Published in final edited form as:
Am J Med. 2007 December ; 120(12): 1084–1089.

Oxidative stress and severe walking disability among older women

Richard D. Semba[a], **Luigi Ferrucci**[b], **Kai Sun**[a], **Jeremy Walston**[a], **Ravi Varadhan**[a], **Jack M. Guralnik**[c], and **Linda P. Fried**[a]

a*Johns Hopkins University School of Medicine, Baltimore, MD*

b*Longitudinal Studies Section, Clinical Research Branch, National Institute on Aging, Baltimore, MD*

c*Laboratory of Epidemiology, Demography, and Biometry, National Institute on Aging, Bethesda, MD*

Abstract

Background—Oxidative stress has been implicated in sarcopenia and the loss of muscle strength with aging, but the relationship between oxidative stress and decline in muscle strength and physical performance has not been well characterized. Serum protein carbonyls are markers of oxidative damage to proteins and are caused by oxidative stress.

Methods—Serum protein carbonyls were measured at baseline and compared with a decline in walking speed and development of severe walking disability (inability to walk or walking speed <0.4 m/sec) over 36 months of follow-up in 545 moderately-severely disabled women, ≥65 years, living in the community in Baltimore, Maryland (the Women's Health and Aging Study I).

Results—After adjusting for age, body mass index, smoking, and chronic diseases, $\log_e$ protein carbonyls (nmol/mg) were associated with a decline in walking speed over 36 months ($P = 0.002$). During follow-up, 154 women (28.2%) developed severe walking disability. After adjusting for the same potential confounders, $\log_e$ protein carbonyls were associated with incident severe walking disability (Hazards Ratio 1.42, 95% C.I. 1.02 – 1.98, $P = 0.037$).

Conclusion—High oxidative stress, as indicated by oxidative damage to proteins, is an independent predictor of decline in walking speed and progression to severe walking disability among older women living in the community.

Keywords

aging; disability; oxidative stress; protein carbonyls; walking

Sarcopenia, or loss of muscle strength and muscle mass, is an important factor underlying mobility difficulties such as severe walking disability and a decline in walking speed in older adults[1] There is initial evidence that excessive oxidative stress is involved in the pathogenesis of age-related sarcopenia and subsequent decline of strength and mobility.[2,3] Reactive oxygen species are formed as intermediates in reduction-oxidation (redox) mostly within mitochondria. Reactive oxygen species are balanced by antioxidant enzymes such as superoxide dismutase,

Correspondence to: Dr. Richard Semba, 550 N. Broadway, Suite 700, Baltimore, MD 21205., Tel. (410) 955-3572, Fax (410) 955-0629, email: rdsemba@jhmi.edu.

catalase, thioredoxin, and glutathione peroxidase, and exogenous antioxidants such as carotenoids, tocopherols, ascorbate, selenium, flavonoids, and other plant polyphenols.

Oxidative stress refers to the condition in which the balance between oxidants and antioxidant defenses is upset and excess reactive oxygen species cause oxidative damage to nucleic acids, proteins, and lipids.[4] Reactive oxygen species have an extremely short half-life and are difficult to measure in humans, but it is possible to measure the damage that oxidative stress causes to protein, lipids, and DNA. Protein carbonyls are the most studied marker of protein oxidation.[5–7] Protein carbonyls represent several pathways of oxidative protein damage and are useful in epidemiologic studies because they are stable and can be measured in serum or plasma.[7]

The relationship between oxidative damage to proteins and functional status has not been characterized in older adults. We hypothesized that higher oxidative stress, as indicated by serum protein carbonyl levels, was associated with an accelerated decline of walking speed and excessive risk of developing severe walking disability among older adults. To address this hypothesis, we examined the relationship between serum protein carbonyl concentrations and walking speed among older women living in the community.

