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Serum Albumin in Relation to Change in Muscle Mass, Muscle Strength, and Muscle Power in Older Men

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Abstract

Objectives—Low serum albumin within the normal range has been posited as a risk factor for the age-related loss of muscle mass and strength. The purpose of this study is to investigate serum albumin in relation to change in muscle mass, grip strength, and leg power.

Design—Prospective cohort

Setting—Six U.S. academic medical centers

Participants—Community-dwelling men aged 65 and older participating in The Osteoporotic Fractures in Men (MrOS) Study

Measurements—Serum albumin was measured at baseline in 5534 participants. Baseline serum albumin was examined in relation to change in appendicular skeletal muscle (ASM) mass, grip strength, and leg power after 2 and 4.6 years. The 2-year change in serum albumin was examined with respect to simultaneous change in these outcomes in 1267 participants.

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Author Contributions:

Caryn Snyder, Lynn Marshall, Jodi A. Lapidus, and Lynn Sakai were responsible for the study concept and design. Lynn Marshall and Peggy M. Cawthon assisted with acquisition of data. Caryn Snyder was responsible for the data analysis and draft of the manuscript. Caryn Snyder, Jodi A. Lapidus, Peggy M. Cawthon, Thuy-Tien Dam, Lynn Sakai, and Lynn Marshall were responsible for interpretation of results and critical revision of the manuscript. All authors gave final approval of the submitted manuscript.

Results—Baseline serum albumin <40 g/L was not associated with 2- or 4.6-year change in ASM mass, grip strength, or leg power before or after adjustment for confounders. There was no association between serum albumin change and change in grip strength. A statistically significant trend was observed between serum albumin change and change in ASM mass but there was substantial overlap across confidence intervals. Participants with a marked decrease (> 3 g/L) and mild decrease (1–2 g/L) in serum albumin over 2 years exhibited a modest loss of –8.9 (95% CI: –25.6, 7.8) watts and –6.3 (95% CI: –21.2, 8.5) watts of leg power, respectively (p for trend=0.02), compared to those with no decrease in albumin concentration.

Conclusion—Serum albumin demonstrated modest and inconsistent trends with loss of muscle mass and function. Low serum albumin within the normal range is not a risk factor for this process among elderly men.

Keywords

aging; sarcopenia; body composition; albumin; men

INTRODUCTION

Prospective studies have demonstrated that muscle mass^{1–3} and muscle strength^{4–9} decline with age. Both men and women lose muscle mass and muscle strength but average annual percent loss is substantially greater among men.^{1,2,9} Although there is great concern about the health consequences of these age-related muscle changes,^{10–13} the factors that contribute to such declines are not well documented.

Loss of muscle mass and muscle strength are likely to have multiple causes and numerous physiologic mechanisms have been proposed.^{10–17} One prominent hypothesis is that loss of muscle mass and strength is a consequence of chronic low-grade inflammation common among the elderly.^{10,11} Others have hypothesized that age-related decline in androgens may be a specific determinant of muscle loss among older men.^{16,17} It has been proposed that low serum albumin may be of etiologic importance because albumin functions in several pathways that could contribute to loss of muscle mass and muscle strength, including sex steroid metabolism.

Albumin is an acute phase reactant¹⁸ and a nonspecific protein transport for numerous hormones including aldosterone, thyroid hormones, and androgens.^{18,19} In the absence of disease states that affect albumin production such as cirrhosis, congestive heart failure, and kidney disease, hypoalbuminemia is considered to represent poor nutritional status and chronic inflammation.²⁰ Modest reductions in serum albumin have been observed from subclinical inflammation²¹ and levels of inflammatory cytokines such as tumor necrosis factor (TNF) – α , C-reactive protein, and interleukin (IL)-6 may inhibit synthesis of albumin or contribute to its degradation.^{21–23}

Low serum albumin has been extensively studied in relation to risk of cardiovascular disease,^{24–26} disability,²⁷ and mortality.^{24,25,28} However, comparatively little is known about the relation of hypoalbuminemia to loss of muscle mass and muscle strength. Two cross-sectional studies reported an association between low serum albumin and low muscle strength²⁹ or muscle mass³⁰ in elderly persons. However, this study design prohibits the ability to discern whether low serum albumin precedes declines in muscle mass or muscle strength. Two longitudinal studies have reported a statistically significant association between low baseline measures of serum albumin and subsequent declines in muscle mass³¹ and grip strength.³² However, neither study examined serum albumin in relation to measures of both muscle mass and strength. In addition, the study of albumin and grip strength suggested the possibility that the association was stronger in men than in women.³²

To advance knowledge about the relation of serum albumin and declines in muscle mass, muscle strength, and muscle power in older men, we conducted a prospective investigation among participants in the Osteoporotic Fractures in Men (MrOS) cohort. In addition, the association of serum albumin change with these outcomes was examined in a large sample of the cohort for whom the 2-year change in serum albumin concentration could be ascertained.

