REJUVENATION RESEARCH
Volume 11, Number 3, 2008

DOI: 10.1089/rej.2007.0581

Carotenoids as Protection Against Disability in Older Persons

Fulvio Lauretani,[1,6] Richard D. Semba,[2] Stefania Bandinelli,[3] Margaret Dayhoff-Brannigan,[2]
Fabrizio Lauretani,[1] Anna Maria Corsi,[1,4] Jack M. Guralnik,[5] and Luigi Ferrucci[6]

Abstract

The purpose was to examine the relationship of total plasma carotenoids, an indicator of fruit and vegetable intake, with walking speed and severe walking disability in older adults. Nine hundred twenty-eight men and women aged 65 to 102 years from the *Invecchiare in Chianti* (Aging in the Chianti Area [InCHIANTI]) study, a population-based cohort in Tuscany, Italy, were studied. Plasma carotenoids were measured at enrollment (1998–2000), and walking speed over 4 meters and 400 meters distance were assessed at enrollment and 6 years later (2004–2006). At enrollment, 85 of 928 (9.2%) participants had severe walking disability (defined as being unable to walk or having a walking speed at the 4-meter walking test < 0.4 m/sec). After adjusting for potential confounders, participants with high total plasma carotenoids were significantly less likely to have prevalent severe walking disability (odds ration [OR] 0.59, 95% confidence interval [CI] 0.38–0.90, $p = 0.01$) and had higher walking speed over 4 meters ($\beta = 0.024$, standard error [SE] $= 0.011$, $p = 0.03$) and over 400 meters ($\beta = 0.019$, SE $= 0.010$, $p = 0.04$). Of 621 participants without severe walking disability at enrollment who were seen 6 years later, 68 (11.0%) developed severe walking disability. After adjusting for potential confounders, higher total plasma carotenoids were associated with a significantly lower risk of developing severe walking disability (OR 0.51, 95% CI 0.30–0.86, $p = 0.01$) and were associated with a less steep decline in 4-meter walking speed over a 6-year follow-up ($n = 579$; $\beta = 0.026$, SE $= 0.012$, $p = 0.03$) and with lower incidence rates of being unable to successfully complete the 400-meter walking test at the 6-year follow-up visit ($\beta = -0.054$, SE $= 0.03$, $p = 0.04$). High plasma carotenoids concentrations may be protective against the decline in walking speed and the development of severe walking disability in older adults.

Introduction

Lower walking speed and walking performance among older adults are associated with a higher incidence of cardiovascular disease, disability, and mortality.[1–3] Understanding the processes that are responsible for the age-associated decline in walking speed is important in order to develop strategies to prevent or delay disability and associated morbidity and mortality among older adults. Two recent cross-sectional epidemiologic studies suggest that low serum levels of carotenoids or low β-carotene intake is associated with low muscle strength, impaired physical function, and severe limitation in walking in older adults. In the Women's Health and Aging Study, low serum carotenoids were associated with poor muscle strength among older women living in the community,[4] and low β-carotene intake was associated with impaired lower extremity performance in older community-dwelling adults in Italy.[5] Then, we recently found in the InCHIANTI study that older community-dwelling men and women with low plasma carotenoid concentrations had a greater decline in hip, knee, and grip muscle strength over a period of 6 years compared to those with high plasma carotenoids.[6]

Serum carotenoids are considered the most valid indicator of fruit and vegetable intake,[7] and thus, carotenoids may be considered as biomarkers for dietary intake of fruits and

[1]Tuscany Regional Agency, Florence, Italy.
[2]Johns Hopkins School of Medicine, Baltimore, Maryland.
[3]Azienda Sanitaria Firenze, Florence, Italy.
[4]Department of Medical and Surgical Critical Care, Thrombosis Centre, University of Florence, Italy.
[5]Laboratory of Epidemiology, Demography and Biometry, National Institute on Aging, Bethesda, Maryland.
[6]Longitudinal Studies Section, Clinical Research Branch, National Institute on Aging, Baltimore, Maryland.

vegetables. There is growing scientific evidence that a relatively high fruit and vegetable intake[8–11] and the type of diet rich in fruits and vegetables, such as the Mediterranean diet,[12–14] improve health and are associated with increased longevity. The exact mechanisms by which higher fruit and vegetable intake may improve health is not completely clear but may relate to the role of dietary antioxidants, such as dietary carotenoids, in protecting against oxidative stress and inflammation.[14,15] It is not clear whether low circulating levels of antioxidant nutrients predict adverse functional outcomes such as severe walking disability, because the previous studies that specifically addressed antioxidant nutrients were cross-sectional.[4,5] To address the hypothesis that low serum carotenoids may predict worsening of physical disability and decline in physical performance, we examined the relationship between plasma total carotenoids at enrollment and the development of severe walking disability and change over time in walking speed over a six-year interval among participants of the InCHIANTI study, a population-based study of older adult living in the Chianti region of Tuscany, Italy.

