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Skeletal Muscle Cutpoints Associated with Elevated Physical Disability Risk in Older Men and Women

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The purpose of this study was to determine skeletal muscle cutpoints for identifying elevated physical disability risk in older adults. Subjects included 4,449 older (≥60 years) participants from the Third National Health and Nutrition Examination Survey during 1988–1994. Physical disability was assessed by questionnaire, and bioimpedance was used to estimate skeletal muscle, which was normalized for height. Receiver operating characteristics were used to develop the skeletal muscle cutpoints associated with a high likelihood of physical disability. Odds for physical disability were compared in subjects whose measures fell above and below these cutpoints. Skeletal muscle cutpoints of 5.76–6.75 and ≤5.75 kg/m^2 were selected to denote moderate and high physical disability risk in women. The corresponding values in men were 8.51–10.75 and ≤8.50 kg/m^2. Compared with women with low-risk skeletal muscle values, women with moderate- and high-risk skeletal muscle values had odds for physical disability of 1.41 (95% confidence interval (CI): 0.97, 2.04) and 3.31 (95% CI: 1.91, 5.73), respectively. The corresponding odds in men were 3.65 (95% CI: 1.92, 6.94) and 4.71 (95% CI: 2.28, 9.74). This study presents skeletal muscle cutpoints for physical disability risk in older adults. Future applications of these cutpoints include the comparison of morbidity risk in older persons with normal muscle mass and those with sarcopenia, the determination and comparison of sarcopenia prevalences, and the estimation of health-care costs attributable to sarcopenia.

activities of daily living; aging; disability evaluation; men; muscle, skeletal; risk; women

Abbreviations: CI, confidence interval; L_{neg}, likelihood ratio for negative result; L_{pos}, likelihood ratio for positive result; NHANES III, Third National Health and Nutrition Examination Survey; SMI, skeletal muscle index.

After reaching a peak in early adult years, skeletal muscle gradually declines beginning at about 45 years (1–3). Consequent to the age-related decrease in muscle mass, which is commonly referred to as "sarcopenia," is a reduction in muscle strength (4–6). Moreover, in severe cases of sarcopenia, physical disability may occur. Because the relation between muscle strength and physical disability in older adults is nonlinear (7), with the largest increase in physical disability occurring when moving from moderate to low strength, there is likely a threshold for muscle mass below which the risk for physical disability increases.

To date, three epidemiologic studies have shown a relation among sarcopenia, functional impairment, and physical disability (8–10). Without exception, these studies used an

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arbitrary cutpoint to determine those subjects with or without sarcopenia. Baumgartner et al. (8) and Melton et al. (9) defined sarcopenia in older adults as a height-adjusted appendicular muscle mass of 2 or more standard deviations below the mean of young adults. Janssen et al. (10) used a similar approach but used muscle mass relative to body weight. Although these three studies demonstrated that sarcopenia is associated with physical disability in older persons, they did not systematically examine the relation between muscle mass and physical disability. Thus, the specific skeletal muscle cutpoint below which physical disability increases is unknown.

Until recently, the size or mass of skeletal muscle could be determined only in small-scale laboratory studies. However, equations for predicting whole-body muscle mass using bioelectrical impedance analysis (11) and anthropometry (12) have recently been developed. With the exception of the anthropometric technique in obese subjects, these methods provide simple, inexpensive, and reliable estimates of whole-body muscle mass in adults (11, 12) that are appropriate for use in large-scale epidemiologic and laboratory-based studies.

The increasing older population, the availability of simple tools for measuring muscle mass (11, 12), and the developing interest of the scientific and medical communities in determining the impact of sarcopenia on morbidity dictate the need to establish the cutpoint at which sarcopenia becomes a significant health problem. Therefore, the main objective of our study was to determine skeletal muscle cutpoints for identifying elevated physical disability risk in older adults.