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.[8] 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.[8]

Standardized questionnaires were administered in the participant's home by trained interviewers. Mini-Mental Status Examination (MMSE) was recorded.[8] 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.[8]

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.[8] Women were categorized as having severe walking disability based upon being unable to walk or having a walking speed <0.4 m/sec.[9] The 0.4 m/sec cut-off point was approximately at the top of the lowest quartile in the WHAS population at baseline[10] and has been shown to predict functional dependence.[11] 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.[8]

There were 1002 women enrolled in the Women's Health and Aging Study I, of whom 753 women participated in the blood drawing and had serum nutrient measurements at baseline. Of the 753 women, 150 had severe walking disability at baseline, 554 of the 753 women did not have severe walking disability at baseline and had at least one follow-up visit, and 49 women did not have severe walking disability at baseline but did not have a follow-up visit (17 dropped out and 32 died). Of the 554 women without severe walking disability at baseline, there were 545 women who had serum available for measurement of serum protein carbonyls. Women who were unable to walk had a greater severity of ADL disability.[8] 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).

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 protein carbonyls were measured using a commercial ELISA (Zentech PC Test, Protein Carbonyl Enzyme Immuno-Assay Kit, Biocell Corp, Papatoetoe, NZ). Protein carbonyls are stable under long term storage at −70° C.[7] The assay has a minimum detectability of 0.02 nmol/mg protein, which is well below that range found in healthy human controls. Intra-assay and interassay CVs for protein carbonyl measurements were 10.1% and 18.2%. Serum IL-6 was measured using a commercial ELISA (Quantikine Human IL-6, R & D Systems, Minneapolis, MN).

Descriptive statistics were used to characterize the study population. Serum protein carbonyls were log-transformed to achieve a normal distribution. Body mass index was categorized as underweight (<18.5 kg/m^2), normal range (18.5–24.9 kg/m^2), overweight (≥25–29.9 kg/m^2) and obese (≥30 kg/m^2) according to World Health Organization criteria.[12] Grouped-time Cox proportional hazards models[13] were used to examine the associations between serum protein carbonyls and the risk of developing severe walking disability because severe walking disability was determined at six-month intervals. Trajectories of walking speed were calculated using generalized estimating equations (GEE).[14] Women who did not have at least one follow-up visit after enrollment because of death, refusal, or loss to follow-up were excluded from the longitudinal analyses. The length of follow-up in longitudinal analyses was 36 months. Women who died, refused further participation, or were lost to follow-up after a follow-up visit were censored according to their severe walking disability status at their last visit in the study. Multiple linear regression models with GEE methods were used to examine the relationship between log protein carbonyls and decline in walking speed. The statistical programs used were SAS (SAS Institute, Cary, NC).

Results

There were 545 women who did not have severe walking disability at baseline, had serum protein carbonyl measurements available, and had at least one follow-up visit. One hundred fifty-four (28.2%) of the women developed severe walking disability during follow-up with an overall rate of severe walking disability of 11.6 per 100 person-years. The characteristics of women who did and did not develop severe walking disability during follow-up are shown in Table 1. Women who developed severe walking disability were older and more likely to be current smokers, have a MMSE score <24, and to be affected by congestive heart failure, peripheral artery disease, and depression. There were no significant differences between women who developed and those who did not develop walking disability by race, education, body mass index, hypertension, coronary artery disease, stroke, osteoarthritis, chronic obstructive pulmonary disease, diabetes, and cancer. Log_e serum protein carbonyls were higher among women who developed compared to those who did not develop severe walking disability ($P = 0.07$).