Subjects and Methods

The study participants consisted of men and women, aged 65 and older, who participated in the *Invecchiare in Chianti* (Aging in the Chianti Area [InCHIANTI]) study, conducted in two small towns in Tuscany, Italy. The rationale, design, and data collection have been described elsewhere, and the main outcome of this longitudinal study is mobility disability.[16] Briefly, in August 1998, 1270 people aged 65 years and older were randomly selected from the population registry of Greve in Chianti (population 11,709) and Bagno a Ripoli (population 4704), and of 1256 eligible subjects, 1155 (90.1%) agreed to participate. Participants received an extensive description of the study and participated after written, informed consent. The participants were seen again for a 3-year follow-up visit from 2001–2003 and 6-year follow-up visit from 2004–2006 at which time they underwent a repeat laboratory testing and assessment of physical performance. The study protocol complied with the Declaration of Helsinki and was approved by the Italian National Institute of Research and Care on Aging Ethical Committee.

Of the 1155 participants 65 years or older seen at enrollment, 1055 (91.3%) participated in the blood drawing. There were 928 (80.3%) participants at enrollment who had both plasma carotenoids and 4-meter walking speed available for this analysis. The subjects who did not participate in the blood drawing were generally older and had greater comorbidity than the subjects who participated in the blood drawing, as reported elsewhere.[17] None of the participants were taking dietary supplements. We found no significant difference of plasma carotenoids levels between participants evaluated versus those not evaluated at the 6-year year follow-up study (carotenoids mean levels: 1.80 versus 1.84 μmol/L, $p = 0.23$, respectively).

Data collection consisted of a home interview, a 24-hour urine collection and a medical evaluation at the study clinic, which took place within 21 days after the home interview. Demographic information were collected included sociodemographic variables (age, gender, and years of education); smoking history was determined from self-report and dichotomized in the analysis as "current smoking" versus "ever smoked" and "never smoked. Pharmacologic treatments were assessed and coded according to Anatomical Therapeutic Chemical (ATC) codes.

Average daily intakes of energy (kcal), carbohydrates, total protein, total lipids, etc., were estimated using the European Prospective Investigation into Cancer and Nutrition food frequency questionnaire, validated in the InCHIANTI population.[18] All participants were examined by a trained geriatrician, and diseases were ascertained according to standard, preestablished criteria and algorithms based upon those used in the Women's Health and Aging Study for coronary heart disease, congestive heart failure, peripheral artery diseases, diabetes mellitus, chronic obstructive pulmonary disease, and osteoarthritis.[19] Weight was measured using a high-precision mechanical scale. Standing height was measured to the nearest 0.1 cm. Body mass index (BMI) was calculated as weight/height^2 (kg/m^2).

In the 4-meter walking test, the participants were instructed to walk at their normal pace over a 4-meter distance, which was repeated twice and the average time used.[20] The 400-meter walking test consisted of a timed walk for 400 meters, and the participants were instructed to walk at a normal steady pace. Participants were asked to walk 20 laps on a 20-meter course as fast as possible at a steady pace. Time per lap completion was collected using a photo-based chronometer and overall gait speed was calculated. A maximum of two standing rests were allowed for two minute intervals each. Participants were classified as unable to complete the 400-meter walking test at follow-up if they: attempted but failed the 400-meter walk, had self-reported difficulty walking 8 meters without help, difficulty keeping feet together for 10 seconds (part of the Frailty and Injuries: Cooperative Studies of Intervention Techniques [FICSIT]) battery, severe dyspnea and dyspnea at rest in the last 3 months, angina/chest pain with intense dyspnea, or were not tested but had evidence of inability to complete the walk (as indicated by inability to complete a 4-meter walk).[21] Reasons why subjects were excluded from performing the 400-meter walking test were reported elsewhere. [22]

Subjects were categorized as having severe walking disability based upon being unable to walk or having a walking speed at the 4-meter walking test less than 0.4 m/sec.[23] The 0.4 m/sec cut-off point was approximately at the top of the lowest quartile in the Women's Health and Aging Study population at baseline[24] and has been shown to predict functional dependence.[25]

