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Do muscle mass, muscle density, strength and physical function similarly influence risk of hospitalization in older adults?

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Abstract

Objectives—To examine the association between strength, function, lean mass, muscle density and risk of hospitalization.

Design—Prospective cohort stud

Setting—Two U.S. clinical centers

Participants—Adults aged 70 – 80 years (N=3,011) from the Health, Aging and Body Composition Study.

Measurements—Measures included grip strength; knee extension strength; lean mass; walking speed; chair stand pace. Thigh computed tomography scans assessed muscle area and density (a proxy for muscle fat infiltration). Hospitalizations were confirmed by local review of medical records. Negative binomial regression models estimated incident rate ratios (IRRs) of hospitalization for race/sex specific quartiles of each muscle/function parameter separately. Multivariate models adjusted for age, body mass index, health status and coexisting medical conditions.

Results—During an average 4.7 years of follow-up, 1,678 (55.7%) participants experienced ≥1 hospitalization. Participants in the lowest quartile of muscle density were more likely to be

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subsequently hospitalized (multivariate IRR: 1.47, 95% CI: 1.24, 1.73) compared to the highest quartile. Similarly, participants with the weakest grip strength were at increased risk of hospitalization (MIRR: 1.52, 95% CI: 1.30, 1.78, Q1 vs. Q4). Comparable results were seen for knee strength, walking pace and chair stands pace. Lean mass and muscle area were not associated with risk of hospitalization.

Conclusion—Weak strength, poor function and low muscle density, but not muscle size or lean mass, were associated with an increased risk of hospitalization. Interventions to reduce the disease burden associated with sarcopenia should focus on increasing muscle strength and improving physical function rather than simply increasing lean mass.

Keywords

hospitalization; lean mass; physical function; muscle fat infiltration; walking speed

Introduction

The loss of strength and muscle mass observed with aging is associated with increased health care costs; direct health care costs due to sarcopenia in the United States in 2000 were estimated to exceed $18.5 billon dollars.[1] Given the increasing size of the older population in the United States, the health care costs associated with sarcopenia are likely to increase. In non-disabled adults, poor physical function including weak muscle strength, slow walking speed, and poor balance has been associated with an increased risk of falls[2–5], fractures[6–8]; subsequent mobility limitation,[9, 12] and hospitalizations.[10] In particular, hospitalizations are an important outcome in older adults, as even short stays in the hospital are associated with an increased risk of subsequent functional decline and disability.[11,12,13,14]

Various imaging techniques are used to assess muscle characteristics: dual x-ray absorptiometry (DXA) scans determine lean mass, and computed tomography (CT) scans are analyzed to determine muscle cross-sectional area and muscle density. Low lean mass, small muscle cross-sectional area and decreased muscle density have been associated with poor strength[15] and increased risk of mobility limitations.[9] However, there is no information regarding how these muscle characteristics may influence the risk of hospitalizations in older adults. Of particular interest is low muscle density, a marker of muscle fat infiltration or myosteatosis, that has been associated with poor metabolic function[16] and may be indicative of a perturbation of muscle function.[17]

Despite the association between lean mass, muscle cross-sectional area and muscle density with objective physical function measures, few reports have considered the relative or joint contributions of these factors when assessing health risks in older adults. Understanding these contributions is important for several reasons. First, if lean mass is not independently associated with adverse health outcomes, then definitions of sarcopenia that rely on lean mass alone (and ignore strength or physical function) may not be as clinically useful as more integrative definitions. Second, the assessment of lean mass, muscle cross-sectional area and muscle density rely on complex imaging procedures whereas measures of physical performance, particularly walking speed, can be cheaply and quickly implemented in clinical settings. If the simple measures capture the risk for adverse events as well as more complex imaging modalities, then methods to identify individuals at risk should consider the less complicated measures. Additionally, the best method of identifying those at risk may be the consideration of both strength and lean mass simultaneously; it may be that strength relative to muscle size (also know as specific force), rather than each component individually, is the important determinant of health risks in older adults.

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In these analyses, we aimed to test the hypothesis that weak muscle strength (grip and knee extension strength); low lean mass (arm and leg); poor physical performance (chair stands, walking speed); low specific force (upper and lower extremities); small thigh muscle area; and low thigh muscle density were associated with increased risk of subsequent hospitalization in non-disabled, community-dwelling older adults using data from the Health, Aging and Body Composition (Health ABC) study, a large observational study of more than 3,000 participants.

Methods

Participants

The Health ABC study consists of 3,075 white and black men and women age 70 – 80 years. Participants were recruited from Medicare beneficiary listings for ZIP codes in the metropolitan areas surrounding Pittsburgh, PA and Memphis, TN. Fifty-two percent of participants were women and 41% were black. To be eligible, participants must not have reported any of the following: difficulty walking one-quarter of a mile, climbing 10 steps, or performing activities of daily living; history of active treatment of cancer in the prior 3 years; or plans to move from the area within 3 years. The baseline examination took place between March 1997 and July 1998. Follow-up for these analyses averaged 4.7 years. Baseline characteristics of the cohort have been described elsewhere.[15,18] Institutional review boards approved this research at all participating institutions, and all participants provided written informed consent.

Muscle strength

Maximal isokinetic knee extension strength was measured using a KinCom 125 AP dynamometer (Chattanooga, TN). Strength (torque, Newton meters [Nm]) was measured at 60 degrees per second. Participants had six attempts to complete up to three reproducible and acceptable trials; the average of the maximal knee extension strength of these three trials was analyzed. A number of participants were excluded from testing or were missing data for this measure, including those with high blood pressure (systolic > 200 mmHg or diastolic > 110 mmHg) and those reporting a history of cerebral aneurysm or stroke/bleeding; bilateral total knee replacement; or severe bilateral knee pain (N=398). Grip strength was measured using Jamar dynamometers (Sammons Preston Rolyan, Bolingbrook, IL, USA), [19] Participants completed two trials per hand; the maximal strength for either hand was used in the analyses. Participants were excluded from the grip strength testing due to recent pain in their wrist or hand; or a history of surgery on the upper extremity in the 3 months prior to baseline (N=12).

