reduce the chances of detecting significant associations.

Fourth, LUTS is a common problem in most elderly men, but remission in symptoms may occur in some individuals.⁴⁷ The operational definition of progression did not distinguish between men who had symptom remission from men who had stable IPSS scores. However, in sensitivity analysis, we excluded 302 men with remission (IPSS change \leq -3); the significant findings on high FV intake and LUTS change remained (data not shown). Also, the measurement of IPSS change over time as a primary outcome could reduce the impact of these fluctuations in our study.

In addition, the study sample consisted of all volunteers who were of a higher educational level and more likely to be married than the general Hong Kong population in the same sex and age groups.⁴⁸ Thus, the results may not be entirely generalizable. However, the selection bias would not affect the estimates of exposure–outcome associations.⁴⁹ Finally, the baseline data were collected more than 10 years ago (2001~2003); thus, new evidence is needed to confirm our findings.

CONCLUSION

This 4-year cohort study among Chinese elderly men indicated that adequate FV intake, especially dark and leafy vegetables, was associated with improved LUTS among

Chinese elderly men, although there was a lack of significant association with ED and sexuality. Clinical trials examining this directly and replication in other ethnic groups are warranted.

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