METHODS

Study Setting

MrOS is a prospective cohort study of 5995 community-dwelling men aged 65 years or older. Men were recruited from March 2000 through April 2002 at six U.S. academic medical centers in Birmingham, Alabama; Minneapolis, Minnesota; Palo Alto, California; Pittsburgh, Pennsylvania; Portland, Oregon; and San Diego, California. Eligible men were at least 65 years of age, able to walk without the assistance of another person, and had at least one native hip. Gait aids were utilized in 3% of MrOS participants and most (90%) of these men used a cane or quad cane. Details regarding the recruitment strategies and study design are described elsewhere.^{33,34} All surviving participants were invited to return for a planned second study visit (Visit 2) from March 2005 through April 2006. In addition, funding for an ancillary study, the Oral and Skeletal Bone Loss in Older Men (MrOS Dental Study), permitted 1353 participants from two study sites to be recruited for an additional clinic visit from September 2002 to May 2003. At each study visit measures relevant to the present analysis were obtained and included whole and regional body composition by dual energy x-ray absorptiometry (DXA), grip strength, and leg power. Serum was collected at the baseline visit and the ancillary study visits but not at Visit 2. The MrOS study protocols were approved by the Institutional Review Board at each enrollment site. All participants gave written informed consent.

Serum Albumin

Main Analytic Cohort—Participants provided a fasting morning blood-draw at baseline. Serum was prepared immediately after phlebotomy and remained frozen at -70°C until assay. MrOS participants with a sufficient quantity of stored serum were selected for the measurement of albumin (Figure 1). There was no material difference between participants whose serum was and was not selected for study inclusion with regard to age, body composition, muscle strength, or muscle power (data not shown). Assays were performed at the Oregon Veterans Administration Clinical Lab in Portland, Oregon using a Roche COBAS Integra 800 automated analyzer (Roche Diagnostics Corp., Indianapolis, IN). The analyzer was calibrated daily and the inter-assay coefficient of variation (CV%) was 2.0% based on a pooled serum sample included in each batch.

Repeat Albumin Measures—During the ancillary study visit, 1340 participants completed a blood-draw. Serum from the baseline visit was available for 1267 (94.5%) of these men and was used to obtain repeat measures of albumin (Figure 1). Before assay, aliquots of serum from the two time points were paired and then randomly ordered. For this study, albumin was analyzed at the Oregon Health & Science University Clinical Laboratory with a Beckman LX 20 analyzer (Beckman-Coulter Instruments, United Kingdom). The analyzer was calibrated daily and, based on two pooled serum samples included in each run, the inter-assay CV% was 1.6% and the intra-assay CV% was 3.4%.

Body Composition

Body composition was measured with dual energy X-ray absorptiometry (DXA) at each visit. All enrollment sites used DXA scanners of the same model and manufacturer (QDR

4500W, Hologic, Inc.; Waltham, MA), certified densitometry technicians, and quality assurance measures to ensure comparability. Intra-site and inter-clinic coefficients of variation were within acceptable limits.³⁴ Participant positioning at visits subsequent to baseline was matched to the baseline scan to enhance the precision of longitudinal measurements. Appendicular skeletal muscle (ASM) mass was defined as the sum of the nonbone, nonfat lean tissue of the extremities and is highly correlated with skeletal muscle mass ($r=0.82$).³⁵ Change in ASM was computed between baseline and visit 2 for the primary analysis. In addition, change in ASM mass was also computed between baseline and the ancillary visit.

Muscle Strength and Power

Grip strength was measured using a JAMAR handheld dynamometer (Sammons Preston, Bolingbrook, Illinois) and two trials were performed for each hand. The average result from all hand measurements was computed. Leg power was assessed using the Nottingham Power Rig.^{36,37} The maximum result from five trials at each visit was computed. Men who could not perform the grip strength or leg power assessments were classified as “unable” and assigned the value from the first percentile in the 5-year age category to which they belonged.³⁸ A total of 92 and 105 men were unable to complete measurements of grip strength and leg power at Visit 1, respectively. At Visit 2, 81 and 230 men were unable to complete these measures. In addition, machine failure at one of the study sites prevented 294 men from completing leg power assessments at Visit 2. Absolute change in leg power and grip strength from the MrOS baseline visit to Visit 2 for the main prospective analysis and between the MrOS baseline visit and baseline ancillary study visit was used for the serum albumin change analysis. Leg power was only assessed at the Portland site during the ancillary study visit ($n=512$).