Blood samples were collected in the morning after a 12-hour fast. Aliquots of serum and plasma were immediately obtained and stored at $-80°$C. Aliquots of plasma were shipped on dry ice to Dr. Semba's laboratory for measurements of plasma carotenoids. Carotenoids were measured using high-performance liquid chromatography (HPLC).[26] Total carotenoids were calculated as the sum of α-carotene, β-carotene, β-cryptoxanthin, lutein/zeaxanthin, and lycopene in micromoles per liter (μmol/L). Within-run and between-run coefficients of variation, respectively, were 7.3% and 9.6% for α-carotene, 4.5% and 5.4% for β-carotene, 2.7% and 3.5% for β-cryptoxanthin, 2.6% and 7.1% for lutein, 6.2% and 6.8% for zeaxanthin, and 7.5% and 7.8% for lycopene.

The level of physical activity in the year prior to the interview was classified on an ordinal scale based on responses to a modified standard questionnaire[27] into: (1) hardly any physical activity; (2) mostly sitting (occasionally walks, easy gardening); 3) light exercise (no sweat) 2–4 hours per week; (4) moderate exercise (sweat) 1–2 hours per week (level 4); (5) moderate exercise more than 3 hours per week; (6) intense exercise (at the limits) more than 3 times per week. For analytical purposes, we grouped the participants as: 1–3 inactive or having light physical activity; 4–5 having moderate physical activity; 6 having intense physical activity.

Variables are reported as means (standard deviations) for normally distributed parameters or as percentages. The present analysis was limited to participants who were seen at enrollment and 6-year follow-up visits. The 6-year interval allowed for characterization a larger decline in walking speed. Means were compared using t test and percentages were compared using χ^2 tests. Logistic regression analysis was used to examine the relationship between total plasma carotenoids and other risk factors with severe walking disability. Linear regression analysis was used to examine the relationship between total plasma carotenoids and other risk factors with walking speed. All analyses were performed using SAS (version 8.2, SAS Institute, Inc., Cary, NC) with a statistical significance level set at $p < 0.05$.

Results

The characteristics of the study population at enrollment are shown in Table 1. At enrollment, 85 of 928 (9.2%) had severe walking disability. Of 843 participants who did not have severe walking disability at enrollment, there were 621 who had walking speed assessed at the 6-year follow-up visit. Of 222 people who were not seen at the 6-year follow-up visit, 160 had died, 48 refused to participate, and 14 moved out of the study area. Of 621 participants seen at the 6-year follow-up visit, 68 (11%) had severe walking disability (42 were unable to walk and 26 had walking speed at the 4-meter walking test < 0.4 m/sec).

The relationship between total plasma carotenoids and other risk factors with prevalent severe walking disability at enrollment and incident severe walking disability at 6 years of follow-up was examined in logistic regression models as shown in Table 2. At baseline, after adjusting for age and gender, participants with higher total plasma carotenoids were less likely to have prevalent walking disability (model 1), and this association was still statistically significant after adjusting for age, gender, education, BMI, current smoking, level of physical activity and total energy intake (model 2) (O.R. 0.59, 95% CI 0.38–0.90, $p = 0.01$). We did not include congestive heart failure, peripheral artery disease, and diabetes mellitus in the final model (model 2) because these variables are considered to be in the causal pathway between poor dietary intake of carotenoids, inflammation, and physical performance. However, when these diseases were included in the final model, in addition to the variables in model 2, higher total plasma carotenoids were still associated with a lower prevalence rates of severe walking disability (OR 0.56, 95% CI 0.32–0.99, $p = 0.04$).

As shown in Table 2, higher total plasma carotenoids were significantly associated with lower incidence rates of severe walking disability at the 6-year follow-up visit after adjusting for age and gender (model 1), and after adjusting by age, gender, education, BMI, current smoking, level of physical activity, and total energy intake (model 2) (OR 0.51, 95% CI 0.30–0.86, $p = 0.01$). Again, when congestive heart failure, peripheral artery disease, and diabetes mellitus were included in the model as covariates, in addition to the covari-

