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LOW SERUM CAROTENOIDS ARE ASSOCIATED WITH A DECLINE IN WALKING SPEED IN OLDER WOMEN

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Abstract

Background and Objectives—Walking speed is an important measure of physical performance that is predictive of disability and mortality. The relationship of dietary factors to changes in physical performance has not been well characterized in older adults. The aim was to determine whether total serum carotenoid concentrations, a marker for fruit and vegetable intake, and serum selenium are related to changes in walking speed in older women.

Subjects and Methods—The relationship between total serum carotenoids and selenium measured at baseline, 12, and 24 months follow-up and walking speed assessed at baseline and every six months for 36 months was examined in 687 moderately to severely disabled women, 65 years or older, living in the community.

Results—Mean total serum carotenoids were associated with mean walking speed over three years of follow-up ($P = 0.0003$) and rate of change of walking speed ($P = 0.007$) in multivariate linear regression models adjusting for age, body mass index, and chronic diseases. Mean serum selenium was associated with mean walking speed over three years of follow-up ($P = 0.0003$) but not with the rate of change of walking speed ($P = 0.26$).

Conclusions—These findings suggest that a higher fruit and vegetable intake, as indicated by higher total serum carotenoid concentrations, may be protective against a decline in walking speed in older women.

Keywords

Aging; carotenoids; disability; walking speed; women

Introduction

Mobility is a key factor in maintaining independence and quality of life with aging. In older adults, slow walking speed is associated with incident cardiovascular disease, disability, and mortality (16,31,32,36,46). An understanding of the biological mechanisms that lead to a decline in walking speed is important in order to develop strategies to prevent or delay disability and associated morbidity and mortality among older adults. Lack of physical activity, smoking, and obesity are modifiable risk factors that have been associated with poor walking speed (13,40,42). The role of diet in the maintenance of walking speed and mobility in older adults

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has not been well characterized, but could potentially be important as a modifiable risk factor. Dietary intake of fruits and vegetables was inversely associated with lower extremity physical performance, activities of daily living, and instrumental activities of daily living in older adults (18). Low serum carotenoids, an indicator of fruit and vegetable intake (12) and low dietary intake of beta-carotene have been associated with poor grip, hip, and knee strength in older women and impaired lower extremity performance in older community-dwelling adults in Italy (6,37).

Selenium is an essential trace element and a normal constituent of the diet. Selenium is a component of selenoproteins, including selenoenzymes such as glutathione peroxidase, selenoprotein-P, and thioredoxin reductase (22). Selenium is best characterized for the role it plays in the glutathione peroxidase enzyme system, a major antioxidant defense system that uses reduced glutathione to reduce oxidative stress by breaking down hydrogen peroxide and lipid peroxides (22). In older adults, low serum selenium concentrations have been associated with poor muscle strength (3,24), increased mortality (35), as well as anemia (38). These findings suggest that selenium could potentially play a role in aging-related outcomes, including walking speed.

New evidence is emerging that a relatively high intake of fruits and vegetables (2,7,27,28,41, 43), are beneficial for health and survival in older adults. The exact mechanisms by which higher fruit and vegetable intake may improve health are not completely clear but may relate to the role of carotenoids and plant polyphenols in protecting against oxidative stress and inflammation (9,10,14). To address the hypotheses that low serum carotenoids and low serum selenium are associated with a decline in walking speed, we examined the relationship between total serum carotenoids and serum selenium at baseline, 12 and 24 months follow-up and change in walking speed assessed every six months for 36 months among older community-dwelling women.

Methods

Subjects in this study were women, aged 65 and older, who participated in the Women's Health and Aging Study I (WHAS I), a population-based study designed to evaluate the causes and course of physical disability in older women living in the community. WHAS I participants were recruited from an age-stratified random sample of women aged 65 years and older selected from Medicare enrollees residing in 12 contiguous zip code areas in Baltimore (17). Women were screened to identify self-reported physical disability that was categorized into four domains. The domains of disability were ascertained in a 20–30 minute home interview that included questions related to (1) mobility and exercise tolerance, i.e., walking for a quarter of a mile, walking up 10 steps without resting, getting in and out of bed or chairs, (2) upper extremity function, i.e., raising your arms up over your head, using your fingers to grasp or handle, lifting or carrying something as heavy as ten pounds, (3) higher functioning tasks (a subset of instrumental activities of daily living, not including heavy housework, i.e., using the telephone, doing light housework, preparing your own meals, shopping for personal items), and (4) basic self-care tasks (a subset of non-mobility dependent activities of daily living, i.e., bathing or showering, dressing, eating, using the toilet). WHAS I enrolled the one-third most disabled women ages 65 and older, those with disability in two or more domains. Of the 1409 women who met study eligibility criteria, 1002 agreed to participate in the study in 1992. There were no major differences in sociodemographic or reported health characteristics between eligible participants and those who declined to participate (17).