MATERIALS AND METHODS

Experimental design

The subjects consisted of 2,276 older (≥60 years) women and 2,223 older men from the Third National Health and Nutrition Examination Survey (NHANES III). Physical disability was assessed using standard questions (13–15). Bioelectrical impedance analysis was used to estimate whole-body muscle mass (11), which was normalized for height (muscle mass (kg)/height $(m)^2$). Receiver operating characteristics were used to develop skeletal muscle cutpoints associated with high and low likelihood ratios for physical disability. Prevalences and odds ratios for disability were compared in subjects falling above and below the skeletal muscle cutpoints.

Study population

NHANES III was conducted by the National Center for Health Statistics to estimate the prevalence of major diseases, nutritional disorders, and risk factors for these diseases. NHANES III was a nationally representative, two-phase, 6-year cross-sectional survey conducted from 1988 through 1994. The complex sampling plan used a stratified, multistage, probability cluster design. The total sample included 33,199 subjects. Full details of the study design, recruitment, and procedures are available elsewhere (16). The full evaluation included a home interview and a physical examination in a mobile center.

Of the total sample, 4,502 subjects were aged 60 years or more and of non-Hispanic White, non-Hispanic Black, and Mexican-American ethnicity. Bioelectrical impedance analysis measures, height and weight (which were needed to compute muscle mass), and physical disability measures were acquired. Other races, in whom the bioelectrical impedance analysis-muscle method has not been validated, were excluded from the data analysis. Informed consent was obtained from all participants, and the protocol was approved by the National Center for Health Statistics.

Physical disability

Physical disability was defined as having difficulty performing activities of daily living using the following two questions: 1) "Because of any impairment or health problem, do you need the help of other persons with personal care needs, such as eating, bathing, dressing, or getting around the home?" and 2) "Because of any impairment or health problem, do you need the help of other persons in handling routine needs, such as everyday household chores, doing necessary business, shopping, or getting around for other purposes?" (16). Subjects were classified as physically disabled if they answered "yes" to one or both of these questions and nondisabled if they answered "no" to both questions. These physical disability questions were selected from the classic works of Rosow and Breslau (13), Lawton and Brody (14), and Katz et al. (15). Physical disability should not to be confused with functional impairment, which is defined as having limitations in mobility performance (e.g, walking 0.25 mile (0.402 km), climbing 10 stairs, lifting/carrying 10 pounds (4.54 kg), standing from a chair). In the framework of the Nagi model of the disablement process, functional impairment precedes physical disability (17, 18).

Body composition

Body weight and height were measured to the nearest 0.1 kg and 0.1 cm using standardized equipment and procedures (19). Bioelectrical impedance analysis resistance (ohms, Ω) was obtained using a Valhalla 1990B Bio-Resistance Body Composition Analyzer (Valhalla Medical, San Diego, California) with an operating frequency of 50 kHz at 800 μA. Whole-body bioelectrical impedance analysis measurements were taken between the right wrist and ankle with the subject in a supine position (20) after the subjects completed a minimum 6-hour fast.

Skeletal muscle mass measurements. Muscle mass was calculated using the bioelectrical impedance analysis equation of Janssen et al. (11): skeletal muscle mass (kg) = [(height^2/bioelectrical impedance analysis resistance × 0.401) + (gender × 3.825) + (age × –0.071)] + 5.102, where height is measured in centimeters; bioelectrical impedance analysis resistance is measured in ohms; for gender, men = 1 and women = 0; and age is measured in years. This bioelectrical impedance analysis equation was developed and cross-validated against magnetic resonance imaging measures of whole-body muscle mass in a sample of 269 men and