Table 1. Characteristics of the Study Population at Enrollment

Characteristic[a]	*All participants (n = 928)*	*Participants free of severe walking disability at baseline who were reevaluated at the 6-year follow-up (n = 621)*
Incident Severe Walking Disability	—	68 (11%)
Age (years)	75.6 (7.4)	73.1 (5.8)
Gender (% female)	55.7	56.7
Education (years)	5.3 (3.3)	5.8 (3.43)
Current smokers (%)	27.3	26.6
Body mass index (kg/m^2)	27.4 (4.1)	27.5 (4.0)
Total plasma carotenoids (μmol/L)	1.08 (0.69)	1.86 (0.67)
Total energy intake (kcal/day)	1912 (559)	1968 (566)
4-meter walking speed (m/sec)	0.97 (0.29)	1.04 (0.23)
400-meter walking speed (m/sec)	1.21 (0.24)	1.25 (0.23)
Severe walking disability (%)	8.4	0
Coronary heart disease (%)	5.9	5.2
Congestive heart failure (%)	5.9	2.3
Peripheral artery disease (%)	6.3	3.5
Diabetes mellitus (%)	10.9	10.0
Chronic obstructive pulmonary disease (%)	8.4	6.0
Physical activity		
Sedentary n (%)	148 (16.0)	80 (13.0)
Light n (%)	727 (78.4)	504 (80.9)
Moderate/high n (%)	53 (5.6)	37 (6.1)

[a]Mean (standard deviation) for continuous variables or percentages as noted.

TABLE 2. RELATIONSHIP BETWEEN TOTAL CAROTENOIDS AND OTHER RISK FACTORS WITH PREVALENT SEVERE WALKING DISABILITY AT ENROLLMENT AND INCIDENT SEVERE WALKING DISABILITY AT SIX YEARS OF FOLLOW-UP

	Baseline prevalent severe Walking disability (85/928)			*6-Year incident Severe walking disability (68/621)*		
Characteristic	*OR*	*95% CI*	p	*OR*	*95% CI*	p
Model 1						
Total plasma carotenoids (μmol/L)	0.41	0.27–0.63	< 0.0001	0.45	0.28–0.75	0.0018
Age (years)	1.17	1.13–1.21	< 0.0001	1.22	1.16–1.28	< 0.0001
Gender (female)	1.22	0.73–2.05	0.44	2.24	1.19–4.20	0.01
Model 2						
Total plasma carotenoids (μmol/L)	0.59	0.38–0.90	0.01	0.51	0.30–0.86	0.01
Age (years)	1.09	1.05–1.14	< 0.0001	1.18	1.13–1.25	< 0.0001
Gender (female)	0.77	0.37–1.61	0.49	1.20	0.54–2.69	0.65
Education (years)	0.90	0.79–1.01	0.07	0.93	0.83–1.04	0.18
Body mass index (kg/m^2)	0.84	0.42–1.65	0.61	1.42	0.63–3.25	0.40
Current smoking	1.26	0.74–2.12	0.39	0.71	0.41–1.22	0.21
Total energy intake (kcal/day)	1.00	0.99–1.00	0.15	1.00	0.99–1.00	0.68
Physical activity (3 levels)	0.10	0.06–0.19	< 0.0001	0.27	0.14–0.53	0.0001

OR, odds ratio; CI, confidence interval.

ates already in model 2, higher total plasma carotenoids were still associated with a significantly lower risk of developing incident severe walking disability (OR 0.44, 95% CI 0.27–0.74, $p = 0.002$).

Univariate and multivariate linear regression models were used to examine the relationship between total plasma carotenoids and walking speed on a 4-meter and 400-meter course (Table 3). At enrollment, higher total plasma carotenoids were associated with faster walking speed on a 4-meter course after adjusting for age and gender (model 1), and after adjusting for age, gender, education, BMI, current smoking, and total energy intake (model 2) ($\beta = 0.024$, SE = 0.011, $p = 0.03$). Similarly, higher total plasma carotenoids were associated with faster walking speed on a 400-meter course after adjusting for age and gender (model 1), and also after adjusting for age, gender, education, BMI, current smoking, and total energy intake (model 2) ($\beta = 0.019$, SE = 0.010, $p = 0.04$).

Univariate and multivariate linear regression models were used to examine the relationship between total plasma carotenoids and a decline in walking speed at the 4-meter walking speed at enrollment and at the 6-year follow-up visit and the inability/ability to successfully complete the 400-meter walking test (Table 4). Higher total plasma carotenoids were associated with significantly faster 4-meter walking speed at follow-up after adjusting for age, gender, and walking speed at enrollment (model 1), and after adjusting for age, gender, 4-meter walking speed at enrollment, education, BMI, current smoking, and total energy intake (model 2) ($\beta = 0.026$, SE = 0.012, $p = 0.03$). Higher total plasma carotenoids were significantly associated with lower incidence rates of being unable to successfully complete the 400-meter walking test

