Do Muscle Mass, Muscle Density, Strength, and Physical Function Similarly Influence Risk of Hospitalization in Older Adults?

Peggy Mannen Cawthon, PhD, MPH, Kathleen M. Fox, MHS, PhD,† Shravanthi R. Gandra, PhD, MBA,‡ Matthew J. Delmonico, PhD, MPH,§ Chiun-Fang Chiou, PhD,‡ Mary S. Anthony, PhD,‡ Ase Sewall, BS,‖ Bret Goodpaster, PhD,# Suzanne Satterfield, MD, DrPH,** Steven R. Cummings, MD,* and Tamara B. Harris, MD, MS,†† for the Health, Aging and Body Composition Study*

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

DESIGN: Prospective cohort study.

SETTING: Two U.S. clinical centers.

PARTICIPANTS: Adults aged 70 to 80 (N = 3,011) from the Health, Aging and Body Composition Study.

MEASUREMENTS: Measurements were of grip strength, knee extension strength, lean mass, walking speed, and 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- and sex-specific quartiles of each muscle and 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 one or more hospitalizations. Participants in the lowest quartile of muscle density were more likely to be subsequently hospitalized (multivariate IRR = 1.47, 95% confidence interval (CI) = 1.24–1.73) than those in the highest quartile. Similarly, participants with the weakest grip strength were at greater risk of hospitalization (multivariate IRR = 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 greater 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.
J Am Geriatr Soc 57:1411–1419, 2009.

Key words: hospitalization; lean mass; physical function; muscle fat infiltration; walking speed

From the *Research Institute, California Pacific Medical Center, San Francisco, California; †Strategic Healthcare Solutions, LLC, Monkton, Maryland; ‡Amgen Inc., Thousand Oaks, California; §University of Rhode Island, Kingston, Rhode Island; ‖Sewall Inc., Bethesda, Maryland; #Division of Endocrinology and Metabolism, School of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania; **Department of Preventative Medicine, University of Tennessee, Memphis, Tennessee; and ††Intramural Research Program, National Institute on Aging, Bethesda, Maryland.

Portions of the analyses in this paper were presented as a poster at the American Geriatrics Society Meeting in Washington, DC, May 2008.

Address correspondence to Peggy M. Cawthon, PhD, MPH, Research Institute, California Pacific Medical Center, 185 Berry Street, Lobby 4, Suite 5700, San Francisco, CA 94107. E-mail: pcawthon@sfcc-cpmc.net

DOI: 10.1111/j.1532-5415.2009.02366.x

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

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 low muscle density have been associated with poor strength[15] and greater risk of mobility limitations,[9] although there is no information regarding how these

0002-8614/09/$15.00

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 and 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 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.

These analyses were designed 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 greater risk of subsequent hospitalization in nondisabled, 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 aged 70 to 80. Participants were recruited from Medicare beneficiary listings for ZIP codes in the metropolitan areas surrounding Pittsburgh, Pennsylvania, and Memphis, Tennessee. Fifty-two percent of participants were female 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 at all participating institutions approved this research, 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° 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 was excluded from testing, including those with high blood pressure (systolic >200 mmHg or diastolic >110 mmHg) and those reporting a history of cerebral aneurysm, stroke, or bleeding; bilateral total knee replacement; or severe bilateral knee pain or were missing data for this measure (n = 398). Grip strength was measured using Jamar dynamometers (Sammons Preston Rolyan, Bolingbrook, IL).[19] Participants completed two trials per hand; the maximal strength for either hand was used in the analyses. Twelve participants were excluded from the grip strength testing because of recent pain in their wrist or hand or a history of surgery on the upper extremity in the 3 months before baseline.

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. Walking speed was not measured for nine 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, they attempted to rise from a chair five times without the use of the arms. The time to complete the repeated chair stands was recorded, and 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 examination; 25 participants had missing data for the chair stands examination.

Dual X-Ray Absorptiometry

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

Muscle Density and Cross-Sectional Area

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 to 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 lower 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 were missing for 429 participants. In a subanalysis, 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 maximal grip strength to mean arm lean mass in kilograms. Specific force data for the upper extremities were missing for 32 participants.