Other baseline measures

Self-reported information on demographic factors, medication use, alcohol consumption, smoking status, medical history, and diet was ascertained at baseline. Participants were measured by study staff for height (cm) with a Harpenden stadiometer (calibrated daily) and weight (kg) with balance beam or digital scales (calibrated weekly) while wearing shoes and light indoor clothing. Race/ethnicity was categorized into five mutually exclusive categories: Caucasian, African American, Asian, Hispanic, and Other (multiracial persons). Smoking status was categorized into “current”, “past”, and “never”. Physical activity was quantified using the Physical Activity Scale for the Elderly (PASE)³⁹ and was based on exercise, leisure, household, and occupational activities commonly performed by older adults. Total caloric intake and protein intake was obtained from a modified food frequency questionnaire developed by Block Dietary Data Systems.⁴⁰ Protein intake was calculated as a percentage of total caloric intake and categorized into quintiles. Alcohol consumption was reported as usual number of drinks per day and was categorized into “0 drinks per week”, “1–7 drinks per week”, and “8+ drinks per week”. Medical history was assessed with questions about physician diagnosed myocardial infarction, angina, congestive heart failure, stroke, hypertension, chronic obstructive pulmonary disease, rheumatoid arthritis, osteoarthritis, diabetes, liver disease, renal disease, cancer, and Parkinson’s disease. All prescription medications recorded by the clinics were stored in an electronic medications inventory database (San Francisco Coordinating Center, San Francisco, CA). Each medication was matched to its ingredient(s) based on the Iowa Drug Information Service (IDIS) Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA).⁴¹ Medications considered in this analysis were oral corticosteroids, statins, nonsteroidal anti-inflammatory medications (NSAIDs), Cox II inhibitors, aspirin, selective serotonin reuptake inhibitors (SSRIs), and thyroid hormone.

Statistical Analysis

Main Prospective Analysis—In the main prospective analysis, we quantified the association of baseline serum albumin with muscle change outcomes among 5534 men. For this analysis, serum albumin concentration was categorized into 1-unit increments of <40 g/L, 40 g/L, 41 g/L, 42 g/L, 43 g/L, 44 g/L, and >44 g/L in order to represent the range of albumin levels observed in the cohort. Few men had albumin levels of <38 g/L (n= 91), 38 g/L (n=110), or 39 g/L (n= 259) and, therefore, were combined into one category. Distributions of baseline characteristics in the primary analytic cohort according to serum albumin category were compared using one way analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables. Multivariable general linear models (GLM) were used to estimate mean change and 95% confidence intervals (CI) of the outcome variables (ASM, grip strength or leg power) within baseline albumin category, with the category of 42 g/L serving as the referent. Two-sided p-values were reported from the F-test and a value of less than 0.05 was considered statistically significant.

The initial model for ASM mass change was adjusted for age, study site, and the baseline ASM measure. Initial models for the grip strength and leg power change variables were adjusted for age, study site, the baseline value of the outcome measure, baseline ASM mass, and change in ASM mass. Models were also assessed without the baseline outcome measure to determine if there were material differences in results. Potential confounding factors were then evaluated with a backward selection process using the change in the point estimate. Candidates were those factors associated with both serum albumin and the outcome variable of interest at $p < 0.25$ in the descriptive analyses. Variables that were not associated with the outcome in the multivariate model were removed sequentially based on the magnitude of the p-value ($p > 0.25$). Finally, variables remaining in the model were dropped one at a time if removal resulted in minimal change to the serum albumin least square mean or model R^2 .

In the serum albumin change analysis, the change in serum albumin concentration over an average of two years of follow-up was categorized as “marked decrease” (> 3 g/L change), “mild decrease” (1 to 2 g/L change), “stable” (0 g/L change), and “increase” (>0 g/L change). The models developed for the primary analysis were additionally adjusted for baseline serum albumin and were used to examine the association between serum albumin change categories and simultaneous change in ASM mass, grip strength, and leg power. Multiple linear regression using generalized linear models was performed for each outcome. Stratification by three baseline serum albumin categories (<40 g/L, 40–42 g/L, and > 43 g/L) was conducted to assess possible interaction between baseline serum albumin and change in serum albumin.

Statistical analyses were performed using SAS software version 9.1 (SAS Institute Inc., Cary, NC).

RESULTS

Study Population

Between the baseline visit and Visit 2, 79 (1.4%) participants voluntarily withdrew from the study and 524 (9.5%) participants died. Of the remaining participants, 95 (1.7%) refused participation in Visit 2, 654 (11.8%) completed the Visit 2 self-administered questionnaire but did not attend the clinic visit, and 4182 (84.8%) completed the entire visit. Men who died or voluntarily withdrew (n=603) or who did not participate in Visit 2 (n=749), respectively, were older at baseline than participants who had Visit 2 clinic measures (mean ($\pm$ SD): 77.5 ($\pm$ SD) and 74.8 ($\pm$ 6.0) compared to 72.8 ($\pm$ 5.4); $p < 0.001$) and were more likely to have a serum albumin concentration less than 40 g/L at baseline (15% and 9%

compared to 7%; $p<0.001$). These participants also had lower baseline measures of grip strength (mean ($\pm$ SD): 34 ($\pm$ 8) and 37 ($\pm$ 8) compared to 39 ($\pm$ 8); $p<0.001$) and leg power (mean ($\pm$ SD): 174 ($\pm$ 63) and 193 ($\pm$ 63) compared to 215 ($\pm$ 61); $p<0.001$).