TABLE 3. RELATIONSHIP BETWEEN TOTAL CAROTENOIDS AND OTHER RISK FACTORS WITH WALKING SPEED AT ENROLLMENT

	400 meters distance (m/sec) (n = 928)			*4 meters distance (m/sec) (n = 928)*		
Characteristic	β	*SE*	p	β	*SE*	p
Model 1						
Total plasma carotenoids (μmol/L)	0.042	0.012	0.005	0.039	0.011	0.001
Age (years)	−0.021	0.001	< 0.0001	−0.021	0.001	< 0.0001
Gender (female)	−0.138	0.016	< 0.0001	−0.157	0.014	< 0.0001
Model 2						
Total plasma carotenoids (μmol/L)	0.024	0.011	0.03	0.019	0.010	0.041
Age (years)	−0.016	0.001	< 0.0001	−0.019	0.001	< 0.0001
Gender (female)	−0.081	0.018	< 0.0001	−0.124	0.016	< 0.0001
Education (years)	0.013	0.002	< 0.0001	0.011	0.002	< 0.0001
Body mass index (kg/m^2)	0.039	0.020	0.047	0.011	0.018	0.53
Current smoking	0.001	0.011	0.89	−0.024	0.010	0.01
Total energy intake (kcal/day)	3×10^{-5}	1×10^{-5}	0.022	3×10^{-5}	1×10^{-5}	0.019
Physical activity (3 levels)	0.146	0.02	< 0.0001	0.096	0.016	< 0.0001

TABLE 4. RELATIONSHIP BETWEEN CAROTENOIDS AND OTHER RISK FACTORS WITH DECLINE OF WALKING SPEED BETWEEN ENROLLMENT AND SIX-YEAR FOLLOW-UP VISIT FOR WALKING AT FOUR AND INABILITY/ABILITY TO PERFORM FOUR HUNDRED METERS DISTANCE

	Inability/ability to perform					
	4 meters distance (m/sec) (579 of 621)[a]			*400 meters distance (202 vs 419)*[b]		
Characteristic	β	*SE*	p	β	*SE*	p
Model 1						
Total plasma carotenoids (μmol/L)	0.037	0.012	0.002	−0.057	0.03	0.03
Age (years)	−0.019	0.002	< 0.0001	0.016	0.004	< 0.0001
Gender (female)	−0.071	0.017	< 0.0001	0.003	0.037	0.93
Walking speed at enrollment (m/sec)	−0.431	0.040	< 0.0001	−0.062	0.094	< 0.0001
Model 2						
Total plasma carotenoids (μmol/L)	0.026	0.012	0.03	−0.054	0.026	0.04
Age (years)	−0.019	0.002	< 0.0001	0.016	0.004	< 0.0001
Gender (female)	−0.093	0.020	< 0.0001	−0.011	0.044	0.79
Walking speed at enrollment (m/sec)[c]	−0.117	0.010	< 0.0001	−0.580	0.099	< 0.0001
Education (years)	0.007	0.002	0.005	−0.002	0.005	0.75
Body mass index (kg/m^2)	0.0001	0.002	0.03	0.035	0.047	0.46
Current smoking	−0.027	0.002	0.97	0.001	0.03	0.96
Total energy intake (kcal/day)	-1×10^{-5}	1×10^{-5}	0.33	1×10^{-5}	1×10^{-5}	0.67
Physical activity (3 levels)	0.042	0.02	0.04	0.078	0.043	0.07

[a]Analyses included only the participants who had timed walking speed available for the distances of 4 meter at both enrollment and 6-year follow-up.
[b]Participants were classified as unable to complete the 400-meter walking test if was attended less than 20 laps or were unable to complete a 4 meter distance walk and able to successfully complete the 400-meter walking test.
[c]Analysis were performed using 4-meter walking speed and 400-meter walking speed, respectively.

at the 6-year follow-up visit after adjusting for age, gender, and 400-meter walking test enrollment (model 1), and after adjusting for age, gender, 400-meter walking speed at enrollment, education, BMI, current smoking, and total energy intake (model 2) ($\beta = -0.054$, SE $= 0.03$, $P = 0.04$).

Discussion

This study shows that a significant association exists between carotenoids and walking ability in older community-dwelling men and women. Our findings are consistent with previous cross-sectional studies showing that lower carotenoid intake and serum levels of carotenoids are associated with low skeletal muscle strength and impaired physical performance.[4,5] As noted previously, serum carotenoids reflect fruit and vegetable intake.[6] Recent data from the Atherosclerosis Risk in Communities study also shows that fruit and vegetable intake is inversely correlated with functional limitations and disability.[28]