Other Measures

Height was measured using wall-mounted stadiometers, and weight was measured using balance beam scales; body mass index (BMI) was calculated as weight (kg)/height(m)^2. Self-reported health was categorized as excellent or very good versus good, fair, or poor. Prevalent medical conditions were ascertained by a combination of self-report, clinic data, and medication use. Medical conditions considered in this analysis included cerebrovascular disease, coronary heart disease, peripheral arterial disease, congestive heart failure, hypertension, hip or knee osteoarthritis, osteoporosis, pulmonary disease, and diabetes mellitus. 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 6 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 using local review. Medicare claims data from the Centers for Medicare and Medicaid Services regarding the number of hospitalizations in the year before the baseline examination were 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 and density, strength, and physical performance were analyzed as race- and sex-specific quartiles, because distribution of each measure differed according to race and sex. When applicable, if participants could not complete a measurement because of physical inability, they were included in statistical models as a separate category (unable). Characteristics of participants were compared according to quartile of each muscle and strength or function parameter (lean mass, strength, muscle area, muscle density, chair stands, and walking performance) separately. Because of space constraints, only the characteristics of participants according to quartile of muscle density are presented in this report. Additionally, characteristics of participants according to race and sex (black female, white female, black male, white male) were compared using analysis of variance for normally distributed continuous variables, Kruskal-Wallis tests for skewed continuous data, and chi-square tests for categorical variables. A P-value threshold of less than .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 (CIs).[23] The highest or best-performing quartile was considered the referent group; linear tests for trend across all quartiles were performed. Negative binomial regression allows for analysis of count data when follow-up time differs according to participant and the underlying distribution follows an negative binomial distribution. Poisson models were considered, but because of 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 per 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 percentage body fat, and self-rated health and for the following medical conditions: cerebrovascular disease, coronary heart disease, peripheral arterial disease, congestive heart failure, hypertension, hip or knee osteoarthritis, osteoporosis, pulmonary disease, and diabetes mellitus.

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 examination was created. The possible values of the summary score ranged from 0 to 4, with 0 indicating ability to perform all tests and 4 indicating poor performance on all four tests. Poor performance for a test was defined as performance in the worst race- or sex-specific quartile or being unable to complete the measure. For each test with poor performance, 1 point was added to the summary score. Next, the risk of hospitalizations according to category of the summary score (0, 1–2, $\geq$3) was estimated in multivariate negative binomial models. Multivariate models were run and adjusted for medical conditions, age, self-rated health, race, sex, and clinical center. To test whether muscle density is independently associated with hospitalization risk, the model was additionally adjusted for muscle density. In a subanalysis, the analysis data set was restricted to the population of participants who had not had any hospitalization in the year before enrollment.

RESULTS

During an average ± standard deviation of 4.7 ± 0.8 years of follow-up, 1,678 (55.7%) participants experienced at least one hospitalization. The mean number of hospitalizations was 1.3 ± 1.9; average days in the hospital was 7.9 ± 15.3 (median 2 days). Men were (N = 903, 60.8%) more likely than women (N = 816, 51.5%) to experience at least one hospitalization ($P<.001$). The difference in hospitalizations between white (N = 975, 54.5%) and black (N = 744, 58.3%) participants was less pronounced ($P=.03$). A total of 10% (n = 325) of participants with baseline data experienced at least one hospitalization in the year before the baseline examination.

The race and sex differences in measures of lean mass, muscle size, muscle density, strength, physical function, and specific force were pronounced in participants in the Health ABC Study, because the values of each parameter differed across the four race and sex categories (Table 1, $P<.001$ for all). In general, black men had the highest lean mass, largest muscle area, and greatest strength, whereas 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 and sex groups. Because the measures of lean mass, muscle size, strength, and function varied according to race and sex, race- and sex-specific quartiles of each parameter were created.