Physical functioning

Participants were asked to walk at their usual pace over 6 meters at least twice. Walking pace (m/s) was calculated from the faster time observed. A walking speed was not measured for 9 participants. Participants were asked to rise from a chair once without using their arms to push off. If they were able to complete a single chair stand, the participant attempted to rise from a chair five times without the use of the arms. The time to complete the repeated chair stands was recorded; number of chair stands per second was calculated and analyzed. Participants unable to complete the single stand or the repeated stand test were considered unable to complete the repeated chair stands exam; 25 participants had missing data for the chair stands exam.

Dual x-ray absorptiometry

To measure lean mass of the upper and lower extremities and percent body fat, whole body dual x-ray absorptiometry (DXA) scans were completed on Hologic 4500A scanners (Hologic, Waltham, MA). Leg lean mass data was missing for 79 participants; arm lean mass data was missing for 21 participants; and 113 participants were missing both total body lean mass and total body percent fat measures.

Muscle density and cross-sectional area

Computed tomography (CT) scans of the thigh were analyzed to determine mid-thigh muscle cross-sectional area and muscle density as described previously.[9,20,21] Briefly, one 10-mm thick axial image was obtained in both legs at the femoral midpoint, defined as the midpoint of the distance between the medial edge of the greater trochanter and the intercondyloid fossa, with scanning parameters of 120 kVp and 200–250 mA. For each participant, skeletal muscle and adipose tissue were distinguished using bimodal image histogram results from the distribution of CT values. Intermuscular and visible intramuscular adipose tissue were distinguished from subcutaneous adipose tissue by drawing a line along the fascial plane surrounding the thigh muscles. Muscle cross-sectional area (cm^2) was defined as the total area of the nonadipose, nonbone tissue within this fascial plane; the mean cross-sectional area of the two legs was analyzed. Muscle density was defined as the mean attenuation coefficient of muscle tissue within the fascial plan (excluding intermuscular and visible intramuscular adipose tissue) and expressed in Hounsfield units (HU), with higher attenuation indicating decreased muscle density. Previous studies have variously described "muscle density" as the mean attenuation coefficient or as muscle fat infiltration[9,20,21] In the Health ABC participants, reproducibility analyses for the muscle density and cross-sectional area measure were completed in a convenience sample of 5%. The coefficients of variation for the measures were less than 5%. Muscle area and density measures were missing for 63 participants.

Specific force and torque

Specific force was determined by taking the ratio of strength to mass for the upper and lower extremities as has been described.[22] For the legs, specific force was calculated as the ratio of average maximal torque (Nm) to the mean leg lean mass in kg. Specific force data for the lower extremities was missing for 429 participants. In a sub-analysis, muscle cross-sectional area, instead of leg lean mass, was used to calculate specific force for the lower extremities. For the arms, specific force was calculated as the ratio of the maximal grip strength to the mean arm lean mass in kg. Specific force data for the upper extremities was missing for 32 participants.

Other measures

Height was measured using wall-mounted stadiometers, and weight was measured using balance beam scales; BMI was calculated as weight (kg)/height$(m)^2$. Self-reported health was categorized as excellent/very good vs. good/fair/poor. Prevalent medical conditions were ascertained by a combination of self-report, clinic data and/or medication use. Medical conditions considered in this analysis included cerebrovascular disease, coronary heart disease, peripheral arterial disease, congestive heart failure, hypertension, hip/knee osteoarthritis, osteoporosis, pulmonary disease, and diabetes. Sixty-five participants were missing data for at least one of the covariates listed above.

Hospitalizations

During follow-up, Health ABC participants were asked to report any hospitalizations, outpatient cancer, fracture, or cardiovascular events. Every six months, they were asked directed questions to elicit information about events of this type. Medical records for each hospitalization were collected centrally; duration of stay and specific diagnosis were confirmed by local review. Medicare claims data from the Centers for Medicare & Medicaid Services (CMS) regarding the number of hospitalizations in the year prior to the baseline exam was also available for all participants.

Statistical methods

Analyses were performed using SAS version 9.1 (SAS Institute, Inc., Cary, NC). Measures of lean mass, muscle size/density, strength and physical performance were analyzed as race and sex specific quartiles, as distribution of each measure differed by race and sex. When applicable, if a participant could not complete a measurement due to physical inability, he or she was included in statistical models as a separate category ("unable.") Characteristics of participants were compared by quartile of each muscle and strength/function parameter (lean mass, strength, muscle area, muscle density, chair stands and walking performance) separately. Due to space constraints, only the characteristics of participants by quartile of muscle density are presented in this report. Additionally, characteristics of participants by race and gender groups (black female, white female, black male, white male) were compared using ANOVA for normally distributed continuous variables; Kruskal Wallis tests for skewed continuous data; and chi-square tests for categorical variables. A p-value threshold of <0.05 was used for all analyses.