Standardized questionnaires were administered in the participant's home by trained interviewers. Mini-Mental Status Examination (MMSE) was recorded (17). Race was assessed in a questionnaire as black, white, or other, current smoking as yes or no, and education as 0–

8, 9–11, 12 years or more than 12 years as the highest level of formal education achieved. Two weeks later, a trained registered full-time study nurse conducted an examination of each study participant in her home, using a standardized protocol that included physical performance measures and a standardized physical examination. Approximately 75% of women also consented to phlebotomy performed during a separate visit by a trained phlebotomist who followed a standardized protocol. Further details on the methods and sampling design of the WHAS studies are published elsewhere (17).

Walking speed was assessed every six months. The participant was asked to walk over a 4-meter course. Participants were instructed to stand with both feet at the starting line and to start walking after a specific verbal command. Timing began when the command was given. In this test, the subject could use a cane, a walker, or other walking aid, but not the aid of another person. The times to complete the first meter and the entire path were recorded. The test was repeated three times, twice at the woman's usual pace, and once at her fastest possible pace. The speed of the faster of the two usual-pace walks was used in the analyses. The length of the walk expressed in meters divided by the time in seconds was used to calculate the walking speed (Guralnik 1995). Demographic characteristics, self-rated health, and information about appetite and eating were measured in the WHAS questionnaires. An interim history of hospitalizations was obtained at each study visit. Chronic diseases were adjudicated by WHAS co-investigators based on the questionnaire, physical examination and physician contact (17).

There were 1002 women enrolled in the Women's Health and Aging Study I, of whom 753 women participated in the blood drawing at baseline. There were no significant differences in race or body mass index between those who did and did not participate in the blood drawing, but women who did and did not participate in the blood drawing were different by age (77.4 vs 80.7 years, respectively, $P < 0.0001$) and were more disabled (17).

Non-fasting blood samples were obtained by venipuncture between 9 AM and 2 PM. Processing, aliquoting, and freezing were carried out at the Core Genetics Laboratory of The Johns Hopkins University School of Medicine following a standardized protocol. Blood samples were delivered to Quest Diagnostics Laboratories (Teterboro, New Jersey) and other aliquots were stored continuously at -70°C until the time of laboratory analyses. Serum carotenoids were measured by high performance liquid chromatography (HPLC) (37). Total carotenoids were calculated as the sum of α -carotene, β -carotene, β -cryptoxanthin, lutein, zeaxanthin, and lycopene in $\mu\text{mol/L}$. The inter-assay CVs for α -carotene, β -carotene, β -cryptoxanthin, lutein, zeaxanthin, lycopene, and α -tocopherol were all $< 12\%$. Plasma selenium was measured by graphite furnace atomic absorption spectrometry using a Perkin Elmer AAnalyst 600 with Zeeman background correction. Samples were diluted 1:4 with a triton-X (Sigma Chemical, St. Louis, MO) and nitric acid solution (Fisher Scientific, Pittsburgh, PA), and the matrix modifier was a palladium and magnesium nitrate solution (both Perkin Elmer, Norwalk, CT). The instrument was calibrated daily using known plasma selenium standards (UTAK Laboratories, Inc., Valencia, CA). The inter-assay CV for selenium was 2%.

Means and proportions were used to describe the study population. Body mass index was categorized as underweight ($< 18.5\text{ kg/m}^2$), normal range ($18.5\text{--}24.9\text{ kg/m}^2$), overweight ($\geq 25\text{--}29.9\text{ kg/m}^2$) and obese ($\geq 30\text{ kg/m}^2$) according to World Health Organization criteria (20). Women who did not have more than one measurement of total serum carotenoids and serum selenium and more than one assessment of walking speed after baseline were excluded from the analyses. The length of follow-up in longitudinal analyses was 36 months. Total serum carotenoids and serum selenium were calculated as the mean of two or three measurements taken at baseline, 12, and 24 months. Mean walking speed was calculated as the mean of all walking speed measurements taken during baseline and follow-up. The slope (rate of change) of walking speed from baseline through follow-up visits was determined separately for each

subject. Linear regression models were used to examine the relationship between total serum carotenoids and other variables with mean walking speed and rate of change of walking speed. The statistical program used was SAS version 9.13 (SAS Institute, Cary, NC).