Participants in the lowest race- and sex-specific quartile of muscle density tended to be older and heavier, have a higher BMI and percentage body fat, have larger muscle cross-sectional area, and have higher levels of leg and arm lean mass than those with higher muscle density (Table 2, $P<.001$ for all). Body weight, percentage body fat, and BMI were moderately correlated with thigh muscle density (coefficient of determination (r^2) = −0.31 for weight, $r^2 = -0.46$ for BMI, $r^2 = -0.51$ for percentage body fat, $P<.001$ for all). Greater grip strength, but not knee extension strength, was modestly associated with higher muscle density ($P=.02$). 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 ($P<.001$). Self-rated health, diabetes mellitus, coronary heart disease, and congestive heart failure were associated with muscle density, with higher prevalence of disease in participants with the lowest muscle density ($P<.05$ 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, $P=.005$). Unexpectedly, higher muscle density was moderately associated with higher prevalence of hypertension ($P=.03$). Peripheral arterial disease and osteoporosis were not associated with muscle density ($P>.05$). 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 models age adjusted for, race, sex, and clinical center, participants in the lowest race- and sex-specific quartile of muscle density had a 1.53 times (95% CI = 1.32–1.78) higher rate of hospitalization than participants in the highest quartile of muscle density (P for trend <.001 across quartiles.) Further adjustment for potential confounding factors (prevalent medical conditions, self-rated health, percentage body fat, and weight) attenuated the results only slightly. Thus, in multivariate models, participants in the lowest muscle density quartile had a 51% higher risk of hospitalization during follow-up than participants in the highest quartile (multivariate IRR (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 and poor physical function (slow walking speed and poor chair stands performance) were associated with greater risk of hospitalizations in the Health ABC cohort. For example, participants in the slowest race- and sex-specific quartile of walking speed had a 70% greater risk of hospitalization (MIRR = 1.70, 95% CI = 1.45–1.98) during follow-up than 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 greater risk of hospitalization 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) greater risk of hospitalization than 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) was 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 hospitalization. In models adjusted for age, race, sex, and clinical center, the risk of hospitalization did not differ between quartiles of arm lean mass (IRR = 1.05, 95% CI = 0.91–1.23 for Q1 vs Q4; P for trend across quartiles = .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 greater risk of hospitalizations than 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 and Q4 or Q3 and Q4, and the P for trend across quartiles was of borderline significance ($P=.09$).

Concurrent poor performance on several measures of strength and function (walking speed, chair stands performance, grip strength, and knee extension strength) was associated with greater risk of hospitalization (Table 4). In models adjusted for age, race, sex, and clinical center, participants who had poor performance on all four examinations had a risk of hospitalization that was 2.45 times higher than participants without poor performance on any examination. Poor performance on just one examination was associated with greater risk of hospitalization than poor performance on no examinations (IRR = 1.35, 95% CI = 1.18–1.54). Adjustment for potential confounding factors somewhat attenuated the associations, although all multivariate models remained highly significant. In the model that adjusted for medical conditions, age, self-rated health, race, sex, clinical center, weight, and percentage fat, participants with poor performance on all four examina-

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 Cohort

	Mean (Range)			
Parameter	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Muscle characteristics (from computed tomography)				
Muscle density, Hounsfield units				
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-ray 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)
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, Nm				
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 force/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/Nm				
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 of Health, Aging and Body Composition Study Participants According to Race- and Sex-Specific Quartile of Muscle Density (Hounsfield Units)*