The number of hospitalizations and person time at risk (follow-up time minus days in hospital) were calculated. Negative binomial regression with robust variance estimators for standard errors (to account for intra-individual dependence of repeat events) was used to estimate incidence rate ratios (IRRs) and 95% confidence intervals.[23] The highest or best performing quartile was considered the referent group; linear test for trend across all quartiles was performed. Negative binomial regression allows for analysis of count data where follow-up time differs by participant and the underlying distribution follows an negative binomial distribution. Poisson models were considered, but due to overdispersion of the data (variance > mean and $\neq 1$), negative binomial models were used. Separate models were run for each predictor variable (muscle density, thigh muscle area, leg lean mass, arm lean mass, walking speed, chair stands/second, grip strength, knee extension strength, specific force for the upper extremities and specific force for the lower extremities.) Participants were included in each of the models if they had no missing data for the predictor variable or the covariates. Models were adjusted for age, sex, race, weight, total body percent fat, self-rated health and for the following medical conditions: cerebrovascular disease, coronary heart disease, peripheral arterial disease, congestive heart failure, hypertension, hip/knee osteoarthritis, osteoporosis, pulmonary disease, and diabetes.

Finally, to determine the effects of concurrent poor performance in several physical performance tests and risk of subsequent hospitalization, a summary score for the measures of grip strength, knee extension strength, walking speed and repeat chair stands exam was created. The possible values of the summary score ranged from 0 to 4, with 0 indicating the ability to perform all tests and 4 indicating poor performance on all 4 tests. Poor performance for a test was defined as performance in the worst race/sex specific quartile or being unable to complete the measure. For each test with poor performance, one point was added to the summary score. Next, the risk of hospitalizations by category of the summary score (0, 1–2, 3 or more) was estimated in multivariate negative binomial models. Multivariate models were run, and adjusted for medical conditions, age, self-rated health, race, sex, clinical center. To test whether muscle density is independently associated with hospitalization risk, the model was additionally adjusted for muscle density. In a sub-analysis, the analysis data set was restricted to the population of participants who had not had any hospitalization in the year prior to enrollment.

Results

During an average of 4.7 years (standard deviation: 0.81 years) of follow-up, 1,678 (55.7%) participants experienced least one hospitalization. The mean number of hospitalizations was 1.3 (SD=1.9); average days in the hospital was 7.9 (standard deviation =15.3; median= 2 days). Men were more likely than women to experience at least one hospitalization: 60.8 % of men (N=903) compared to 51.5% (N=816) of women were hospitalized during follow-up. (p<.001) The difference in hospitalizations between white and black participants was less pronounced: 54.4% (N=975) of white participants were hospitalized during follow-up, compared to 58.3% (N=744) of black participants. (p=0.033) A total of 10% (N=325) of participants with baseline data experienced at least one hospitalization in the year prior to the baseline exam.

The race and sex differences in measures of lean mass, muscle size, muscle density, strength, physical function and specific force were pronounced among participants in the Health ABC study, as the values of each parameter differed across the four race and sex categories (Table 1, p<0.001 for all). In general, black men had the highest lean mass, largest muscle area and the greatest strength while white women had the lowest lean mass, smallest muscle area and lowest strength. White men walked the fastest and completed more chair stands per second than the other race/sex groups. Since the measures of lean mass, muscle size, strength and function varied by race and sex, race and sex specific quartiles of each parameter were created.

Participants in the lowest race/sex specific quartile of muscle density tended to be older; heavier; have a higher BMI and percent body fat; have larger muscle cross-sectional area; and higher levels of leg and arm lean mass than those with higher muscle density (Table 2, p<0.001 for all). Body weight, percent body fat, and BMI were moderately correlated with thigh muscle density ($r^2=-0.31$ for weight, $r^2=-0.46$ for BMI, and, $r^2=-0.51$ for percent body fat, p<.001 for all). Greater grip strength, but not knee extension strength, was modestly associated with higher muscle density. (p=0.022). Specific force of the upper and lower extremities, walking speed, and chair stands per second were all associated with muscle density, with better performance associated with higher muscle density (p<0.001). Self-rated health, diabetes, coronary heart disease, and congestive heart failure were associated with muscle density, with higher prevalence of disease in participants with the lowest muscle density (p<0.05 for all). Participants in the middle two quartiles of muscle density (Q2 and Q3) tended to have higher prevalence of pulmonary disease than those in the lowest (Q1) or highest quartile (Q4, p=0.005). Unexpectedly, higher muscle density was moderately associated with higher prevalence of hypertension (p=0.03). Peripheral arterial disease and osteoporosis were not associated with muscle density (p>0.05). As the quartile of muscle density increased, the average number of hospitalizations and days in the hospital decreased (p<.001).

Thigh muscle density was associated with risk of hospitalization during follow-up. In age, race, sex and clinical center adjusted models, participants in the lowest race and sex specific quartile of muscle density had a 1.53- fold (95% CI: 1.32, 1.78) higher rate of hospitalization than participants in the highest quartile of muscle density (p-for trend <0.001 across quartiles.) Further adjustment for potential confounding factors (prevalent medical conditions, self-rated health, percent body fat, and weight) only slightly attenuated the results. Thus, in multivariate models, participants in the lowest muscle density quartile had a 51% higher risk of hospitalization during follow-up compared to participants in the highest quartile (MIRR: 1.51, 95% CI: 1.27, 1.81; *p* for trend, <.001; Table 3).

There was an association between measures of muscle strength and function and hospitalization risk. Weak knee extension and grip strength, as well as poor physical function (slow walking speed and poor chair stands performance) were associated with increased risk of hospitalizations in the Health ABC cohort. For example, participants in the slowest race/sex specific quartile of walking speed had a 70% increased risk of hospitalization (MIRR: 1.70, 95% CI: 1.45, 1.98) during follow-up, compared to participants with the fastest walking speed after adjustment for multiple confounding factors. Although lean mass was not associated with hospitalization risk, poor specific force of muscle was associated with increased hospitalizations during follow-up. Participants in the lowest quartile of lower extremities specific force had a 65% (MIRR 1.65, 95% CI: 1.39, 1.96) increased risk of hospitalization compared to those in the highest quartile after multivariate adjustment. When CT muscle cross-sectional area was substituted for leg lean mass in the definition of specific force of the lower extremities, the results were similar and the conclusions unchanged. (data not shown).