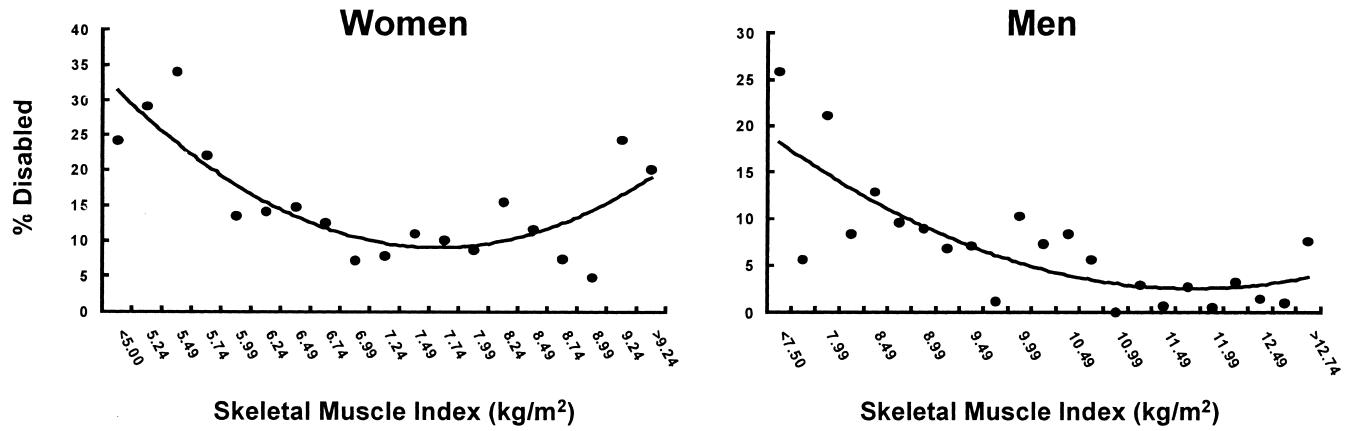

FIGURE 1. Percentage of women and men with physical disability according to skeletal muscle index (muscle mass (kg)/height (m)^2), Third National Health and Nutrition Examination Survey, 1988–1994. The points represent the prevalence of physical disability for the subjects that fit within each 0.25-kg/m^2 range of skeletal muscle index. The regression lines were derived and fit using polynomial regression analyses.

women who varied widely in age (18–86 years) and adiposity (body mass index, 16–48 kg/m^2). In that study, the correlation between bioelectrical impedance analysis-predicted and magnetic resonance imaging-measured muscle mass was 0.93 with a standard error of the estimate of 9 percent (11). Absolute muscle mass (kg) was normalized for height (muscle mass (kg)/height (m)^2) and termed the skeletal muscle index (SMI).

Covariates for multivariate odds ratio analysis

Age and race. Age was included in the multivariate analysis as a continuous variable. Race was coded as 0 for non-Hispanic Whites, 1 for non-Hispanic Blacks, and 2 for Hispanics.

Health behaviors. Alcohol consumption was graded as being none (0 drinks/month), moderate (1–15 drinks/month), or heavy (>15 drinks/month). Subjects were considered current smokers if they smoked cigarettes, cigars, or pipe tobacco at the time of the interview; previous smokers if they smoked 100 cigarettes, 20 cigars, or 20 pipes of tobacco in their lifetime; and nonsmokers if they smoked less than these amounts.

Comorbidity. The chronic illnesses included in the present study were coronary heart disease (myocardial infarction, congestive heart failure), stroke, cancer, lung disease (chronic bronchitis, emphysema), diabetes mellitus other than gestational diabetes, and arthritis (rheumatoid and osteoarthritis). These conditions were considered present for those who had ever been told by a physician that they had the condition.

Body fat. Body fat is related to physical disability independently of lean body mass or muscle mass (21, 22). Fat mass is also correlated to muscle mass (23, 24). Thus, to determine the independent effect of SMI on physical disability, it was important to control for fat mass in our analyses. Lean body mass was calculated using the gender-specific bioelectrical impedance analysis formulas of Sun et al. (25), which were developed for use in epidemiologic studies. Fat mass was subsequently determined by subtracting lean body mass from body weight. Fat mass was normalized for height (kg/m^2) and included in the multivariate analysis as a continuous variable.