Results

There were 742 women who had total serum carotenoids, serum selenium, and walking speed assessed at baseline, of whom 22 were unable to walk at baseline and were excluded from the analyses. An additional 33 women did not have walking speed and/or serum carotenoids and selenium assessed during follow-up and were not included in the analysis. The demographic, nutritional, and disease characteristics of the 687 women in the study are shown in Table 1.

Univariate linear regression models were used to examine the relationship between demographic factors, serum total carotenoids, serum selenium, body mass index, and chronic diseases and mean walking speed (mean of all walking measurements assessed during 36 months of follow-up) as shown in Table 2. Older age, lower level of education, MMSE score <24, hypertension, coronary artery disease, congestive heart failure, stroke, diabetes, depression, osteoarthritis, and chronic renal disease were significantly associated with lower mean walking speed. White race, overweight, obesity, serum total carotenoids, and serum selenium were significantly associated with higher mean walking speed.

Total serum carotenoids and serum selenium were associated with mean walking speed (both $P = 0.0003$) in multivariate linear regression models adjusting for age, body mass index, and chronic diseases (Table 3). Older age, MMSE score <24, stroke, diabetes, depression, and chronic renal failure were also significantly associated with mean walking speed in the final multivariate model. Scatterplots of the relationship between total serum carotenoids and mean walking speed and serum selenium and mean walking speed are shown in Figures 1a and 2a.

Univariate linear regression models were used to examine the relationship between demographic factors, serum total carotenoids, serum selenium, body mass index, and chronic diseases and change in walking speed (slope of walking speed from baseline through six-month follow-up visits as assessed during 36 months of follow-up) as shown in Table 4. Older age, lower level of education, MMSE score <24, peripheral artery disease, congestive heart failure, diabetes, depression, and chronic renal disease were significantly associated with a decline in walking speed. White race, overweight, obesity, serum total carotenoids, and serum selenium were significantly associated with an increase in walking speed in univariate analyses.

Total serum carotenoids were associated with change in walking speed ($P = 0.007$) in multivariate linear regression models adjusting for age, body mass index, and chronic diseases. Serum selenium was not associated with change in walking speed in the same model. Older age, MMSE score <24, stroke, diabetes, depression, and chronic renal failure were also significantly associated with a decline in walking speed in the final multivariate model. Scatterplots of the relationship between total serum carotenoids and slope of decline in walking speed and serum selenium and slope of decline in walking speed are shown in Figures 1b and 2b.

Discussion

This study suggests that low total serum carotenoid concentrations, a marker for fruit and vegetable intake, are associated with low walking speed and greater decline of walking speed during three years of follow-up. The strengths of this study are that serum carotenoid concentrations were measured in the study participants two or three times during a two year period, and walking speed was measured every six months for a three year period. The results of the present study are consistent with findings from the InCHIANTI study in which total

plasma carotenoids at enrollment were independent predictors of a decline in walking speed among older community-dwelling men and women (25).

Fruits and vegetables are rich sources of antioxidants, including the carotenoids, vitamin C, flavonoids, and other polyphenols. It cannot be determined from this study whether serum carotenoids play a direct biological role as a determinant of walking speed, since there are other constituents in fruits and vegetables that, acting alone or in concert with other substances, could play a role. A high fruit and vegetable intake has been shown to be protective against inflammation, cardiovascular disease, and mortality in prospective studies (2,27,28,41). Intervention studies show that increased consumption of fruits and/or vegetables and related products reduces inflammation (1,19,21,45).

The direction of the association between total serum carotenoids and serum selenium and decline in walking speed cannot necessarily be determined from the design of this longitudinal study, since total serum carotenoids, serum selenium, and walking speed were repeatedly measured during follow-up. It is possible that women with poor walking speed were unable to shop, prepare meals, and eat healthier diets compared with women who had better walking speed, thus raising the issue of reverse causality. However, other longitudinal studies have shown that at baseline, low serum/plasma carotenoid and selenium concentrations are predictive of subsequent declines in walking speed (25), and mortality (26,35).