Neither muscle size nor lean mass (leg or arm) were strongly associated with risk of hospitalizations. No significant association was seen in age or multivariate adjusted models between thigh muscle area or leg lean mass and risk of hospitalizations. In age, race, sex and clinical center adjusted models, the risk of hospitalization did not differ between quartile of arm lean mass. (IRR: 1.05, 95% CI: 0.91, 1.23, for Q1 vs. Q4; p for trend across quartiles=0.55). In multivariate models, the association between arm lean mass and hospitalization risk was of borderline significance: participants in the lowest quartile of arm lean mass had a somewhat higher risk of hospitalizations compared to those in the highest quartile. (MIRR: 1.31, 95% CI: 1.01, 1.69). There was no difference in hospitalization risk between participants in Q2 vs. Q4 or Q3 vs. Q4 and the p for trend across quartiles was of borderline significance. (p=0.090).

Concurrent poor performance on several measures of strength and function (walking speed, chair stands performance, grip strength and knee extensions strength) was associated with increased risk of hospitalizations (Table 4). In models adjusted for age, race, sex and clinical center, participants who had poor performance on all four exams had a risk of hospitalizations 2.45-fold higher than those participants without poor performance on any exam. Poor performance on just one exam was associated with an increased risk of hospitalization compared to poor performance on no exams. (IRR: 1.35, 95% CI: 1.18, 1.54). Adjustment for potential confounding factors somewhat attenuated the associations. However, all multivariate models remained highly significant. In the model that adjusted for medical conditions, age, self-rated health, race, sex, clinical center, weight and percent fat, participants with poor performance on all four exams had a risk of hospitalization 1.88-fold higher (95% CI: 1.27, 2.78) than participants without poor performance on any exam. Adding muscle density to the model resulted in essentially unchanged effect estimates. Both concurrent poor performance and muscle density remained independent predictors of hospitalization risk. When the analysis was restricted to participants who did not experience at least one hospitalization in the year prior to the baseline exam, the results were slightly attenuated but remained statistically significant. For example, in the age, clinical center, race and sex adjusted model (Model 1), as the number of physical exams with poor performance increased, so did the risk of hospitalization (p for trend, <.001). For example, participants with poor performance in one exam were about 26% more likely to experience a hospitalization (IRR, 1.26 (95% CI: 1.10, 1.45) compared to those having no exams with poor performance. Additionally, participants with poor performance in all four exams were 2.14-fold more likely to experience a hospitalization compared to those having no exams with poor performance (IRR: 2.14, 95% CI: 1.43. to 3.19). Similar results were found for the multivariate models (Models 2 and 3) in Table 4: the IRRs for number of exams with poor performance remained significant after sub-setting to participants without a hospitalization in the year prior to baseline (p for trend for all <.001).

Discussion

Worse physical function, muscle weakness, decreased muscle density and low specific force of muscle are associated with an increased risk of hospitalization over nearly 5 years of follow-up in black and white men and women who were free from disability at the baseline examination. These associations were not explained by adjustment for body size or prevalent medical conditions. Concurrent poor performance in multiple tests of muscle strength and function was also associated with an increased risk of hospitalization; excluding participants with at least one hospitalization prior to the baseline exam only slightly attenuated these associations. Thus, even among healthy, non-disabled older adults, poor physical function is associated with an increased risk of hospitalization. However, neither lean mass (measured at arm or leg) nor muscle area was associated with hospitalization risk. These results suggest that measures of strength, function, specific force and density may be more important than measures of lean mass alone in assessing health risks in older adults.

Participants in the lowest quartile of muscle density had a 51% higher risk of hospitalizations compared to those in the highest quartile. Low muscle density, as measured by the muscle attenuation coefficient, is a marker for increased muscle fat infiltration or myosteatosis, and higher intramuscular fat stores. The muscle density measures in Health ABC exclude most inter-muscular adipose tissue depots. However, extracellular adipose tissue that is smaller than the pixel resolution of the scanner may not have been completely excluded.[24] Other studies have reported that the correlation between muscle density (also known as the thigh muscle attenuation coefficient) and lipid content within muscle fibers was $r=-0.43$; the correlation between thigh muscle attenuation and muscle triglyceride (TG) content was $r=-0.58$.[24] In Health ABC, low muscle density has been associated with increased risk of functional limitation[9], poorer strength[20] and worse metabolic function.[16] Others have hypothesized that intramuscular lipid is a critical component of metabolic and physical derangement of muscle function.[17]

In these analyses, lean mass was not independently associated with increased risk of hospitalizations. A previous report from this cohort demonstrated that strength declines more quickly than muscle mass in older adults.[25] This report also noted that while loss of lean mass was independently associated with loss of strength, maintenance or gain of lean mass was not associated with increases in or maintenance of muscle strength. Additionally, while both lower extremity muscle mass (thigh muscle cross-sectional area) and poor strength were associated with increased risk of mobility limitation, the association between decreased muscle mass and mobility limitation was explained by poorer strength.[9] Thus, interventions to improve muscle function and reduce disease and disability in older adults should aim to improve muscle strength, not just increase muscle size or overall lean mass. The results of these analyses also indicate that operational definitions of sarcopenia that rely solely on muscle mass may not be as clinically useful as definitions that would include measures of function or strength. Finally, treatments (either pharmacologic or behavioral) that increase muscle density may be particularly important for reducing the burden of disability and poor health outcomes that are associated with poor function.