Statistical analysis

The Intercooled Stata 7 program (Stata Corporation, College Station, Texas) was used to properly weight the sample and to take into account the complex sampling strategy of the NHANES III design. The purpose of weighting the sample was to produce statistical estimates that would have been obtained if the entire US population had been sampled.

Receiver operating characteristics analysis was used to develop skeletal muscle cutpoints associated with physical disability. For each gender, the relative frequencies of subjects with and without physical disability were determined at SMI intervals of 0.25 kg/m^2. These relative frequencies represent sensitivity (true positives) and specificity (true negatives) values. In the next step, the likelihood ratios for positive [sensitivity/(1 – specificity)] and negative [(1 – sensitivity)/specificity] results were calculated at the 0.25-kg/m^2 intervals. The goal of this analysis is to find a cutpoint that maximizes the likelihood ratio for positive results (L_{pos}) while minimizing the likelihood ratio for negative results (L_{neg}) (26). When no single cutpoint has both a high L_{pos} and a low L_{neg} value, as was the case for our analysis, two cutpoints can be selected—one with a relatively high L_{pos} and one with a relatively low L_{neg} (26). We selected the two cutpoints by looking for large changes in the L_{pos} and L_{neg} values when moving from one SMI interval to the next and by visually examining the relation between SMI and physical disability (figure 1). The selection of two cutpoints allowed us to classify our subjects into one of three categories: 1) high risk = subjects with SMI values below the L_{pos} cutpoint, 2) moderately increased risk = subjects with SMI

TABLE 1. Subject characteristics, Third National Health and Nutrition Examination Survey, 1988–1994

	Women	Men
Sample size (no.)	2,276	2,223
Weighted size (no.)*	19,434,291	14,668,613
Age (mean years)	71 (8)†	70 (7)
Weight (mean kg)	68.2 (15.0)	81.2 (14.6)
Height (mean cm)	159 (7)	173 (7)
Body mass index (mean kg/m^2)	27.0 (5.5)	26.6 (4.3)
Fat mass (mean kg)	26.1 (9.8)	21.6 (7.5)
Lean body mass (mean kg)	42.2 (6.3)	59.6 (9.0)
Skeletal muscle mass (mean kg)	17.9 (3.2)	29.7 (4.2)
Skeletal muscle index (mean kg/m^2)	7.04 (1.11)	9.86 (1.18)

* The weighted sample sizes are a reflection of the number of subjects and the sample weights.
† Numbers in parentheses, standard deviation.

values between the L_{pos} and L_{neg} cutpoints, and 3) low risk = subjects with SMI values above the L_{neg} cutpoint. For simplicity we have referred to the L_{pos} and L_{neg} cutpoints as the high-risk and moderately increased risk cutpoints, respectively, in the Results and Discussion sections.

The prevalences of physical disability were compared in those with low-risk, moderately increased risk, and high-risk SMI values using χ^2 statistics. Multiple logistic regression analysis was used to examine the associations between sarcopenia and physical disability. Dummy variables were created to compute odds ratios for these factors. Odds ratios were computed prior to and after controlling for the influence of age, race, health behaviors, comorbidity, and body fat.

RESULTS

Table 1 contains the descriptive characteristics of the subjects. Based on our definition, 15.7 percent of the older women and 6.9 percent of the older men were physically disabled ($p < 0.001$). SMI was 40.1 percent higher in men than women ($p < 0.001$).