Baseline Serum Albumin

In the main prospective analysis, the mean ($\pm$ SD) serum albumin concentration was 42.7 ($\pm$ 2.4) g/L (range: 25–51 g/L). A total of 91 (1.6%) of the participants had clinically low serum albumin measures at baseline (< 38 g/L). Participants with a serum albumin concentration less than 40 g/L were older (75.4 years and 72.4 years, respectively) and more likely to be African American, nondrinkers, and less physically active than participants in higher serum albumin categories (Table 1). They were also more likely to take an oral corticosteroid and less likely to use a statin medication. In addition, a significant cross-sectional association was observed between baseline serum albumin concentration and measures of grip strength and leg power ($p<0.0001$; Table 1). Among the men with repeat measures of serum albumin, the intraclass correlation coefficient for the albumin measured at baseline and 2 years later was 0.61.

Main Prospective Analysis

Serum albumin concentration at baseline was not associated with measures of change in muscle mass or muscle function (Table 2). The absolute difference in mean ASM mass change between the highest and lowest albumin categories was 0.20 kg before adjustment and no significant association was apparent ($p=0.53$) after multiple adjustment for potential confounding factors. Results were virtually identical when the model did and did not include adjustment for the baseline ASM value. In addition, results remained the same using ASM values scaled for participant height (data not shown). Analysis of grip strength change and leg power change also demonstrates no variation according to baseline albumin concentration. The results remained null when serum albumin was entered in each model as a continuous variable or dichotomized variable with a cut-point of 40 g/L (data not shown).

Serum Albumin Change Analysis

Among the 1267 participants with two serum albumin measures, the baseline concentration was 41.7 ($\pm$ 3.1) g/L and the average change in albumin was -0.79 ($\pm$ 2.77) g/L. Baseline serum albumin concentration examined in this sample in relation to 2-year change in ASM mass, grip strength, and leg power were null and similar to those reported in Table 2 for the primary analytic cohort (data not shown).

The absolute difference in mean ASM mass change between men with a marked decrease in serum albumin compared to men with an increase in serum albumin was 0.12 kg before adjustment (Table 3). Although a statistically significant trend was observed ($p=0.03$), there was substantial overlap in the confidence intervals across categories. Results were similar when modeled with and without the baseline ASM value. Analysis of grip strength change demonstrated little variation according to albumin change category. A positive trend ($p=0.01$) was observed between serum albumin change categories and simultaneous change in leg power over an average of two years of follow-up in men at the Portland site. Participants with a marked decrease (> 3 g/L) and mild decrease (1–2 g/L) in serum albumin concentration exhibited an average loss of -8.9 (95% CI: $-25.6, 7.8$) watts and -6.3 (95% CI: $-21.2, 8.5$) watts of leg power, respectively (Table 3). An absolute loss of this magnitude corresponds to a percent change in leg power of -4.5% (95% CI: $-12.4\%, 3.5\%$) and -2.9% ($-10.0\%, 4.1\%$), respectively. Stratification demonstrated that baseline serum albumin concentration did not modify the association between change in serum albumin and change in ASM mass, grip strength, or leg power (data not shown).

DISCUSSION

Among men aged 65 years and older, a single measure of serum albumin was not associated with either short term or longer term loss of muscle mass, muscle strength, or muscle power. Moreover, serum albumin change was not associated with simultaneous change in muscle strength. A statistically significant trend was observed between serum albumin change and concurrent change in leg power and ASM mass. However, the magnitude of change was small and there was considerable overlap in the confidence intervals. In addition, the opposing directions of these trends are unusual and may be indicative of a spurious association.

Two longitudinal studies have reported a small but statistically significant association between serum albumin concentration and subsequent change in measures of muscle mass³¹ and muscle strength.³² The current study may appear to contradict past research findings but the magnitude of change is similar. The lowest and highest serum albumin categories in the MrOS cohort exhibited an adjusted mean loss of -0.97 (95% CI: $-1.11, -0.083$) kg and -0.87 (95% CI: $-0.95, -0.79$) kg ASM mass, respectively, over an average of 4.6 years of follow-up. The Health, Aging, and Body Composition Study (Health ABC) reported comparable loss of ASM mass over 5 years in the lowest and highest serum albumin categories after adjusting for a similar set of confounders (mean ($\pm$ SD): -0.93 (± 0.06) kg and -0.73 (± 0.05) kg, respectively).³¹ The difference in mean ASM mass change between the highest and lowest serum albumin categories was small (0.10 kg in MrOS and 0.21 kg in Health ABC) in both study populations. Schalk and colleagues (2005) reported a statistically significant trend between serum albumin concentration and change in grip strength after 3 years of follow-up in elderly men from the Longitudinal Aging Study Amsterdam (LASA). The maximum measurement of the right and left hand were summed in the LASA study to determine the grip strength outcome variable. The lower three serum albumin quartiles exhibited a loss of grip strength that was similar in magnitude (approximately -11.5 kg, -11.0 kg, and -10.0 kg) and only the highest serum albumin quartile differed from the other categories. The grip strength difference between the highest and lowest serum albumin quartiles was a modest 5 kg in men.³² There was no association between serum albumin quartiles and 3-year change in grip strength among women in this study (one-sided p for trend= 0.06) or between baseline serum albumin and change in grip strength after 6 years in men or women.³²