The strongest risks for hospitalization in these analyses were for the lower extremity (walking speed and knee extension strength). Walking speed is a complex trait that may be influenced by a number of factors, including poor cardiovascular function and cognitive decline.[26,27] The results reported here are consistent with other published reports: decreased walking speed has previously been associated with hospitalization and mortality in this and other cohorts.[10,28] Assessment of walking speed is inexpensive and simple to implement. Thus, walking speed alone may be an ideal measure for identifying individuals at risk of poor outcomes, including hospitalizations. On the other hand, in this study, upper extremity strength was also associated with risk of hospitalizations, so poor upper extremity strength (even with robust lower extremity function) should be considered a possible risk factor for future adverse health outcomes.

There are several strengths of the current study. The Health ABC study is a large, well characterized cohort of a diverse group of older adults. Additionally, hospitalization records are collected in a complete and systematic manner and reviewed by experts, and co-morbid conditions are very well defined. However, a few limitations should be noted. First, the study participants were quite healthy at baseline, and this might limit the generalizability of these findings to other groups, such as non-ambulatory populations or the infirm. This selection bias may cause an underestimation of the observed associations, because disabled persons (who are likely to have both poorer muscle strength and lower muscle mass) were excluded from the study. However, any study or intervention trial in the older persons focusing on mobility loss is likely to suffer from the same limitation. Secondly, while sub-analyses were completed restricting the analysis set to participants who did not experience a hospitalization in the year prior to the baseline exam, the temporal association between poor performance and risk of hospitalization cannot be fully established. It is possible that those participants who did experience a hospitalization before the baseline exam had poorer physical function that contributed to the hospitalization. Without measures of physical function preceding the first hospitalization of every participant throughout old age, it will be impossible to concretely establish the temporality of the association. It is reassuring, however, that poor physical function is not simply a maker of previous hospitalization. Third, although the analyses were essentially unchanged by adjustment for co-existing medical conditions, factors that were not measured might explain the associations observed.

In conclusion, low muscle strength, poor physical performance, and low muscle density (but not muscle size or lean mass) are associated with increased risk of hospitalization in adults aged 70–79 years. Interventions to improve muscle strength and physical performance may reduce not only future disability but might also reduce the large economic burden associated with hospitalizations should poor muscle strength and function be causally related to subsequent hospitalizations.

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References

1. Janssen I, Shepard DS, Katzmarzyk PT, et al. The healthcare costs of sarcopenia in the United States. J Am Geriatr Soc. 2004; 52:80–85. [PubMed: 14687319]
2. Graafmans WC, Ooms ME, Hofstee HM, et al. Falls in the elderly: a prospective study of risk factors and risk profiles. Am J Epidemiol. 1996; 143:1129–1136. [PubMed: 8633602]

3. Moreland JD, Richardson JA, Goldsmith CH, et al. Muscle weakness and falls in older adults: a systematic review and meta-analysis. J Am Geriatr Soc. 2004; 52:1121–1129. [PubMed: 15209650]
4. Stevens JA, Olson S. Reducing falls and resulting hip fractures among older women. MMWR Recomm Rep. 2000; 49:3–12. [PubMed: 15580729]
5. Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med. 1988; 319:1701–1707. [PubMed: 3205267]
6. Cawthon PM, Fullman RL, Marshall L, et al. Physical performance and risk of hip fractures in older men. J Bone Miner Res. 2008; 23:1037–1044. [PubMed: 18302496]
7. Cummings SR, Nevitt MC, Browner WS, et al. Risk factors for hip fracture in white women. Study of Osteoporotic Fractures Research Group. N Engl J Med. 1995; 332:767–773. [PubMed: 7862179]
8. Lewis CE, Ewing SK, Taylor BC, et al. Predictors of Non-Spine Fracture in Elderly Men: The MrOS Study. J Bone Miner Res. 2007; 22:211–219. [PubMed: 17059373]
9. Visser M, Goodpaster BH, Kritchevsky SB, et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. J Gerontol A Biol Sci Med Sci. 2005; 60:324–333. [PubMed: 15860469]
10. Penninx BW, Ferrucci L, Leveille SG, et al. Lower extremity performance in nondisabled older persons as a predictor of subsequent hospitalization. J Gerontol A Biol Sci Med Sci. 2000; 55:M691–697. [PubMed: 11078100]
11. Hirsch CH, Sommers L, Olsen A, et al. The natural history of functional morbidity in hospitalized older patients. J Am Geriatr Soc. 1990; 38:1296–1303. [PubMed: 2123911]
12. Sager MA, Franke T, Inouye SK, et al. Functional outcomes of acute medical illness and hospitalization in older persons. Arch Intern Med. 1996; 156:645–652. [PubMed: 8629876]
13. Ferrucci L, Guralnik JM, Pahor M, et al. Hospital diagnoses, Medicare charges, and nursing home admissions in the year when older persons become severely disabled. JAMA. 1997; 277:728–734. [PubMed: 9042845]
14. Gill TM, Allore HG, Holford TR, et al. Hospitalization, restricted activity, and the development of disability among older persons. JAMA. 2004; 292:2115–2124. [PubMed: 15523072]
15. Newman AB, Haggerty CL, Goodpaster B, et al. Strength and muscle quality in a well-functioning cohort of older adults: the Health, Aging and Body Composition Study. J Am Geriatr Soc. 2003; 51:323–330. [PubMed: 12588575]
16. Goodpaster BH, Krishnaswami S, Harris TB, et al. Obesity, regional body fat distribution, and the metabolic syndrome in older men and women. Arch Intern Med. 2005; 165:777–783. [PubMed: 15824297]
17. Unger RH, Orci L. Lipoapoptosis: its mechanism and its diseases. Biochim Biophys Acta. 2002; 1585:202–212. [PubMed: 12531555]
18. Visser M, Deeg DJ, Lips P, et al. Skeletal muscle mass and muscle strength in relation to lower-extremity performance in older men and women. J Am Geriatr Soc. 2000; 48:381–386. [PubMed: 10798463]
19. Harkonen R, Harju R, Alaranta H. Accuracy of the Jamar dynamometer. J Hand Ther. 1993; 6:259–262. [PubMed: 8124439]
20. Goodpaster BH, Carlson CL, Visser M, et al. Attenuation of skeletal muscle and strength in the elderly: The Health ABC Study. J Appl Physiol. 2001; 90:2157–2165. [PubMed: 11356778]
21. Visser M, Kritchevsky SB, Goodpaster BH, et al. Leg muscle mass and composition in relation to lower extremity performance in men and women aged 70 to 79: the health, aging and body composition study. J Am Geriatr Soc. 2002; 50:897–904. [PubMed: 12028178]
22. Newman AB, Kupelian V, Visser M, et al. Sarcopenia: alternative definitions and associations with lower extremity function. J Am Geriatr Soc. 2003; 51:1602–1609. [PubMed: 14687390]
23. Byers AL, Allore H, Gill TM, et al. Application of negative binomial modeling for discrete outcomes: a case study in aging research. J Clin Epidemiol. 2003; 56:559–564. [PubMed: 12873651]
24. Goodpaster BH, Kelley DE, Thaete FL, et al. Skeletal muscle attenuation determined by computed tomography is associated with skeletal muscle lipid content. J Appl Physiol. 2000; 89:104–110. [PubMed: 10904041]