The relation between SMI and physical disability in women is shown in figure 1. A SMI of ≤6.75 kg/m^2 was selected as the moderately increased risk cutpoint, and a SMI of ≤5.75 kg/m^2 was selected as the high-risk cutpoint (table 2). The prevalence of women with physical disability decreased from 25.8 percent in those with high-risk SMI values to 14.1 percent in those with moderately increased risk SMI values to 10.8 percent in those with low-risk SMI values ($p < 0.001$ for trend). By comparison with women with low-risk SMI values, the unadjusted and adjusted odds ratios for physical disability in women with moderately increased SMI values were 1.37 (95 percent confidence interval (CI): 0.98, 1.90; $p = 0.063$) and 1.41 (95 percent CI: 0.97, 2.04; $p = 0.072$). The unadjusted and adjusted odds ratios for physical disability in women with high-risk SMI values were 2.96 (95 percent CI: 1.92, 4.58; $p < 0.001$) and 2.93 (95 percent CI: 1.66, 5.19; $p < 0.001$).

The relation between SMI and physical disability in men is shown in figure 1. A SMI of ≤10.75 kg/m^2 was selected as the moderately increased risk cutpoint, and a SMI of ≤8.50 kg/m^2 was selected as the high-risk cutpoint (table 3). The prevalence of men with physical disability decreased from 14.8 percent in those with high-risk SMI values to 8.1 percent in those with moderately increased risk SMI values to 2.8 percent in those with low-risk SMI values ($p < 0.001$ for trend). By comparison with men with low-risk SMI values, the unadjusted and adjusted odds ratios for physical disability in men with moderately increased risk SMI values were 3.49 (95 percent CI: 1.95, 6.25; $p < 0.001$) and 3.65 (95 percent CI: 1.92, 6.94; $p < 0.001$). The unadjusted and adjusted odds ratios for physical disability in men with high-risk SMI values were 6.96 (95 percent CI: 3.72, 13.05; $p < 0.001$) and 4.71 (95 percent CI: 2.28, 9.74; $p < 0.001$).

Table 4 presents the distribution of the population according to the SMI cutpoints: 9.4 percent of the older women and 11.2 percent of the older men had SMI values within the high-risk range, and 21.9 percent of the older women and 53.1 percent of the older men had SMI values within the moderately increased risk range. Table 4 also contains a summary of the prevalences and odds ratios for physical disability according to the SMI cutpoints. Within both genders, physical disability increased in a graded fashion (p for trend < 0.001) when moving from the low-risk through the high-risk categories. To further explore the potential influence of age on the sarcopenia cutpoints, we examined separately the associations between SMI and physical disability in the subjects aged 60–74 years and those aged ≥75 years. Independently of gender and age group, the odds ratios for physical disability increased in a graded fashion (p for trend < 0.05) when moving from the low-risk through the high-risk categories.

The SMI cutpoints that were determined from physical disability were also used to predict four functional limitation measures (difficulty or inability to walk 0.25 mile, climb 10 stairs, lift/carry 10 pounds, stand up from a chair). In men, the likelihood of having difficulty or being unable to walk 0.25 mile [1.00, 1.02 (95 percent CI: 0.70, 1.49), 2.70 (95

TABLE 2. Likelihood ratio for disability in women, Third National Health and Nutrition Examination Survey, 1988–1994*

SMI† cutpoint (kg/m^2)	Not at risk (cumulative)‡	At risk (cumulative)‡	L_{pos}† value	L_{neg}† value
≤4.99	244,188	77,672	2.14	0.98
≤5.24	398,128	140,694	2.38	0.97
≤5.49	653,441	271,837	2.80	0.93
≤5.74	1,353,178	469,537	2.34§	0.88
≤5.99	2,315,934	618,512	1.80	0.87
≤6.24	3,783,220	860,183	1.53	0.85
≤6.49	5,007,784	1,071,468	1.44	0.81
≤6.74	6,767,403	1,320,624	1.32	0.79§
≤6.99	8,767,300	1,476,493	1.14	0.85
≤7.24	10,571,215	1,628,368	1.04	0.94
≤7.49	11,839,069	1,784,338	1.02	0.96
≤7.74	13,129,384	1,929,585	0.99	1.03
≤7.99	14,114,415	2,022,951	0.97	1.17
≤8.24	14,893,931	2,166,173	0.98	1.14
≤8.49	15,376,482	2,229,199	0.98	1.23
≤8.74	15,754,002	2,259,198	0.97	1.45
≤8.99	16,054,753	2,274,260	0.95	1.83
≤9.24	16,299,124	2,352,377	0.97	1.71
≥9.25	16,923,897	2,510,394		