Walking speed is strongly related to sarcopenia, or loss of muscle mass and strength (23). Oxidative stress has been postulated to be an underlying biological mechanism for sarcopenia (15), and with aging, increased oxidative damage to DNA, protein, and lipids occurs in skeletal muscle with associated atrophy and loss of muscle fibers (4,30,33). Serum carotenoids play an important role in reducing oxidative stress through the quenching of hydroxyl radicals and reducing lipid peroxidation (29). Low serum carotenoids were independently predictive of subsequent increases in serum IL-6 among older community-dwelling women (44). Elevated serum IL-6 concentrations are associated with an increased risk of reduced physical function and sarcopenia (11,34) and the development of disability (5).

Modifiable risk factors that may protect against the decline of walking speed include greater physical activity, avoidance of smoking, and prevention of obesity (13,40,42). Adoption of a healthy diet that is high in fruits and vegetables, fiber, and low in saturated fats has been shown to reduce cardiovascular risk factors (10). A Mediterranean-style diet that is high in fruits and vegetables has attracted much interest because of an apparent protective effect against cardiovascular disease (8,39). Whether a similar healthy diet can protect against the decline of physical function in older adults remain unknown and could be addressed in controlled trials.

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Figure 1. Scatterplot of total serum carotenoids and (a) mean walking speed, and (b) slope of decline in walking speed

Figure 2. Scatterplot of serum selenium and (a) mean walking speed, and (b) slope of decline in walking speed

Table 1

Characteristics of study subjects from the Women's Health and Aging Study I at baseline

Characteristic		N	Mean or %	SD
Age (y)	65–69.9	133	19.4	---
	70–74.9	162	23.6	---
	75–79.9	133	19.4	---
	80–84.9	83	12.1	---
	85–89.9	133	19.4	---
	90	43	6.2	---
White (%)		492	71.6	---
Education <12 years (%)		446	65.2	---
MMSE <24 (%)		111	16.1	---
Current smoker (%)		81	11.8	---
Body mass index (kg/m ²) (%)	<18.5	22	3.5	---
	18.5–24.9	162	25.4	---
	25.0–29.9	221	34.6	---
	≥30	233	36.5	---
Total serum carotenoids (μmol/L)		687	2.08	0.95
Serum selenium (μg/L)		687	117	18.0
Hypertension (%)		397	57.8	---
Coronary heart disease (%)		164	23.9	---
Peripheral artery disease (%)		153	22.3	---
Congestive heart failure (%)		69	10.0	---
Stroke (%)		34	4.9	---
Diabetes mellitus (%)		114	16.6	---
Chronic obstructive lung disease (%)		189	27.5	---
Depression (%)		113	16.4	---
Osteoarthritis (%)		380	55.3	---
Cancer (%)		79	11.5	---
Renal disease (%)		57	8.6	---

Table 2

Univariate linear regression analysis of serum carotenoids and selenium, demographic factors, and chronic diseases with mean walking speed during three years of follow-up

Characteristic		Beta	SE	P
Age (y)	65–69.9	---	---	---
	70–74.9	−0.093	0.033	0.005
	75–79.9	−0.107	0.035	0.002
	80–84.9	−0.232	0.039	<0.0001
	85–89.9	−0.312	0.035	<0.0001
	90	−0.478	0.049	<0.0001
White		0.123	0.026	<0.0001
Education <12 years		−0.132	0.024	<0.0001
MMSE score <24		−0.215	0.031	<0.0001
Current smoker		0.041	0.037	0.26
Body mass index (kg/m ²) (%)	<18.5	0.027	0.069	0.69
	18.5–24.9	---	---	---
	25.0–29.9	0.098	0.030	0.001
	≥30	0.061	0.029	0.04
Total serum carotenoids (μmol/L)		0.050	0.012	<0.0001
Serum selenium (μg/L)		0.004	0.0006	<0.0001
Hypertension		−0.052	0.024	0.032
Coronary heart disease		0.006	0.028	0.81
Peripheral artery disease		−0.107	0.028	0.0002
Congestive heart failure		−0.128	0.039	0.001
Stroke		−0.252	0.054	<0.0001
Diabetes mellitus		−0.104	0.031	0.001
Chronic obstructive lung disease		0.031	0.026	0.24
Depression		−0.169	0.031	<0.0001
Osteoarthritis		−0.048	0.024	0.05
Cancer		0.058	0.037	0.12
Renal disease		−0.148	0.043	0.0006