Grouped-time univariate Cox proportional hazards models were used to examine the relationship between demographic and health characteristics and the development of severe walking disability. Log_e serum protein carbonyls, older age, current smoking, log_e IL-6, MMSE score <24, congestive heart failure, peripheral artery disease, diabetes mellitus, and depression were significantly associated with an increased risk of developing severe walking disability. In a final multivariate grouped-time Cox proportional hazards model that adjusted for the factors that were significant in univariate analyses, log_e serum protein carbonyls were associated with an increased risk of developing severe walking disability (H.R. 1.42, 95% C.I. 1.02–1.98, $P = 0.037$) (Table 2). Serum IL-6 was not included in the model because it is a considered to be in the causal pathway between oxidative stress and severe walking disability. When log_e IL-6 was included in the previous multivariate model, log_e serum protein carbonyls (H.R. 1.39, 95% C.I. 0.99–1.94, $P = 0.053$) and log_e serum IL-6 (H.R. 1.24, 95% C.I. 0.98–1.60, $P = 0.07$) were associated with severe walking disability with a slight reduction in the magnitude of the association. An alternative multivariate model was explored that included hospitalizations, since hospitalizations are known to increase the risk of disability. When hospitalizations were included in the multivariate model with the same variables in the first multivariate model above, log_e serum protein carbonyls were associated with severe walking disability (H.R. 1.41, 95% C.I. 1.02–1.94, $P = 0.039$).

Multiple linear regression was used to examine the relationship between serum protein carbonyls and other factors with a decline in walking speed (Table 3). In a final model adjusting for age, current smoking, MMSE score <24, congestive heart failure, peripheral artery disease, diabetes mellitus, depression, and study visit, log_e serum protein carbonyls were associated with a decline in walking speed (beta = −0.064, SE = 0.02, $P = 0.002$). IL-6 was not included in the final model because it is considered to be in the causal pathway between oxidative protein damage and decline in walking speed. When IL-6 was added to the previous model, log_e protein carbonyls (beta = −0.057, SE = 0.031, $P = 0.006$) and log_e IL-6 (beta = −0.064, SE = 0.016, $P < 0.0001$) were associated with a decline in walking speed. An alternative multiple linear regression model was explored that included hospitalizations in addition to the variables in the first model above. When hospitalizations were included in the multivariate model, log_e protein carbonyls were associated with a decline in walking speed (beta = −0.062, SE = 0.02, $P = 0.002$).

Discussion

This study shows that older community-dwelling women with higher oxidative stress, as indicated by oxidative damage to proteins, are experiencing an accelerated decline in walking

speed and are at higher risk of developing severe walking disability. To our knowledge, this is the first study to examine the relationship between oxidative stress and the development of severe walking disability in a population of older adults living in the community. These findings are consistent with the idea that the aging-related decline in muscle strength may be attributed in part to oxidative stress. Increased oxidative damage to DNA, protein, and lipids has been described in skeletal muscle with atrophy and loss of muscle fibers with aging.[2,3,15,16] A limitation of this study is that markers of oxidative damage were not measured directly in skeletal muscle, which would be invasive and difficult to conduct in a large epidemiologic study. However, serum protein carbonyls are a general measure of oxidative protein damage and have been shown to correlate with oxidative protein damage in tissues.[7]

Oxidative stress is considered a basic underlying biological mechanism for atherosclerosis, coronary artery disease, peripheral artery disease, stroke, Alzheimer's disease, and other common morbid conditions in older adults. Oxidative damage to proteins can lead to the loss of structural integrity of cells, compromise cellular function, and increase susceptibility to proteolysis.[17–20] Oxidative stress can also damage lipids and impair cell structure and function[21] and can damage DNA, resulting in strand breaks, DNA-DNA and DNA-protein crosslinks, and other oxidation and fragmentation products.[22] The present study is limited in that oxidative damage to lipids and DNA were not measured. In addition to damaging biomolecules directly, reactive oxygen species can trigger redox sensitive transcription factors such as NF-kappa B and AP-1 that are involved in the upregulation of inflammatory cytokines such as interleukin-6.[23,24] In the present study, when IL-6 was included in multivariate analyses that examined the relationship between serum protein carbonyls and severe walking disability and decline in walking speed, the magnitude of the relationship of each factor with the outcome was slightly reduced.

A limitation of this study is that the study population included only women, and the findings cannot necessarily be extrapolated to men. In addition, the women represented moderately to severely disabled community-dwelling women, however, this population is the subset that is at highest risk of progression to severe walking disability. Another limitation is that serum protein carbonyls are still an experimental tool rather than a laboratory test that is used or available for clinical use. Since this is an observational study, it is not possible to infer that increased oxidative stress causes functional decline, as increased protein carbonyls could be a marker for individuals at increased risk for other reasons. It is also not possible to control for unmeasured or unknown covariates that might affect the apparent interaction between oxidative damage (as measured by serum protein carbonyls) and decline in walking speed.