The null results from the main prospective analysis of the MrOS study population persisted regardless of the duration of follow-up and use of an upper or lower extremity measure of muscle function. These results do not deviate substantially from past findings when evaluating magnitude of change. The apparent differences across study populations may be due to differences in analysis methods. For example, the analysis of data from the LASA study population used a one-sided, trend p -value.³² This methodology can result in smaller p -values than the two-sided p -value that was reported in the present study. In addition, much of the research conducted on this topic has utilized large sample sizes. This can result in associations that are small in magnitude with highly statistically significant p -values.

Albumin is one of the most commonly measured serum proteins and is used to gauge nutritional status or disease severity in elderly patients.²⁰ The utility of this serum protein as a marker for the age-related loss of muscle mass and muscle function appears plausible from a biological perspective. However, the limited longitudinal research available on this topic questions the use of serum albumin measures for this purpose. Serum albumin can decline in response to physiologic stress,¹⁸ renal and liver disease,^{18,42} inflammation,^{21–23} and major surgery.¹⁹ In addition, serum albumin has been reported to decrease by as much as 5 g/L in ambulatory individuals following eight hours of bed rest⁴³ and can vary as much as 11 g/L

from the use of different laboratory techniques for measurement.⁴⁴ It has been argued that the decline of serum albumin in response to non-adverse conditions makes it a questionable prognostic indicator in individual patients.²⁰ More importantly, the results of the available literature are not compelling and do not support the clinical use of serum albumin as a risk factor for the age-related loss of muscle mass and muscle function.

The potential bias in the current study is unlikely to explain the null results. Participants who died, voluntarily withdrew, or did not participate in the Visit 2 clinic visit were more likely to have a serum albumin concentration below 40 g/L and have lower measures of grip strength and leg power at baseline. However, the MrOS cohort captured a large proportion of men at the follow-up visit. Misclassification can occur in any study evaluating a baseline serum measure in relation to the development of subsequent disease if the concentration of serum protein fluctuates over time. The intraclass correlation coefficient ($r=0.61$) determined in a sample of the MrOS cohort a priori indicates moderate repeatability of this measure over time. When the analysis was repeated in men with outcome measures available after two years of follow-up, the results remained the same. The results also remained null with and without adjustment for the baseline outcome measure.

Strengths of this study include the availability of a multitude of participant demographic, body composition, serum, dietary, and lifestyle factors. We have added to the literature by examining change in serum albumin concentration in relation to measures of both muscle mass and muscle function. In addition, we also examined both upper and lower extremity measures of muscle function. The MrOS study is a cohort of relatively healthy elderly men and a possible limitation is that there was not enough variation in the exposure or outcome to capture the nature of the association. However, the magnitude of change in outcomes was similar to other elderly study populations^{31,32} and the LASA study demonstrated a similar distribution of participants with clinically low serum albumin (<38 g/L).³² Another limitation is the inability to adjust for inflammation. Previous literature has found that adjustment for inflammatory cytokines attenuates the association between serum albumin and change in muscle mass³¹ and muscle strength.³² The direction of confounding is unlikely to explain the null findings in the current study but could partially explain the statistically significant trends observed in the serum albumin change analysis. Finally, the MrOS study population is a cohort of primarily white men and the results may or may not be generalizable to women or other racial groups.

Understanding the etiology of the progressive decline of muscle mass and muscle function with age is an important topic in geriatric research. A low concentration of serum albumin within the normal range has been posited as a potential risk factor due to the biologic plausibility and observation of statistically significant associations that were small in magnitude. The results of this study and the limited body of research on this topic question the utility of serum albumin as a prognostic indicator for this process within the ranges observed in community-dwelling elderly. The investigation of potential risk factors for the age-related loss of muscle mass and muscle function should instead focus on more specific measures of physiologic change such as pro-inflammatory cytokines, growth factor hormones, androgens, and the neuronal and structural changes in skeletal muscle.

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Figure 1.

Derivation of the main analytic cohort and serum albumin change analytic population from the MrOS cohort including dates, study sites, and measures obtained at each study visit.