Sarcopenia, defined as loss of muscle mass and muscle strength, plays a central role in disability and contributes to mobility disability, difficulty with activities of daily living, and increased risk of falls and hospitalizations.[29] Oxidative stress has been postulated to be an underlying biologic mechanism for sarcopenia.[30] With aging, increased oxidative damage to DNA, protein, and lipids has been described in skeletal muscle with associated atrophy and loss of muscle fibers.[31] Whether oxidative stress is the initiating event in the causal pathway leading to sarcopenia is unclear. Serum carotenoids play an important role in reducing oxidative stress through the quenching of hydroxyl radicals and reducing lipid peroxidation.[32] By reducing free radical concentrations, carotenoids may modulate redox balance and activation of nuclear factor κB (NF-κB),[33] a major transcriptional factor involved in the upregulation of interleukin-6 (IL-6).[34] Low serum carotenoids are independent predictors of subsequent increase in serum IL-6 concentration, which, in turn, is associated with an increased risk of reduced physical function and sarcopenia[35,36] and the development of disability.[19,37] Low serum carotenoids were independently predictive of subsequent increases in serum IL-6 among older community-dwelling women.[38] Our results suggest that the biologic pathway for the proposed role of oxidative stress in the pathogenesis of sarcopenia[3,4,39] may begin with a low intake of dietary antioxidants, such as carotenoid-rich fruits and vegetables, with a resulting increase in oxidative stress, activation of NF-κB, and upregulation of IL-6.

Limitation of the study is the loss to follow-up of respondents may have biased the results. Then, other factors not considered in the analyses may explain the study findings. Finally plasma carotenoid measurements at the 6-year follow-up visit were not available. Therefore, whether change over time in carotenoids cause walking disability in older persons should be tested in future studies.

The strengths of this investigation are the representative nature of the study population and the fact that walking speed was tested over both 4- and 400-meter distances. The results showed a strong and consistent relationship between total plasma carotenoids and both prevalent and incident severe walking disability, as well as walking speed tested at the two different distances. Higher total plasma carotenoids were significantly associated with a lower decline in walking speed between enrollment and the 6-year follow-up visit for the 4-meter distance and with lower incidence rates of being unable to successfully complete the 400-meter walking test at the 6-year follow-up visit.

The intake of energy and nutrients decreases with older age.[40] The prevention of undernutrition may potentially reduce the risk of disability, however, such a hypothesis would need to be tested through controlled trials. Given that the carotenoids are biologic markers for fruit and vegetable intake[6] and that fruits and vegetables contain a complex mix of antioxidants, fiber, and vitamins, dietary modification may be an effective strategy to limit, at least in part, the decline of health and physical function that is often observed in aging persons. Such an approach has been taken with the Dietary Approaches to Stop Hypertension Studies[41], and recently a short-term randomized trial showed that a Mediterranean-style diet reduces cardiovascular risk factors.[42] In addition, recent data suggest that a Mediterranean-style diet that is high in fruits and vegetables may have a protective effect against cardiovascular disease.[43] Further studies are needed to verify whether nutritional interventions that increase intake of fruits and vegetables may prevent the decline in physical performance and slow down the progression to disability among older adults.

Acknowledgments

This work was supported by National Institute on Aging Contracts N01-AG-916413, N01-AG-821336, N01-AG-5-0002, and NIA Grant R01 AG027012. This research was supported in part by the Intramural Research Program, National Institute on Aging, National Institutes of Health.