25. Goodpaster BH, Park SW, Harris TB, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. J Gerontol A Biol Sci Med Sci. 2006; 61:1059–1064. [PubMed: 17077199]

26. Ferrucci L, Bandinelli S, Benvenuti E, et al. 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. [PubMed: 11129752]

27. Ferrucci L, Bandinelli S, Cavazzini C, et al. Neurological examination findings to predict limitations in mobility and falls in older persons without a history of neurological disease. Am J Med. 2004; 116:807–815. [PubMed: 15178496]

28. Cesari M, Kritchevsky SB, Penninx BW, et al. Prognostic value of usual gait speed in well-functioning older people--results from the Health, Aging and Body Composition Study. J Am Geriatr Soc. 2005; 53:1675–1680. [PubMed: 16181165]

Table 1

Race and sex-specific quartile cut-points for various muscle composition, strength and physical function parameters for the Health, Aging, and Body Composition (Health ABC) cohort.

		Mean (Range: Min, Max)			
Muscle characteristics (from computed tomography)		**Quartile 1**	**Quartile 2**	**Quartile 3**	**Quartile 4**
Muscle density (HU)	Black women	23.3 (2.42,28.0)	30.5 (28.0,32.4)	34.7 (32.4,37.5)	40.9 (37.5,49.6)
	White women	26.0 (8.37,30.4)	32.9 (30.4,35.0)	37.1 (35.0,39.4)	42.9 (39.4,70.1)
	Black men	28.9 (8.55,32.9)	34.9 (32.9,36.9)	39.2 (36.9,41.6)	45.1 (41.7,54.5)
	White men	29.1 (7.94,33.2)	35.4 (33.2,37.6)	39.7 (37.7,41.9)	45.2 (41.9,55.1)
Thigh muscle area (cm^2)	Black women	159 (95.5,180)	192 (180,203)	213 (203,225)	245 (225,311)
	White women	137 (96.3,152)	161 (152,169)	178 (169,187)	206 (188,302)
	Black men	216 (115,244)	260 (244,277)	291 (277,307)	341 (307,452)
	White men	208 (151,228)	240 (228,253)	266 (253,280)	304 (280,404)
Lean mass (from dual energy x-day absorptiometry)					
Leg lean mass (kg)	Black women	5.66 (3.89,6.31)	6.72 (6.31,7.15)	7.52 (7.15,7.96)	8.91 (7.96,12.6)
	White women	5.00 (3.70,5.44)	5.76 (5.45,6.05)	6.38 (6.05,6.76)	7.38 (6.76,11.7)
	Black men	7.69 (5.33,8.56)	8.96 (8.57,9.41)	9.90 (9.43,10.4)	11.5 (10.4,14.1)
	White men	7.45 (5.36,8.05)	8.45 (8.06,8.83)	9.22 (8.83,9.65)	10.5 (9.65,13.4)
Arm lean mass (kg)	Black women	1.88 (1.26,2.09)	2.24 (2.09,2.37)	2.51 (2.37,2.68)	3.01 (2.69,4.03)
	White women	1.59 (1.17,1.75)	1.84 (1.75,1.93)	2.03 (1.93,2.14)	2.38 (2.14,3.38)
	Black men	3.01 (1.90,3.33)	3.58 (3.33,3.81)	3.99 (3.81,4.22)	4.67 (4.22,5.75)
	White men	2.80 (2.03,3.05)	3.23 (3.05,3.40)	3.57 (3.40,3.77)	4.10 (3.77,5.14)
Physical function					
Walking speed (m/s)	Black women	0.80 (0.42,0.91)	0.97 (0.92,1.03)	1.09 (1.04,1.15)	1.29 (1.16,1.75)
	White women	0.93 (0.66,1.04)	1.12 (1.05,1.18)	1.24 (1.19,1.30)	1.46 (1.31,1.98)
	Black men	0.87 (0.40,0.99)	1.07 (1.00,1.12)	1.19 (1.13,1.26)	1.40 (1.27,1.94)
	White men	1.01 (0.63,1.13)	1.20 (1.14,1.26)	1.35 (1.27,1.43)	1.59 (1.44,2.00)
Chair stands/second	Black women	0.23 (0.13,0.27)	0.31 (0.28,0.33)	0.36 (0.34,0.39)	0.47 (0.40,1.82)
	White women	0.26 (0.09,0.30)	0.34 (0.31,0.36)	0.39 (0.37,0.41)	0.48 (0.42,0.83)
	Black men	0.25 (0.13,0.28)	0.31 (0.29,0.33)	0.36 (0.34,0.40)	0.48 (0.41,0.78)