¹ASM: Appendicular skeletal muscle

Table 1
Baseline characteristics by serum albumin category in men aged 65 years and older; the MrOS study

	Baseline Serum Albumin Categories								
Number (%)	< 40 g/L 460 (8.3)	40 g/L 454 (8.2)	41 g/L 722 (13.1)	42 g/L 989 (17.9)	43 g/L 898 (16.2)	44 g/L 885 (16.0)	> 44 g/L 1126 (20.3)	p-value ¹	
	mean (± SD)								
Age (years)	75.4 (± 6.1)	75.3 (± 6.1)	74.1 (± 6.0)	73.8 (± 5.9)	73.2 (± 5.8)	73.1 (± 5.5)	72.4 (± 5.5)	<0.0001	
Body Mass Index (kg/m ²)	27.4 (± 4.3)	27.6 (± 4.3)	27.5 (± 4.0)	27.6 (± 3.8)	27.6 (± 3.9)	27.4 (± 3.6)	27.0 (± 3.5)	0.005	
Total Body Fat (kg)	21.9 (± 8.0)	22.1 (± 7.7)	22.0 (± 7.3)	22.2 (± 7.4)	22.1 (± 7.2)	21.6 (± 6.7)	21.0 (± 6.3)	0.003	
Baseline ASM Mass (kg) ²	23.8 (± 3.5)	24.1 (± 3.4)	24.3 (± 3.6)	24.3 (± 3.5)	24.5 (± 3.5)	24.5 (± 3.4)	24.2 (± 3.5)	0.01	
Baseline Grip Strength (kg)	35.4 (± 8.2)	37.0 (± 7.9)	37.6 (± 8.2)	38.8 (± 8.1)	39.0 (± 8.3)	39.4 (± 8.0)	39.7 (± 7.9)	<0.0001	
Baseline Leg Power (watts)	190 (± 60)	198 (± 60)	202 (± 63)	210 (± 63)	214 (± 66)	212 (± 63)	213 (± 62)	<0.0001	
Daily Protein Intake (% kcal)	15.8 (± 2.9)	16.0 (± 2.7)	15.9 (± 2.8)	16.1 (± 2.9)	16.2 (± 3.0)	16.1 (± 3.1)	16.2 (± 2.9)	0.11	
	n (%)								
Race								0.0001	
Caucasian	400 (87.0)	420 (92.5)	667 (92.4)	891 (90.1)	821 (91.4)	795 (89.8)	1008 (89.5)		
African American	37 (8.0)	20 (4.4)	27 (3.7)	38 (3.8)	28 (3.1)	35 (4.0)	36 (3.2)		
Asian	13 (2.8)	7 (1.5)	13 (1.8)	25 (2.5)	15 (1.7)	20 (2.3)	42 (3.7)		
Hispanic	9 (2.0)	5 (1.1)	11 (1.5)	19 (1.9)	23 (2.6)	17 (1.9)	28 (2.5)		
Smoking Status								0.19	
Never	177 (38.5)	178 (39.3)	256 (35.5)	371 (37.5)	336 (37.4)	318 (35.9)	429 (38.1)		
Former	260 (56.5)	260 (57.4)	441 (61.1)	577 (58.3)	528 (58.8)	537 (60.7)	675 (60.0)		
Current	23 (5.0)	15 (3.3)	25 (3.5)	41 (4.2)	34 (3.8)	30 (3.4)	22 (2.0)		
Alcohol Consumption								0.0003	
0 drinks/week	194 (42.2)	173 (38.1)	255 (35.3)	330 (33.4)	318 (35.5)	291 (32.9)	392 (34.9)		
1–7 drinks/week	204 (44.4)	211 (46.5)	369 (51.1)	473 (47.9)	434 (48.4)	427 (48.3)	499 (44.4)		