References

1. Woo J, Ho SC, Yu AL. Walking speed and stride length predicts 36 months dependency, mortality, and institutionalization in Chinese aged 70 and older. J Am Geriatr Soc 1999;47:1257–1260.
2. Rolland Y, Lauwers-Cances V, Cesari M, Vellas B, Pahor M, Grandjean H. Physical performance measures as predictors of mortality in a cohort of community-dwelling older French women. Eur J Epidemiol 2006;21:113–122.
3. Newman AB, Simonsick EM, Naydeck BL, Boudreau RM, Kritchevsky SB, Nevitt MC, Pahor M, Satterfield S, Brach JS, Studenski SA, Harris TB. Association of long-distance corridor walk performance with mortality, cardiovascular disease, mobility limitation, and disability. JAMA 2006;295:2018–2026.
4. Semba RD, Blaum C, Guralnik JM, Totin D, Ricks MO, Fried LP. Low carotenoid and vitamin E status are associated with indicators of sarcopenia among older women living in the community. Aging Clin Exp Res 2003;15:482–487.
5. Cesari M, Pahor M, Bartali B, Cherubini A, Penninx BW, Williams GR, Atkinson H, Martin A, Guralnik JM, Ferrucci L. Antioxidants and physical performance in elderly persons: the Invecchiare in Chianti (InCHIANTI) study. Am J Clin Nutr 2004;79:289–294.
6. Lauretani F, Semba RD, Bandinelli S, et al. Low plasma carotenoids and skeletal muscle strength decline over six years. J Gerontol A Biol Sci Med Sci 63:376–383.
7. Food and Nutrition Board, Institute of Medicine. Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids. Washington, D.C.: National Academy Press, 2000.
8. Liu S, Manson JE, Lee IM, Cole SR, Hennekens CH, Willett WC, Buring JE. Fruit and vegetable intake and risk of cardiovascular disease: the Women's Health Study. Am J Clin Nutr 2000;72:922–928.
9. Bazzano LA, He J, Ogden LG, Cole SR, Hennekens CH, Willett WC, Buring JE. Fruit and vegetable intake and risk of cardiovascular disease in US adults: the first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. Am J Clin Nutr 2002;76:93–99.
10. Steffen LM, Jacobs DR Jr, Stevens J, Shahar E, Carithers T, Folsom AR. Associations of whole-grain, refined-grain, and fruit and vegetable consumption with risks of all-cause mortality and incident coronary artery disease and ischemic stroke: the Atherosclerosis Risk in Communities (ARIC) Study. Am J Clin Nutr 2003;78:383–390.
11. Lopez-Garcia E, Schulze MB, Fung TT, Fung TT, Meigs JB, Rifai N, Manson JE, Hu FB: Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. Am J Clin Nutr 2004;80:1029–1035.
12. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med 2003;348:2599–2608.
13. Chrysohoou C, Panagiotakos DB, Pitsavos C, Das UN, Stefanadis C. Adherence to the Mediterranean diet attenuates inflammation and coagulation process in healthy adults: the Atttica Study. J Am Coll Cardiol 2004;44:152–158.
14. Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, D'Armiento M, D'Andrea F, Giugliano D. Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. JAMA 2004;292:1440–1446.
15. Fung TT, McCullough ML, Newby PK, Manson JE, Meigs JB, Rifai N, Willett WC, Hu FB. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. Am J Clin Nutr 2005; 82: 163-173.
16. Ferrucci L, Bandinelli S, Benvenuti E, Di Iorio A, Macchi C, Harris TB, Guralnik JM. Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. J Am Geriatr Soc 2000;48:1618–1625.
17. Schrager MA, Metter EJ, Simonsick E, Ble A, Bandinelli S, Lauretani F, Ferrucci L.Sarcopenic obesity and inflammation in the InCHIANTI study. J Appl Physiol 2007;102:919–925.
18. Pisani P, Faggiano F, Krogh V, Palli D, Vineis P, Berrino F. Relative validity and reproducibility of a food frequency dietary questionnaire for use in the Italian EPIC centres. Int J Epidemiol 1997;26(Suppl 1):S152–S160.
19. Guralnik JM, Fried LP, Simonsick EM, Kasper D, Lafferty ME. The Women's Health and Aging Study: Health and Social Characteristics of Older Women with Disability. Bethesda, MD: National Institute on Aging. NIH Publication No. 95-4009, 1995
20. Bandinelli S, Pozzi M, Lauretani F, Phillips C, Shumway-Cook A, Guralnik JM, Ferrucci L. Adding challenge to performance-based tests of walking: The Walking InCHIANTI Toolkit (WIT). Am J Phys Med Rehabil 2006;85:986–991.
21. Rolland YM, Cesari M, Miller ME, Penninx BW, Atkinson HH, Pahor M. Reliability of the 400-m usual-pace walk test as an assessment of mobility limitation in older adults. J Am Geriatr Soc 2004;52:972–976.
22. Marsh AP, Miller ME, Saikin AM, Rejeski WJ, Hu N, Lauretani F, Bandinelli S, Guralnik JM, Ferrucci L. Lower extremity strength and power are associated with 400-meter