There are behavioral and lifestyle changes that are known to reduce oxidative stress, and these include cessation of smoking, as cigarette smoke is a well-documented source of oxidative stress,[7] adopting a healthy Mediterranean-style diet characterized by high intake of fruits, vegetables, whole grains, nuts, and olive oil,[25–28] and increasing regular exercise and physical activity.[29,30] Future studies should include characterization of long-term effects of such behavioral and lifestyle changes upon oxidative stress and mortality, and additional studies need to be conducted that include the full spectrum from non-disabled to disabled people living in the community. Future studies are needed to examine the relationship between oxidative damage to other biomolecules and adverse outcomes in older adults.

Acknowledgements

This work was supported by National Institute on Aging Grant R01 AG027012, NIH-NCRR, OPD-GCRC grant RR00722, and NIA Contract N01-AG12112. This research was supported in part by the Johns Hopkins Older Americans' Independence Center and the Intramural Research Program, National Institute on Aging, NIH.

References

1. Lauretani F, Russo CR, Bandinelli S, et al. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. J Appl Physiol 2003;95:1851–1860. [PubMed: 14555665]
2. Mecocci P, Fanó G, Fulle S, et al. Age-dependent increases in oxidative damage to DNA, lipids, and proteins in human skeletal muscle. Free Radic Biol Med 1999;26:303–308. [PubMed: 9895220]
3. Pansarasa O, Bertorelli L, Vecchiet J, et al. Age-dependent changes of antioxidant activities and markers of free radical damage in human skeletal muscle. Free Radic Biol Med 1999;27:617–622. [PubMed: 10490283]
4. Sies, H. Oxidative stress. Introductory remarks. In: Sies, H., editor. Oxidative Stress. London: Academic Press; 1985. p. 1-8.
5. Chevion M, Berenshtein E, Stadtman ER. Human studies related to protein oxidation: protein carbonyl content as a marker of damage. Free Radic Res 2000;33:S99–S108. [PubMed: 11191280]
6. Beal MF. Oxidatively modified proteins in aging and disease. Free Radic Biol Med 2002;32:797–803. [PubMed: 11978481]
7. Dalle-Donne I, Rossi R, Giustarini D, et al. Protein carbonyl groups as biomarkers of oxidative stress. Clin Chim Acta 2003;329:23–38. [PubMed: 12589963]
8. Guralnik, JM.; Fried, LP.; Simonsick, EM., et al. The Women's Health and Aging Study: Health and Social Characteristics of Older Women with Disability. Bethesda, MD: National Institute on Aging; 1995. NIH Publication No. 95-4009
9. Ferrucci L, Harris TB, Guralnik JM, et al. Serum IL-6 level and the development of disability in older persons. J Am Geriatr Soc 1999;47:639–646. [PubMed: 10366160]
10. Rantanen T, Guralnik JM, Ferrucci L, et al. Coimpairments as predictors of severe walking disability in older women. J Am Geriatr Soc 2001;49:21–27. [PubMed: 11207838]
11. Tinetti ME, Inouye SK, Gill TM, Doucette JT. Shared risk factors for falls, incontinence, and functional dependence. JAMA 1995;273:1348–1353. [PubMed: 7715059]
12. James PT, Leach R, Kalamara E, Shayeghi M. The worldwide obesity epidemic. Obes Res 2001;9:228S–233S. [PubMed: 11707546]
13. Prentice RL, Gloeckler LA. Regression analysis of grouped survival data with application to breast cancer data. Biometrics 1978;34:57–67. [PubMed: 630037]
14. Diggle, PJ.; Liang, KY.; Zeger, SL. Analysis of Longitudinal Data. Oxford, Clarendon Press; 1994.
15. Gianni P, Jan KJ, Douglas MJ, et al. Oxidative stress and the mitochondrial theory of aging in human skeletal muscle. Exp Gerontol 2004;39:1391–1400. [PubMed: 15489062]
16. Bua EA, McKiernan SH, Wanagat J, et al. Mitochondrial abnormalities are more frequent in muscles undergoing sarcopenia. J Appl Physiol 2002;92:2617–2624. [PubMed: 12015381]
17. Stadtman ER. Protein oxidation and aging. Free Radic Res 2006;40:1250–1258. [PubMed: 17090414]
18. Davies KJA, Lin SW, Pacifici RE. Protein damage and degradation by oxygen radicals. IV. Degradation of denatured protein. J Biol Chem 1987;262:9914–9920. [PubMed: 3036878]
19. Agarawal S, Sohal RS. Differential oxidative damage to mitochondrial proteins during aging. Mech Ageing Dis 1995;85:59–63.
20. Grune T, Shringarpure R, Sitte N, Davies K. Age-related changes in protein oxidation and proteolysis in mammalian cells. J Gerontol Biol Sci 2001;56A:B459–B467.
21. Stark G. Functional consequences of oxidative membrane damage. J Membr Biol 2005;205:1–16. [PubMed: 16245038]
22. Evans MD, Cooke MS. Factors contributing to the outcome of oxidative damage to nucleic acids. BioEssays 2004;26:533–542. [PubMed: 15112233]
23. Kabe Y, Ando K, Hirao S, et al. Redox regulation of NF-κB activation: distinct redox regulation between the cytoplasm and the nucleus. Antioxid Redox Signal 2005;7:395–403. [PubMed: 15706086]
24. Karin M, Takahashi T, Kapahi P, et al. Oxidative stress and gene expression: the AP-1 and NF-κB connections. Biofactors 2001;15:87–89. [PubMed: 12016332]

