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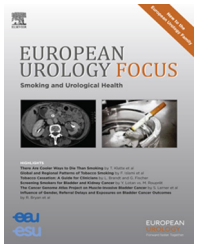

Platinum Priority – Aging Male
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Dietary Antioxidants and Longitudinal Changes in Lower Urinary Tract Symptoms in Elderly Men: The Osteoporotic Fractures in Men Study

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Abstract

Background: Antioxidants can potentially alter the progression of lower urinary tract symptoms (LUTS) through anti-inflammatory mechanisms.
Objective: To determine if dietary antioxidants are associated with reduced likelihood of LUTS progression or increased likelihood of LUTS remission in untreated elderly men.
Design, setting, and participants: A prospective cohort study of 1670 US men aged 65–100 yr.
Outcome measurements and statistical analysis: Baseline variables included the American Urological Association Symptom Index, dietary intake assessed via a 69-item Block food frequency questionnaire (FFQ), demographics, lifestyle characteristics, quality of life (SF-12), and medication use. LUTS was assessed at four time points over a mean ± standard deviation period of 6.9 ± 0.4 yr. Group-based trajectory modeling was performed for men without prostate cancer who did not undergo LUTS treatment with medication or surgery during follow-up (n = 1670). Analyses were stratified by LUTS symptoms at baseline. For men with mild baseline LUTS, we examined the likelihood of LUTS progression relative to LUTS stability. For men with moderate baseline LUTS, we analyzed the likelihood of both LUTS progression relative to LUTS stability and LUTS remission relative to progression. Odds ratios and 95% confidence intervals were estimated for quartiles of daily antioxidant intake using multivariable logistic regression.
Results and limitations: None of the dietary antioxidants (vitamin C, vitamin E, β-carotene, α-carotene, β-cryptoxanthin, lycopene, lutein/zeaxanthin) was associated with a lower probability of LUTS progression or LUTS remission. The study was limited by use of the brief Block FFQ, which contains only 69 food items and may have biased results toward the null hypothesis because of nondifferential misclassification.
Conclusions: In this large cohort of US men, there were no significant associations between multiple dietary antioxidants and LUTS progression or remission over 7 yr.
Patient summary: In a large cohort of elderly men, there were no significant longitudinal associations between multiple dietary antioxidants and lower urinary tract symptoms (LUTS). Our data suggest that dietary antioxidant consumption may not influence the natural history of LUTS in older men.

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1. Introduction

Lower urinary tract symptoms (LUTS) are common among elderly men and have substantial global adverse effects on male health [1,2]. LUTS have been associated with higher mortality and morbidity [3] and billions of US dollars in annual health care expenditure [4]. Since obesity and exercise have been associated with higher and lower risks of LUTS, respectively [5,6], lifestyle changes might potentially prevent LUTS progression. Dietary constituents, especially antioxidants, are candidate lifestyle targets for LUTS prevention. Since antioxidants have potent anti-inflammatory properties, an increase in dietary antioxidant consumption might decrease LUTS via modulation of inflammatory pathways involved in the pathogenesis of LUTS and benign prostatic hyperplasia (BPH) [7].

At least three studies have reported inverse associations between LUTS or BPH and consumption of antioxidants or foods rich in antioxidants, including β-carotene [8–10], lutein [8], lycopene [9,10], total carotenoids [10], vitamin C [8], vitamin E and selenium [9], vegetables [11–14], and fruits [13,15]. Higher consumption of fruits and vegetables (including those rich in β-carotene and lycopene) has also been associated with a lower risk of BPH incidence [8,11].

Since most of the prior studies were cross-sectional, temporal associations between dietary antioxidants and LUTS remain unclear. Moreover, to the nest of our knowledge, no studies have examined potential associations between dietary antioxidants and the risk of LUTS progression in elderly men. Given the high prevalence of LUTS in this population [2], the development of relatively straightforward dietary interventions to prevent LUTS progression in elderly men may substantially inform the clinical care of men with LUTS. Therefore, we examined the association between baseline dietary antioxidant intake and subsequent LUTS progression over a 7-yr period in elderly men. We hypothesized that higher baseline consumption of dietary antioxidants is associated with a lower probability of LUTS progression.