walk time in older adults: the InCHIANTI study. J Gerontol A Biol Sci Med Sci 2006;61:1186–1193.
23. Ferrucci L, Harris TB, Guralnik JM, Tracy RP, Corti MC, Cohen HJ, Penninx B, Pahor M, Wallace R, Havlik RJ. Serum IL-6 level and the development of disability in older persons. J Am Geriatr Soc 1999;47:639–646.
24. Rantanen T, Guralnik JM, Ferrucci L, Penninx BW, Leveille S, Sipilä S, Fried LP. Coimpairments as predictors of severe walking disability in older women. J Am Geriatr Soc 2001;49:21–27.
25. Tinetti ME, Inouye SK, Gill TM, Doucette JT. Shared risk factors for falls, incontinence, and functional dependence. JAMA 1995;273:1348–1353.
26. van Lettow M, Harries AD, Kumwenda JJ, Zijlstra EE, Clark TD, Taha TE, Semba RD. Micronutrient malnutrition and wasting in adults with pulmonary tuberculosis with and without HIV co-infection in Malawi. BMC Infect Dis 2004; 4:61.
27. Ainsworth, BE, Haskell, WL, Leon, AS, Jacobs DR Jr, Montoye HJ, Sallis JF, Paffenbarger RS Jr.Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc 1993;25:71–80.
28. Houston DK, Stevens J, Cai J, Haines PS. Dairy, fruit and vegetables intakes and functional limitations and disability in a biracial cohort: the Atherosclerosis Risk in Communities Study. Am J Clin Nutr 2005;81:515–522.
29. Morley JE, Baumgartner RN, Roubenoff R, Mayer J, Nair KS. Sarcopenia. J Lab Clin Med 2001; 137: 231–243.
30. Gianni P, Jan KJ, Douglas MJ, Stuart PM, Tarnopolsky MA. Oxidative stress and the mitochondrial theory of aging in human skeletal muscle. Exp Gerontol 2004;39:1391–1400.
31. Mecocci P, Fanó G, Fulle S, MacGarvey U, Shinobu L, Polidori MC, Cherubini A, Vecchiet J, Senin U, Beal MF. Age-dependent increases in oxidative damage to DNA, lipids, and proteins in human skeletal muscle. Free Radic Biol Med 1999;26:303–308.
32. Mayne ST. Antioxidant nutrients and chronic disease: use of biomarkers of exposure and oxidative stress status in epidemiologic research. J Nutr 2003;133:933S–940S.
33. Kabe Y, Ando K, Hirao S, Yoshida M, Handa H. Redox regulation of NF-κB activation: distinct redox regulation between the cytoplasm and the nucleus. Antioxid Redox Signal 2005;7:395–403.
34. Ershler WB, Keller ET. Age-associated increased interleukin-6 gene expression, late-life diseases, and frailty. Annu Rev Med 2000;51:245–270.
35. Ferrucci L, Penninx BW, Volpato S, Harris TB, Bandeen-Roche K, Balfour J, Leveille SG, Fried LP, Md JM. Change in muscle strength explains accelerated decline of physical function in older women with high interleukin-6 serum levels. J Am Geriatr Soc 2002;50:1947–1954
36. Payette H, Roubenoff R, Jacques PF, Dinarello CA, Wilson PW, Abad LW, Harris T. Insulin-like growth factor-1 and interleukin 6 predict sarcopenia in very old community-living men and women: the Framingham Heart Study. J Am Geriatr Soc 2003;51:1237–1243.
37. Cappola AR, Xue QL, Ferrucci L, Guralnik JM, Volpato S, Fried LP. Insulin-like growth factor 1 and interleukin-6 contribute synergistically to disability and mortality in older women. J Clin Endocrinol Metab 2003;88:2019–2025.
38. Walston J, Xue Q, Semba RD, Ferrucci L, Cappola AR, Ricks M, Guralnik J, Fried LP. Antioxidants, inflammation, and mortality among women living in the community. Am J Epidemiol 2006;163:18–26.
39. Weindruch R. Interventions based on the possibility that oxidative stress contributes to sarcopenia. J Gerontol A Biol Sci Med Sci 1995;50:157–161.
40. Bartali B, Salvini S, Turrini A, Ferrucci L, Cappola AR, Ricks M, Guralnik J, Fried LP. Age and disability affect dietary intake. J Nutr 2003;133:2868–2873.
41. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, Bray GA, Vogt TM, Cutler JA, Windhauser MM, Lin PH, Karanja N. A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med 1997;336:1117–1124.
42. Estruch R, Martinez-Gonzalez MA, Corella D, Salas-Salvadó J, Ruiz-Gutiérrez V, Covas MI, Fiol M, Gómez-Gracia E, López-Sabater MC, Vinyoles E, Arós F, Conde M, Lahoz C, Lapetra J, Sáez G, Ros E; PREDIMED Study Investigators. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. Ann Intern Med 2006;145:1–11.
43. Serra-Majem L, Roman B, Estruch R. Scientific evidence of interventions using the Mediterranean diet: a systematic review. Nutr Rev 2006;64:S27–S47.

Address reprint requests to:
Luigi Ferrucci, M.D., Ph.D.
National Institute on Aging
Longitudinal Studies Section
Clinical Research Branch
ASTRA Unit
Harbor Hospital 5th Floor
3001 South Hanover Street
Baltimore, MD 21225

E-mail: ferruccilu@grc.nia.nih.gov

Received: May 29, 2007
Accepted: December 6, 2007