	Baseline Serum Albumin Categories							
Number (%)	< 40 g/L 460 (8.3)	40 g/L 454 (8.2)	41 g/L 722 (13.1)	42 g/L 989 (17.9)	43 g/L 898 (16.2)	44 g/L 885 (16.0)	> 44 g/L 1126 (20.3)	p-value ¹
8+ drinks/week	62 (13.5)	70 (15.4)	98 (13.6)	185 (18.7)	144 (16.1)	166 (18.8)	232 (20.7)	
PASE Score ³	140 ± 72	141 ± 71	146 ± 68	150 ± 71	149 ± 68	147 ± 67	147 ± 65	0.09
Leisure exercise subscore ⁴	34 ± 33	33 ± 31	34 ± 33	38 ± 36	35 ± 33	36 ± 33	37 ± 33	0.02
Household activities subscore	89 ± 45	90 ± 45	96 ± 44	95 ± 44	98 ± 42	94 ± 44	95 ± 42	0.009
Anti-inflammatory Use ⁵	98 (21.3)	85 (18.7)	140 (19.4)	194 (19.6)	164 (18.3)	176 (19.9)	221 (19.6)	0.91
Cox II Inhibitors	37 (8.0)	33 (7.3)	48 (6.7)	54 (5.5)	43 (4.8)	49 (5.5)	65 (5.8)	0.20
NSAIDS	67 (14.6)	57 (12.6)	98 (13.6)	147 (14.9)	124 (13.8)	133 (15.0)	163 (14.5)	0.89
Oral Corticosteroid Use	33 (7.2)	15 (3.3)	23 (3.2)	16 (1.6)	9 (1.0)	13 (1.5)	7 (0.6)	<0.0001
Aspirin Use	110 (23.9)	113 (24.9)	139 (19.3)	215 (21.7)	200 (22.3)	166 (18.8)	232 (20.6)	0.07
SSRI Use ⁶	12 (2.6)	14 (3.1)	21 (2.9)	22 (2.2)	27 (3.0)	28 (3.2)	25 (2.2)	0.77
Thyroid Hormone Use	35 (7.6)	39 (8.6)	52 (7.2)	72 (7.3)	43 (4.8)	70 (7.9)	57 (5.1)	0.01
Statin Use	83 (18.0)	99 (21.8)	172 (23.8)	260 (26.3)	232 (25.8)	230 (26.0)	341 (30.3)	<0.0001
Angina	80 (17.4)	60 (13.2)	99 (13.7)	132 (13.4)	131 (14.6)	122 (13.8)	175 (15.5)	0.37
Myocardial Infarction	67 (14.6)	59 (13.0)	106 (14.7)	137 (13.9)	123 (13.7)	125 (14.1)	166 (14.7)	0.97
Stroke	31 (6.7)	29 (6.4)	37 (5.1)	50 (5.1)	63 (7.0)	43 (4.9)	58 (5.2)	0.30
Congestive Heart Failure	27 (5.9)	25 (5.5)	35 (4.9)	44 (4.5)	36 (4.0)	53 (6.0)	66 (5.9)	0.36
Hypertension	186 (40.4)	183 (40.3)	299 (41.4)	422 (42.7)	380 (42.3)	394 (44.5)	531 (47.2)	0.06
COPD ⁷	57 (12.4)	56 (12.3)	96 (13.3)	97 (9.8)	86 (9.6)	99 (11.2)	100 (8.9)	0.03
Diabetes Mellitus	61 (13.3)	48 (10.6)	83 (11.5)	108 (10.9)	94 (10.5)	101 (11.4)	126 (11.2)	0.83
Arthritis or Gout	229 (49.8)	228 (50.2)	347 (48.1)	470 (47.5)	434 (48.3)	409 (46.2)	538 (47.8)	0.84
Osteoarthritis	96 (20.9)	83 (18.3)	144 (19.9)	186 (18.8)	175 (19.5)	183 (20.7)	232 (20.6)	0.86

	Baseline Serum Albumin Categories							
Number (%)	< 40 g/L 460 (8.3)	40 g/L 454 (8.2)	41 g/L 722 (13.1)	42 g/L 989 (17.9)	43 g/L 898 (16.2)	44 g/L 885 (16.0)	> 44 g/L 1126 (20.3)	p-value <i>I</i>
Rheumatoid Arthritis	35 (7.6)	22 (4.9)	44 (6.1)	54 (5.5)	46 (5.1)	42 (4.8)	50 (4.4)	0.22
Cancer	135 (29.4)	134 (29.5)	219 (30.3)	283 (28.6)	267 (29.7)	260 (29.4)	305 (27.1)	0.80

¹ One-way analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables

² ASM: Appendicular skeletal muscle

³ PASE: Physical Activity Scale for the Elderly

⁴ Nonparametric ANOVA to accommodate a skewed distribution

⁵ Anti-inflammatory drug use is defined as the use of a Cox II inhibitor, ibuprofen, naproxen sodium, or another nonsteroidal anti-inflammatory agent (NSAID) at least 3 times per week

⁶ SSRI: Selective serotonin reuptake inhibitor

⁷ COPD: Chronic obstructive pulmonary disease

Table 2

Baseline serum albumin concentration in relation to change in ASM mass, grip strength, and leg power after an average of 4.6 years of follow-up in men aged 65 and older within the main analytic cohort; the MrOS study.