2. Patients and methods

This study used data collected in the Osteoporotic Fractures in Men Study (MrOS), a prospective study of community-dwelling men enrolled from six US sites [16,17]. The study was designed to evaluate risk factors for fracture, falls, and other conditions relevant to aging men, including prostate disease and LUTS [17]. From March 2000 to April 2002, 5994 men age 65–100 yr who could walk unassisted and had at least one natural hip for bone density measurement were enrolled. The six sites were Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Pittsburgh, PA; Portland, OR; and San Diego, CA. The study protocol was approved by the institutional review boards at all participating institutions, and all men gave written informed consent.

Baseline measures collected at clinic visits included basic demographic data, lifestyle information (alcohol use, cigarette smoking), medical conditions, self-rated health, quality of life (short-form 12, SF-12 [18]), and physical activity information based on the Physical Activity Scale for the Elderly (PASE) [19]. Height and weight were measured at the clinic visit and body mass index (BMI) was computed (kg/m^2) [20]. Medications and supplements were brought to the baseline clinic visit and were inventoried by study staff and matched to ingredients according to on the Iowa Drug Information Service drug vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA, USA) [21].

Dietary data were collected at baseline using a brief Block food frequency questionnaire (FFQ) [22,23], which contains 69 items specifically drawn from foods most frequently consumed by elderly US men according to an analysis of data from the Third National Health and Nutrition Examination Survey (NHANES III) [22]. The Block FFQ is a validated, robust instrument used in observational research to measure nutrient intake, including antioxidant micronutrients. The brief Block FFQ asks about consumption frequency and portion size for each item. Gram estimates of foods were calculated as the gram weight for the chosen portion size multiplied by the consumption frequency. Nutrients were then estimated using the average amount of a nutrient in a food multiplied by the gram weight consumed. Nutrients from supplements were calculated separately from food estimates. Total intake was calculated as the sum of the nutrient estimates from food plus supplement nutrient estimates, when applicable. Supplement information was available only for the antioxidants vitamin C, vitamin E, and β-carotene.

At baseline and approximately every 2 yr (2002–2004, 2005–2006, and 2007–2009), follow-up data were collected on lower urinary tract health, including the American Urological Association Symptom Index (AUA-SI) and history of LUTS treatment. Additional follow-up occurred every 4 mo via mailed questionnaires to collect reports of deaths and incident prostate cancer cases, which were adjudicated by study physicians using death certificates and pathology reports.

The following baseline variables were classified into categories for the analysis. BMI was classified as normal ($<$25.0 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese ($\geq$30.0 kg/m^2) [20]. Depressed mood was defined as an SF-12 mental component score $\leq$45 points [24]. Alcohol consumption was classified as never, $\leq$14 drinks/wk, or $>$14 drinks/wk; problem drinking was defined as a CAGE (Cutting down, Annoyance by criticism, Guilty feeling, and Eye-openers) [25] score of $>$1. Central nervous system (CNS) medication was defined as use of antiepileptics, benzodiazepines, antidepressants, opioids, or sedatives at baseline. Participants missing medication information were coded as nonusers after analyses showed no difference between nonusers and those with missing data.

We first restricted the MrOS cohort to 3594 men who had no history of prostate cancer and no prior or current treatment for LUTS, including surgery or medication (α-blockers, antispasmodics, anticholinergics, 5α-reductase inhibitors). These men were then followed through the fourth AUA-SI assessment (2007–2009). During follow-up, the cohort for trajectory analysis was further restricted to 1740 men who remained free from diagnosed prostate cancer, reported no surgery or medication use for LUTS, and completed all four AUA-SI assessments. A figure demonstrating how the analytic cohort was ascertained for the trajectory analysis has been previously published [26]. The same study demonstrated no significant differences in LUTS trajectory among men with a history of stroke and those who used CNS medications [26], so we did not exclude them from the present analysis.

Outcomes for this analysis were LUTS trajectories. Details of the trajectory method were reported previously [26]. In brief, group-based trajectory modeling was performed using the AUA-SI data from all four time points. Trajectory modeling uses the maximum likelihood method and applies a semiparametric mixed model to longitudinal data (PROC TRAJ for SAS 9.1) [27–29]. The four trajectory types identified were stable (n = 1277), progressing (n = 345), and remitting (n = 98) LUTS groups, and one very small group (n = 20) in which the LUTS trajectory increased and then decreased during follow-up. We identified three LUTS progression trajectories during follow-up: men who progressed from mild to moderate LUTS; men who progressed from moderate to severe LUTS; and men who progressed from low-moderate to high-moderate LUTS [26].

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