25. Lopes HF, Martin KL, Nashar K, et al. DASH diet lowers blood pressure and lipid-induced oxidative stress in obesity. Hypertension 2003;41:422–430. [PubMed: 12623938]

26. Sanchez-Moreno C, Cano MP, de Ancos B, et al. Consumption of high-pressurized vegetable soup increases plasma vitamin C and decreases oxidative stress and inflammatory biomarkers in healthy humans. J Nutr 2004;134:3021–3025. [PubMed: 15514269]

27. Rao LG, Mackinnon ES, Josse RG, et al. Lycopene consumption decreases oxidative stress and bone resorption markers in postmenopausal women. Osteoporos Int 2007;18:109–115. [PubMed: 16941193]

28. Machowetz A, Poulsen HE, Gruendel S, et al. Effect of olive oils on biomarkers of oxidative DNA stress in Northern and Southern Europeans. FASEB J 2007;21:45–52. [PubMed: 17110467]

29. Lazarevic G, Antic S, Cvetkovic T, et al. A physical activity programme and its effects on insulin resistance and oxidative defense in obese male patients with type 2 diabetes mellitus. Diabetes Metab 2006;32:583–590. [PubMed: 17296511]

30. Rector RS, Warner SO, Liu Y, et al. Exercise and diet induced weight loss improves measures of oxidative stress and insulin sensitivity in adults with characteristics of the metabolic syndrome. Am J Physiol Endocrinol Metab. 2007 May 1;[Epub ahead of print]

Table 1

Characteristics of Women Who Developed and Did Not Develop Severe Walking Disability in the Women's Health and Aging Study I