Outcome	Serum Albumin Category (n)							
	< 40 g/L (253–291)	40 g/L (291–328)	41 g/L (459–538)	42 g/L (650–749)	43 g/L (585–664)	44 g/L (586–682)	> 44 g/L (756–862)	p-trend ¹
ASM Mass Change								
Mean (± SD)	–1.02 (± 1.47)	–0.98 (± 1.27)	–0.88 (± 1.32)	–0.90 (± 1.22)	–0.85 (± 1.14)	–0.81 (± 1.22)	–0.82 (± 1.27)	
Adjusted Mean ²	–0.98	–0.92	–0.85	–0.88	–0.85	–0.80	–0.85	0.11
Baseline Adjusted Mean ^{2,3}	–0.97	–0.92	–0.84	–0.88	–0.85	–0.80	–0.87	0.25
Baseline Adjusted 95% CI	(–1.11, –0.083)	(–1.05, –0.78)	(–0.95, –0.74)	(–0.97, –0.79)	(–0.94, –0.75)	(–0.89, –0.71)	(–0.95, –0.79)	
Grip Strength Change								
Mean (± SD)	–2.21 (± 5.89)	–2.70 (± 5.42)	–2.28 (± 4.85)	–2.79 (± 6.02)	–2.58 (± 5.50)	–2.75 (± 5.52)	–2.68 (± 5.81)	
Adjusted Mean ⁴	–2.02	–2.64	–2.23	–2.77	–2.55	–2.68	–2.60	0.23
Baseline Adjusted Mean ^{3,4}	–2.45	–2.81	–2.45	–2.74	–2.51	–2.53	–2.46	0.55
Baseline Adjusted 95% CI	(–3.05, –1.86)	(–3.38, –2.25)	(–2.88, –2.01)	(–3.10, –2.37)	(–2.90, –2.12)	(–2.92, –2.15)	(–2.80, –2.11)	
Leg Power Change								
Mean (± SD)	–17.6 (49.4)	–24.8 (51.3)	–23.5 (47.2)	–17.6 (52.2)	–20.8 (54.7)	–18.6 (51.2)	–14.4 (50.8)	
Adjusted Mean ⁵	–22.3	–31.1	–31.1	–25.0	–29.3	–27.4	–26.4	0.74
Baseline Adjusted Mean ^{3,5}	–28.5	–35.1	–33.8	–27.8	–31.4	–29.7	–28.8	0.19
Baseline Adjusted 95% CI	(–35.8, –21.2)	(–42.3, –27.9)	(–40.2, –27.3)	(–33.9, –21.7)	(–37.6, –25.1)	(–36.0, –23.5)	(–34.9, –22.7)	

¹Multiple linear regression using generalized linear models

²Adjusted for participant age and study site

³Adjusted for the baseline value of the outcome in addition to the other listed confounding factors

⁴Adjusted for participant age, study site, baseline appendicular skeletal muscle (ASM) mass, and ASM mass change

⁵Adjusted for participant age, study site, baseline ASM mass, ASM mass change, Cox II Inhibitor Use, rheumatoid arthritis, and smoking status

Table 3

Change in serum albumin concentration in relation to change in ASM mass, grip strength, and leg power after an average of 2 years of follow-up in men aged 65 and older within the serum albumin change analytic population; the MrOS study.

Outcome	Serum Albumin Change Category (n)				p-trend ¹
	Marked Decrease -3 g/L (84-296)	Mild Decrease -1 to -2 g/L (161-383)	Stable 0 g/L (116-200)	Increase >0 g/L (223-365)	
ASM Mass Change (kg)					
Mean (± SD)	-0.10 (± 0.97)	-0.12 (± 0.90)	-0.13 (± 1.11)	-0.22 (± 0.89)	
Adjusted Mean ²	-0.05	-0.11	-0.16	-0.24	0.02
Baseline Adjusted Mean ³	-0.06	-0.12	-0.15	-0.24	0.03
95% CI	(-0.17, 0.06)	(-0.21, -0.03)	(-0.28, -0.02)	(-0.34, -0.14)	
Grip Strength Change (kg)					
Mean (± SD)	0.47 (± 4.50)	0.77 (± 4.04)	1.03 (± 4.70)	0.95 (± 4.56)	
Adjusted Mean ⁴	0.42	0.66	1.05	1.10	0.07
Baseline Adjusted Mean ³	0.51	0.75	0.87	1.08	0.14
95% CI	(-0.03, 1.05)	(0.31, 1.19)	(0.25, 1.49)	(0.61, 1.54)	
Leg Power Change (watts) ⁵					
Mean (± SD)	-7.9 (± 34.7)	-2.4 (± 35.0)	8.5 (± 48.5)	3.8 (± 36.9)	
Adjusted Mean ⁶	-10.0	-5.6	6.3	3.0	0.01
Baseline Adjusted Mean ³	-8.9	-6.3	5.4	2.1	0.02
95% CI	(-25.6, 7.8)	(-21.2, 8.5)	(-10.5, 21.3)	(-12.1, 16.4)	

¹ Multiple linear regression using generalized linear models

² Adjusted for participant age and study site

³ Adjusted for the baseline value of the outcome in addition to the other listed confounding factors

⁴ Adjusted for participant age, study site, baseline ASM mass, and ASM mass change

⁵ Leg power assessments were only performed at the Portland site (n=512)

⁶ Adjusted for participant age, study site, baseline ASM mass, ASM mass change, Cox II Inhibitor Use, rheumatoid arthritis, and smoking status