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, mean ± SD	74 ± 2.9	73.7 ± 3	73.5 ± 2.9	73.2 ± 2.7	<.001
Height, cm, mean ± SD	166.7 ± 9.3	166.2 ± 9.5	166.4 ± 9.2	165.4 ± 9.4	.06
Weight, kg, mean ± SD	83.6 ± 15.3	77.3 ± 14.3	73.3 ± 12.5	68.3 ± 12.7	<.001
Percentage total body fat, mean ± SD	38.4 ± 7.06	35.6 ± 7.61	34.2 ± 7.48	31.8 ± 7.5	<.001
Body mass index, kg/cm^2, mean ± SD	30.1 ± 4.8	27.9 ± 4.5	26.5 ± 4.1	24.9 ± 3.9	<.001
Thigh muscle area, cm^2, mean ± SD	229.1 ± 57.4	228.1 ± 58.5	219.7 ± 52.5	214.1 ± 52.0	<.001
Total lean mass, kg, mean ± SD	51.2 ± 10.6	49.8 ± 10.8	48.2 ± 9.6	46.6 ± 9.8	<.001
Leg lean mass, kg, mean ± SD	8.2 ± 1.9	8.0 ± 1.9	7.7 ± 1.7	7.4 ± 1.7	<.001
Arm lean mass, kg, mean ± SD	2.9 ± 0.9	2.9 ± 0.9	2.8 ± 0.8	2.7 ± 0.8	<.001
Walking speed, m/s, mean ± SD	1.10 ± 0.24	1.18 ± 0.23	1.20 ± 0.23	1.22 ± 0.25	<.001
Chair stands per second, mean ± SD	0.33 ± 0.14	0.37 ± 0.12	0.37 ± 0.11	0.39 ± 0.13	<.001
Grip strength, kg, mean ± SD	31.7 ± 10.8	32.8 ± 11.2	33.2 ± 10.9	33.1 ± 10.7	.02
Knee extension strength, torque, Nm, mean ± SD	103.6 ± 39.6	108.5 ± 39.5	106.7 ± 37.8	107.0 ± 36.7	.14
Upper extremity muscle specific force, kg force/kg lean mass, mean ± SD	10.9 ± 2.6	11.6 ± 2.4	12 ± 2.6	12.2 ± 2.4	<.001
Lower extremity muscle specific force, Nm/kg lean mass, mean ± SD	12.4 ± 3.3	13.4 ± 3.1	13.7 ± 3.3	14.4 ± 3.1	<.001
Self-rated health excellent to very good, n (%)	88 (11.7)	109 (14.5)	99 (13.2)	117 (15.5)	<.001
Diabetes mellitus, n (%)	139 (18.5)	105 (13.9)	115 (15.4)	95 (12.7)	.01
Coronary heart disease, n (%)	159 (21.6)	136 (18.3)	141 (19.1)	111 (15)	.008
Peripheral arterial disease, n (%)	34 (4.7)	40 (5.4)	39 (5.3)	36 (4.9)	.92
Congestive heart failure, n (%)	13 (1.8)	12 (1.6)	9 (1.2)	4 (0.5)	.02
Hypertension, n (%)	141 (18.8)	169 (22.4)	143 (19)	177 (23.5)	.03
Osteoporosis, n (%)	79 (10.7)	79 (10.6)	66 (9)	74 (10)	.68
Pulmonary disease, n (%)	29 (3.9)	41 (5.5)	34 (4.5)	22 (2.9)	.005
Number of times hospitalized, mean ± SD	1.6 ± 2	1.4 ± 2.1	1.2 ± 1.8	1.0 ± 1.6	<.001
Days in hospital, mean ± SD	9.9 ± 16.3	8.4 ± 15.8	7.1 ± 14.8	6.3 ± 14.1	<.001

* Because the race and sex distributions for each quartile are fixed, the distributions of these factors are not reported in this comparison table.
SD = standard deviation.

tions had a risk of hospitalization that was 1.88 times higher than (95% CI = 1.27–2.78) participants without poor performance on any examination. Adding muscle density to the model resulted in essentially unchanged effect estimates. 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 before the baseline examination, the results were slightly attenuated but remained statistically significant. For example, in model adjusted for the age, clinical center, race, and sex (Model 1), as the number of physical examinations with poor performance increased, so did the risk of hospitalization (*P* for trend <.001). Participants with poor performance in one examination were about 26% more likely to experience a hospitalization (IRR = 1.26, 95% CI = 1.10–1.45) than those having no examinations with poor performance. Additionally, participants with poor performance in all four examinations were 2.14 times as likely to experience a hospitalization as those having no examinations with poor performance (IRR = 2.14, 95% CI = 1.43–3.19). Similar results were found for the multivariate models (Models 2 and 3) in Table 4; the IRRs for number of examinations with poor performance remained significant after subsetting to participants without a hospitalization in the year before baseline (*P* for trend for all <.001).