		Mean (Range: Min, Max)			
Muscle characteristics (from computed tomography)		Quartile 1	Quartile 2	Quartile 3	Quartile 4
	White men	0.29 (0.18,0.33)	0.36 (0.34,0.39)	0.42 (0.40,0.45)	0.55 (0.46,1.63)
Strength					
Grip strength (kg)	Black women	17.4 (6.00,21.0)	23.0 (22.0,25.0)	27.0 (26.0,29.0)	33.6 (30.0,80.0)
	White women	16.0 (8.00,19.0)	21.2 (20.0,23.0)	24.0 (24.0,25.0)	28.6 (26.0,42.0)
	Black men	29.0 (12.0,34.0)	38.0 (36.0,41.0)	43.9 (42.0,47.0)	53.7 (48.0,98.0)
	White men	28.8 (14.0,33.0)	36.2 (34.0,39.0)	41.0 (40.0,43.0)	48.7 (44.0,78.0)
Knee extension strength (N-m)	Black women	54.8 (17.1,70.3)	79.0 (70.4,86.4)	92.7 (86.4,101)	115 (101,165)
	White women	52.9 (12.3,66.2)	72.4 (66.2,79.0)	84.5 (79.0,90.8)	103 (91.0,159)
	Black men	86.4 (35.1,109)	123 (110,137)	147 (137,159)	182 (159,255)
	White men	92.8 (39.3,110)	120 (110,130)	141 (130,151)	171 (151,462)
Specific force					
Upper extremities (kg focre/kg lean mass)	Black women	7.80 (3.04,9.32)	10.2 (9.32,11.2)	12.0 (11.2,12.9)	14.9 (12.9,36.5)
	White women	8.94 (4.88,10.5)	11.4 (10.5,12.3)	13.1 (12.3,13.9)	15.3 (13.9,22.5)
	Black men	8.56 (4.27,9.68)	10.5 (9.69,11.2)	12.0 (11.3,12.7)	14.3 (12.7,28.6)
	White men	9.02 (5.58,10.3)	11.0 (10.3,11.6)	12.3 (11.6,13.0)	14.3 (13.0,24.0)
Lower extremities (kg/N-m)	Black women	7.76 (2.65,9.89)	11.1 (9.89,12.3)	13.3 (12.3,14.2)	16.0 (14.2,20.3)
	White women	9.14 (2.08,11.0)	12.0 (11.0,13.0)	13.8 (13.0,14.8)	16.3 (14.8,24.4)
	Black men	9.49 (3.01,11.8)	13.2 (11.8,14.4)	15.6 (14.4,16.6)	18.3 (16.6,24.4)
	White men	11.0 (4.77,12.8)	13.8 (12.8,14.7)	15.6 (14.7,16.5)	18.4 (16.5,37.4)

Table 2

Characteristics (mean, ± or N, %) of the Health, Aging, and Body Composition study (Health ABC) participants by race and gender specific quartile of muscle density (HU).*

Characteristic	Quartile 1 (N= 752) Least dense muscle	Quartile 2 (N= 753)	Quartile 3 (N= 752)	Quartile 4 (N= 754) Most dense muscle	p-value
Age (years)	74 ± 2.9	73.7 ± 3	73.5 ± 2.9	73.2 ± 2.7	<.001
Height (cm)	166.7 ± 9.3	166.2 ± 9.5	166.4 ± 9.2	165.4 ± 9.4	0.064
Weight (kg)	83.6 ± 15.3	77.3 ± 14.3	73.3 ± 12.5	68.3 ± 12.7	<.001
Percent total body fat (%)	38.4 ± 7.06	35.6 ± 7.61	34.2 ± 7.48	31.8 ± 7.5	<.001
Body mass index (kg/cm^2)	30.1 ± 4.8	27.9 ± 4.5	26.5 ± 4.1	24.9 ± 3.9	<.001
Thigh muscle area (cm^2)	229.1 ± 57.4	228.1 ± 58.5	219.7 ± 52.5	214.1 ± 52.0	<.001
Total lean mass (kg)	51.2 ± 10.6	49.8 ± 10.8	48.2 ± 9.6	46.6 ± 9.8	<.001
Leg lean mass (kg)	8.2 ± 1.9	8.0 ± 1.9	7.7 ± 1.7	7.4 ± 1.7	<.001
Arm lean mass (kg)	2.9 ± 0.9	2.9 ± 0.9	2.8 ± 0.8	2.7 ± 0.8	<.001
Walking speed (m/sec)	1.10 ± 0.24	1.18 ± 0.23	1.20 ± 0.23	1.22 ± 0.25	<.001
Chair stands per second	0.33 ± 0.14	0.37 ± 0.12	0.37 ± 0.11	0.39 ± 0.13	<.001
Grip strength (kg)	31.7 ± 10.8	32.8 ± 11.2	33.2 ± 10.9	33.1 ± 10.7	0.022
Knee extension strength (Torque, N-m)	103.6 ± 39.6	108.5 ± 39.5	106.7 ± 37.8	107.0 ± 36.7	0.144
Upper extremities muscle specific force (kg force/kg lean mass)	10.9 ± 2.6	11.6 ± 2.4	12 ± 2.6	12.2 ± 2.4	<.001
Lower extremities muscle specific force (N-m/kg lean mass)	12.4 ± 3.3	13.4 ± 3.1	13.7 ± 3.3	14.4 ± 3.1	<.001
Self-rated health (excellent/very good)	88 (11.7)	109 (14.5)	99 (13.2)	117 (15.5)	<.001
Diabetes	139 (18.5)	105 (13.9)	115 (15.4)	95 (12.7)	0.011
Coronary heart disease	159 (21.6)	136 (18.3)	141 (19.1)	111 (15)	0.008
Peripheral arterial disease	34 (4.7)	40 (5.4)	39 (5.3)	36 (4.9)	0.915
Congestive heart failure	13 (1.8)	12 (1.6)	9 (1.2)	4 (0.5)	0.016
Hypertension	141 (18.8)	169 (22.4)	143 (19)	177 (23.5)	0.033
Osteoporosis	79 (10.7)	79 (10.6)	66 (9)	74 (10)	0.675
Pulmonary disease	29 (3.9)	41 (5.5)	34 (4.5)	22 (2.9)	0.005
Number of times hospitalized	1.6 ± 2	1.4 ± 2.1	1.2 ± 1.8	1.0 ± 1.6	<.001
Days in hospital	9.9 ± 16.3	8.4 ± 15.8	7.1 ± 14.8	6.3 ± 14.1	<.001