Table 3

Multivariate model for serum carotenoids and selenium and other factors with mean walking speed during three years of follow-up

Characteristic		Beta	SE	P
Age (y)	65–69.9	---	---	---
	70–74.9	−0.107	0.030	0.0005
	75–79.9	−0.111	0.032	0.006
	80–84.9	−0.243	0.037	<0.0001
	85–89.9	−0.326	0.033	<0.0001
	≥90	−0.446	0.047	<0.0001
MMSE score <24	−0.113	0.027	<0.0001	
Body mass index (kg/m ²) (%)	<18.5	0.042	0.058	0.45
	18.5–24.9	---	---	---
	25.0–29.9	0.072	0.025	0.005
	≥30	−0.013	0.025	0.6
Total serum carotenoids (μg/L)	0.038	0.010	0.0003	
Serum selenium (μmol/L)	0.002	0.00005	0.0003	
Congestive heart failure	−0.065	0.034	0.05	
Stroke	−0.231	0.047	<0.0001	
Diabetes mellitus	−0.112	0.028	<0.0001	
Chronic obstructive lung disease	0.030	0.024	0.2	
Depression	−0.107	0.027	<0.0001	
Renal disease	−0.076	0.036	0.03	

Table 4

Univariate linear regression analysis of serum carotenoids and selenium, demographic factors, and chronic diseases with slope of mean walking speed over three years of follow-up

Characteristic		Beta	SE	P
Age (y)	65–69.9	---	---	---
	70–74.9	−0.008	0.003	0.008
	75–79.9	−0.006	0.003	0.06
	80–84.9	−0.015	0.004	0.0001
	85–89.9	−0.019	0.004	<0.0001
	≥90	−0.033	0.005	<0.0001
White		0.005	0.002	0.05
Education <12 years		−0.006	0.002	0.01
MMSE score <24		−0.010	0.003	0.0009
Current smoker		−0.002	0.003	0.5
Body mass index (kg/m ²) (%)	<18.5	0.004	0.006	0.48
	18.5–24.9	---	---	---
	25.0–29.9	0.006	0.002	0.035
	≥30	0.008	0.002	0.004
Total serum carotenoids (μmol/L)		0.004	0.003	0.0018
Serum selenium (μg/L)		0.0001	0.00006	0.0025
Hypertension		−0.002	0.002	0.31
Coronary heart disease		−0.001	0.002	0.51
Peripheral artery disease		−0.006	0.002	0.03
Congestive heart failure		−0.009	0.003	0.009
Stroke		−0.008	0.005	0.14
Diabetes mellitus		−0.008	0.003	0.005
Chronic obstructive lung disease		0.001	0.002	0.68
Depression		−0.011	0.003	0.0002
Osteoarthritis		−0.001	0.002	0.57
Cancer		−0.004	0.003	0.26
Renal disease		−0.015	0.004	0.0002

Table 5

Multivariate model for serum carotenoids and selenium and other factors with slope of mean walking speed over three years of follow-up

Characteristic		Beta	SE	P
Age (y)	65–69.9	---	---	---
	70–74.9	−0.009	0.003	0.006
	75–79.9	−0.006	0.003	0.07
	80–84.9	−0.014	0.004	0.0005
	85–89.9	−0.018	0.003	<0.0001
	≥90	−0.029	0.005	<0.0001
MMSE score <24		−0.003	0.003	0.25
Body mass index (kg/m ²) (%)	<18.5	0.005	0.006	0.37
	18.5–24.9	---	---	---
	25.0–29.9	0.005	0.002	0.04
	≥30	0.005	0.002	0.07
Total serum carotenoids (μg/L)		0.003	0.001	0.007
Serum selenium (μmol/L)		0.00006	0.00006	0.26
Congestive heart failure		−0.006	0.003	0.08
Stroke		−0.004	0.005	0.41
Diabetes mellitus		−0.009	0.003	0.002
Depression		−0.008	0.003	0.004
Renal disease		−0.011	0.003	0.003