DISCUSSION

Worse physical function, muscle weakness, low muscle density, and low specific force of muscle were associated with greater risk of hospitalization over nearly 5 years of follow-up in black and white men and women who were free from disability at baseline examination. Adjustment for body size or prevalent medical conditions did not explain these associations. Concurrent poor performance on multiple tests of muscle strength and function was also associated with greater risk of hospitalization; excluding participants with at least one hospitalization before the baseline examination attenuated these associations only slightly. Thus, even in healthy, nondisabled older adults, poor physical function is associated with greater risk of hospitalization, although 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

Table 3. Hospitalizations According to Category of Muscle Strength and Function Parameters for Men and Women in the Health, Aging and Body Composition Cohort

Characteristic	N	Total Events	N with >1 Event	Multivariate-Adjusted* Incidence Rate Ratio (95% Confidence Interval)					P for Trend
				Unable	Quartile 1	Quartile 2	Quartile 3	Quartile 4	
Muscle characteristic									
Muscle density	2,675	3,433	1,471	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	2,675	3,433	1,471	N/A	1.18 (0.95–1.47)	1.04 (0.86–1.25)	1.03 (0.87–1.21)	1.00 (ref)	.14
Lean mass									
Leg lean mass	2,713	3,501	1,496	N/A	1.23 (0.93–1.63)	1.02 (0.81–1.28)	1.02 (0.85–1.22)	1.00 (ref)	.14
Arm lean mass	2,722	3,518	1,503	N/A	1.31 (1.01–1.69)	1.15 (0.94–1.42)	1.19 (1.00–1.42)	1.00 (ref)	.09
Physical function									
Walking speed	2,705	3,491	1,493	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	2,706	3,490	1,493	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)	.001
Strength									
Grip strength	2,714	3,496	1,497	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	2,419	3,010	1,306	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	2,713	3,496	1,497	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	2,411	2,998	1,301	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 percentage body fat, weight, age, self-rated health, sex, race, clinical center, and comorbid conditions (cerebrovascular disease, coronary heart disease, congestive heart failure, hypertension, peripheral arterial disease, pulmonary disease, and diabetes mellitus).

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 than those in the highest quartile. Low muscle density, as measured according to the muscle attenuation coefficient, is a marker for greater muscle fat infiltration, or myosteatosis, and greater intramuscular fat stores. The muscle density measures in Health ABC exclude most intermuscular adipose tissue depots, although 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 coefficient between muscle density (also known as the thigh muscle attenuation coefficient) and lipid content within muscle fibers was −0.43 and between thigh muscle attenuation and muscle triglyceride (TG) content was −0.58.[24] In Health ABC, low muscle density has been associated with greater 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]

Table 4. Risk of Hospitalization According to Summary Physical Performance Score

Number of Physical Examinations with Poor Performance	N	Incidence Rate Ratio (95% Confidence Interval)		
		Model 1: Adjusted for Age, Clinical Center, Race, and Sex*	Model 2: Multivariate Adjusted†	Model 3: Model 2 Adjustments Plus Muscle Density‡
0	1,200	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	2.47 (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 grip strength, knee extension strength, walking speed, and repeat chair stand examination. Poor performance was defined as performance in lowest race- and sex-specific quartile of a measure or unable to complete the measure.

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

† Adjusted for total percentage body fat, weight, age, self-rated health, sex, race, clinical center, comorbid conditions (cerebrovascular disease, coronary heart disease, congestive heart failure, hypertension, peripheral arterial disease, pulmonary disease, and diabetes mellitus). In Model 2 (n = 2,395), 2,977 hospitalizations occurred in 1,295 participants.