*Since the race and gender distributions for each quartile are fixed, the distributions of these factors are not reported in this comparison table.

HU = Hounsfield Units

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Table 3

Multivariate adjusted* incidence rate ratios (95% confidence interval) for hospitalizations by category of muscle, strength and function parameters for men and women in the Health, Aging, and Body Composition (Health ABC) cohort.

	N	Total events	N with ≥1 event	Unable	Quartile 1	Quartile 2	Quartile 3	Quartile 4	p for trend
Muscle characteristics									
Muscle density	2675	3433	1471	N/A	1.51 (1.27,1.81)	1.24 (1.06,1.46)	1.13 (0.96,1.32)	1.00 (ref)	<.001
Thigh muscle area	2675	3433	1471	N/A	1.18 (0.95,1.47)	1.04 (0.86,1.25)	1.03 (0.87,1.21)	1.00 (ref)	0.139
Lean mass									
Leg lean mass	2713	3501	1496	N/A	1.23 (0.93,1.63)	1.02 (0.81,1.28)	1.02 (0.85,1.22)	1.00 (ref)	0.137
Arm lean mass	2722	3518	1503	N/A	1.31 (1.01,1.69)	1.15 (0.94,1.42)	1.19 (1.00,1.42)	1.00 (ref)	0.090
Physical function									
Walking speed	2705	3491	1493	N/A	1.70 (1.45,1.98)	1.41 (1.21,1.65)	1.20 (1.03,1.39)	1.00 (ref)	<.001
Chair stands/second	2706	3490	1493	1.42 (1.03,1.96)	1.23 (1.05,1.45)	1.16 (1.00,1.36)	1.06 (0.91,1.24)	1.00 (ref)	0.001
Strength									
Grip strength	2714	3496	1497	1.61 (1.00,2.59)	1.56 (1.31,1.85)	1.15 (0.99,1.33)	1.19 (1.03,1.39)	1.00 (ref)	<.001
Knee extension strength	2419	3010	1306	2.03 (1.16,3.57)	1.68 (1.40,2.01)	1.40 (1.17,1.67)	1.19 (1.00,1.41)	1.00 (ref)	<.001
Specific force									
Upper extremities	2713	3496	1497	1.61 (1.00,2.60)	1.38 (1.17,1.63)	1.24 (1.06,1.45)	1.13 (0.97,1.32)	1.00 (ref)	<.001
Lower extremities	2411	2998	1301	2.07 (1.18,3.64)	1.65 (1.39,1.96)	1.43 (1.21,1.69)	1.29 (1.08,1.52)	1.00 (ref)	<.001

*Adjusted for total percent body fat, weight, age, self-rated health, sex, race, clinical center, co-morbid conditions (cerebrovascular disease, CHD, CHF, hypertension, PPAD, pulmonary disease, diabetes)

Table 4

Risk of hospitalization (incidence rate ratios, 95% confidence interval) by summary physical performance score*

Number of physical exams with poor performance	N	Model 1: Age, clinical center, race, and sex adjusted †	Model 2: Multivariate adjusted ‡	Model 3: Model 2 adjustments plus muscle density §
0	1200	1.00 (ref)	1.00 (ref)	1.00 (ref)
1	808	1.36 (1.19,1.55)	1.27 (1.10,1.45)	1.25 (1.08,1.43)
2	406	1.73 (1.47,2.04)	1.61 (1.36,1.91)	1.57 (1.32,1.86)
3	179	1.95 (1.56,2.44)	1.72 (1.36,2.17)	1.63 (1.28,2.07)
4	54	2.457 (1.71,3.56)	1.88 (1.27,2.78)	1.80 (1.20,2.69)
p for trend		<.001	<.001	<.001

* Performance tests included include grip strength, knee extension strength, walking speed and repeat chair stands exam. Poor performance is defined as performance in lowest race and sex specific quartile of a measure or unable to complete the measure.

† In age, clinical center, race and sex adjusted models (N=2,645), 3,299 hospitalizations occurred in 1,444 participants.

‡ Adjusted for total percent body fat, weight, age, self-rated health, sex, race, clinical center, co-morbid conditions (cerebrovascular disease, CHD, CHF, hypertension, PPAD, pulmonary disease, diabetes) In model 2, (N=2,395), 2,977 hospitalizations occurred in 1,295 participants.

§ The IRR (95% CI) for muscle density in this model was: quartile 1: 1.40 (1.15, 1.70); quartile 2: 1.25 (1.05, 1.49); quartile 3: 1.09 (0.92, 1.30); quartile 4: 1.00 (referent), p for trend = 0.008.