Characteristic	Incident Severe Walking Disability (n = 154)	No Incident Severe Walking Disability (n = 391)	*P*
Age category (%)			<0.0001
≤69 years	13.3	23.0	
70–74.9	21.2	27.5	
75–79.9	16.8	20.5	
80–84.9	15.3	11.7	
85–89.9	24.6	14.4	
≥90	8.9	2.9	
Race (white) (%)	71.9	74.5	0.47
Education <12 years (%)	64.0	62.0	0.61
Current smoking (%)	16.3	10.7	0.04
Body mass index (%)			
<18.5 kg/m^2	4.2	2.5	0.76
18.5–24.9	26.6	25.5	
25.0–29.9	33.3	36.8	
≥30	35.9	35.2	
MMSE score <24 (%)	17.2	10.7	0.017
Chronic diseases			
Hypertension (%)	56.7	57.1	0.92
Coronary heart disease (%)	22.2	24.0	0.6
Congestive heart failure (%)	11.8	6.6	0.021
Peripheral artery disease (%)	25.1	17.9	0.029
Stroke (%)	3.4	4.7	0.45
Osteoarthritis (%)	48.8	52.2	0.42
Chronic obstructive pulmonary disease (%)	28.6	28.3	0.95
Diabetes mellitus (%)	17.7	12.5	0.07
Depression (%)	18.2	11.5	0.018
Cancer (%)	9.9	13.6	0.18
Log_e serum protein carbonyls (nmol/mg)	−2.41 (0.037)	−2.50 (0.025)	0.07
Log_e serum IL-6 (pg/mL)	0.96 (0.052)	0.83 (0.033)	0.046

Table 2

Grouped-time Multivariate Cox Proportional Hazard Models for Demographic and Health Characteristics and Incidence of Severe Walking Disability in the Women's Health and Aging Study I (*N* = 545)

Characteristic	Multivariate H.R.	95% C.I.	*P*
Log_e serum protein carbonyls (nmol/mg)	1.42	1.02–1.98	0.037
Age (year)			
≤69 years	1.00	---	---
70–74.9	1.47	0.86–2.53	0.16
75–79.9	1.33	0.74–2.39	0.33
80–84.9	2.87	1.56–5.28	0.0007
85–89.9	3.08	1.74–5.48	0.0001
≥90	5.96	2.69–13.18	<0.0001
Current smoking	1.63	1.01–2.65	0.045
Body mass index[1]			
<18.5	1.31	0.55–3.11	0.54
18.5–24.9	1.00	---	---
25.0–29.9	0.89	0.59–1.35	0.59
≥30	1.24	0.81–1.90	0.32
MMSE <24	1.17	0.74–1.83	0.50
Congestive heart failure	1.78	1.07–2.88	0.026
Peripheral artery disease	1.09	0.74–1.62	0.65
Diabetes mellitus	1.69	1.10–2.59	0.015
Depression	1.42	0.93–2.17	0.11

[1] For body mass index, 18.5–24.9 kg/m^2 was used as the reference category.

Table 3

Multivariate Linear Regression Model for Decline in Walking Speed in the Women's Health and Aging Study I (*N* = 545)

Characteristic	Beta	S.E.	*P*
Log_e serum protein carbonyls (nmol/mg)	−0.064	0.02	0.002
Age (years)			
≤69	---	---	---
70–74.9	−0.134	0.031	<0.0001
75–79.9	−0.121	0.031	0.0001
80–84.9	−0.276	0.036	<0.0001
85–89.9	−0.377	0.032	<0.0001
≥90	−0.464	0.042	<0.0001
Study Visit			
Second	0.005	0.011	0.64
Third	−0.028	0.011	0.013
Fourth	−0.051	0.012	<0.0001
Fifth	−0.058	0.013	<0.0001
Sixth	−0.070	0.014	<0.0001
Seventh	−0.107	0.015	<0.0001
Current smoking	−0.044	0.032	0.16
Body mass index[1]			
<18.5	−0.009	0.064	0.89
18.5–24.9	---	---	---
25.0–29.9	0.011	0.026	0.67
≥30	−0.087	0.026	0.001
MMSE <24	−0.138	0.028	<0.0001
Congestive heart failure	−0.079	0.032	0.015
Peripheral artery disease	−0.017	0.025	0.50
Diabetes mellitus	−0.142	0.028	<0.0001
Depression	−0.089	0.027	0.001

[1] For body mass index, 18.5–24.9 kg/m^2 was used as the reference category.