‡ The incidence rate ratio (IRR) (95% confidence interval (CI)) for muscle density in this model was 1.40 (95% confidence interval (CI) = 1.15–1.70) for Quartile 1, 1.25 (95% CI = 1.05–1.49) for Quartile 2, 1.09 (95% CI = 0.92–1.30) for Quartile 3, and 1.00 (referent) for Quartile 4; *P* for trend = .008.

In these analyses, lean mass was not independently associated with greater risk of hospitalization. A previous report from this cohort demonstrated that strength declines more quickly than muscle mass in older adults.[25] This report also noted that, although 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, although lower extremity muscle mass (thigh muscle cross-sectional area) and poor strength were associated with greater risk of mobility limitation, poorer strength explained the association between lower muscle mass and mobility limitation.[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 (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 a number of factors, including poor cardiovascular function and cognitive decline, may influence.[26,27] The results reported here are consistent with other published reports; slower walking speed has previously been associated with hospitalization and mortality in this and other cohorts.[11,28] 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 hospitalization, although in this study, upper extremity strength was also associated with risk of hospitalization, 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 comorbid conditions are 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 nonambulatory populations or those who are infirm. This selection bias may cause an underestimation of the observed associations, because disabled persons (who are likely to have poorer muscle strength and lower muscle mass) were excluded from the study, although any study or intervention trial in older adults focusing on mobility loss is likely to suffer from the same limitation. Second, although subanalyses were completed restricting the analysis set to participants who did not experience a hospitalization in the year before the baseline examination, the temporal association between poor performance and risk of hospitalization cannot be fully established. It is possible that participants who experienced a hospitalization before the baseline examination 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, although it is reassuring that poor physical function is not simply a maker of previous hospitalization. Third, although adjustment for coexisting medical conditions barely changed the analyses, 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 greater risk of hospitalization in adults aged 70 to 79. Interventions to improve muscle strength and physical performance might not only reduce future disability, but might also reduce the large economic burden associated with hospitalization should poor muscle strength and function be causally related to subsequent hospitalizations.

ACKNOWLEDGMENTS

The authors would like to thank Dr. Lynn Marshall for her critique of an earlier version of this manuscript, and Andrea Benard and Hilsa Ayonayon for their administrative assistance with the publication. The Health ABC Study is funded by National Institute on Aging (NIA) Contracts N01-AG-6-2101, N01-AG-6-2103, and N01-AG-6-2106. This research was supported in part by the Intramural Research Program of the National Institutes of Health, NIA, and by Amgen.

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

P. Cawthon received research funds from Amgen, Inc. to complete statistical analyses and prepare the manuscript. K. Fox received consultant funds from Amgen, Inc. to manage the analyses. S. Gandra, C. Chiou, and M. Anthony are employees of Amgen, Inc. and own stock or stock options in Amgen, Inc. A. Sewall received research funds from Amgen, Inc. to program the statistical analyses.

Author Contributions: All authors contributed to the conception and design, analysis and interpretation of the data, and drafting the article and revising it critically for important intellectual content, and all will provide final approval of the manuscript to be published.

Sponsor's Role: None.

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.
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.
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.
4. Stevens JA, Olson S. Reducing falls and resulting hip fractures among older women. MMWR Recomm Rep 2000;49:3–12.
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.
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.
7. Cummings SR, Nevitt MC, Browner WS et al. Risk factors for hip fracture in white women. N Engl J Med 1995;332:767–773.
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.

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;60A:324–333.
10. 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.
11. Penninx BW, Ferrucci L, Leveille SG et al. Lower extremity performance in non-disabled older persons as a predictor of subsequent hospitalization. J Gerontol A Biol Sci Med Sci 2000;55A:M691–M697.
12. 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.
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.
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.
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.
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.
17. Unger RH, Orci L. Lipoapoptosis: Its mechanism and its diseases. Biochim Biophys Acta 2002;1585:202–212.
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.
19. Harkonen R, Harju R, Alaranta H. Accuracy of the Jamar dynamometer. J Hand Ther 1993;6:259–262.
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.
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.
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.
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.
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.
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;61A:1059–1064.
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.
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.
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.