* Equations: sensitivity = cumulative frequency at risk/total at risk; specificity = 1 − (total not-at-risk cumulative frequency/total not at risk); L_{pos} = sensitivity/1 − specificity; L_{neg} = 1 − sensitivity/specificity.

† SMI, skeletal muscle index; L_{pos}, likelihood ratio for positive result; L_{neg}, likelihood ratio for negative result.

‡ The numbers of subjects at risk and not at risk are weighted sample sizes.

§ Value represents the L_{pos} or L_{neg} value selected to denote the SMI cutpoint.

percent CI: 1.77, 4.10)] and lift/carry 10 pounds [1.00, 1.32 (95 percent CI: 0.82, 2.11), 2.37 (95 percent CI: 1.40, 4.00)] increased in a graded fashion (p for trend < 0.01) when moving from the low-risk to moderately increased risk to high-risk categories. In women, the likelihood of having difficulty or being unable to climb 10 stairs [1.00, 1.23 (95 percent CI: 0.89, 1.70), 2.35 (95 percent CI: 1.48, 3.75)] and lift/carry 10 pounds [1.00, 1.11 (95 percent CI: 0.81, 1.52), 2.74 (95 percent CI: 1.72, 4.37)] increased in a graded fashion (p for trend < 0.01) when moving from the low-risk to moderately increased risk to high-risk categories.

DISCUSSION

We identified skeletal muscle cutpoints that are associated with elevated physical disability risk in order to give researchers some insight into the interpretation of the risk involved with specific skeletal muscle values. Our findings demonstrate that the likelihood of physical disability was increased to a high degree when SMI values were ≤5.75 kg/m^2 in women and ≤8.50 kg/m^2 in men, and that physical disability was increased to a moderate degree when SMI values fell between 5.76 and 6.75 kg/m^2 in women and between 8.51 and 10.75 kg/m^2 in men. These cutpoints can be used to determine whether older subjects have normal muscle, moderate sarcopenia, or severe sarcopenia.

Three previous studies have shown a relation among sarcopenia, functional impairment, and physical disability (8–10). Baumgartner et al. (8) reported that sarcopenia is independently associated with physical disability in 808 older men and women. Melton et al. (9) reported that sarcopenia is associated with having difficulty walking in 345 older men. Using the NHANES III data set, Janssen et al. (10) reported that the likelihood of functional impairment and physical disability is approximately twofold greater in older men and threefold greater in older women with severe sarcopenia by comparison with older men and women with a normal muscle mass, respectively. Without exception, these studies used an arbitrary cutpoint to determine subjects with sarcopenia. Specifically, Baumgartner et al. (8) and Melton et al. (9) defined sarcopenia as height-adjusted appendicular (arm + leg) muscle mass of 2 or more standard deviations below the mean of young adults. Janssen et al. (10) used a similar approach but used whole-body muscle mass relative to body weight.

The cutoff values derived in the present study are for whole-body muscle mass, which can be estimated using a variety of widely available techniques including magnetic resonance imaging (1, 27, 28), total-body potassium counting (29), bioelectrical impedance analysis (11), and anthropometry (12, 30). Dual-energy x-ray absorptiometry-measured appendicular muscle can also predict whole-body

TABLE 3. Likelihood ratio for disability in men, Third National Health and Nutrition Examination Survey, 1988–1994*

SMI† cutpoint (kg/m^2)	Not at risk (cumulative)‡	At risk (cumulative)‡	L_{pos}† value	L_{neg}† value
≤7.49	189,163	65,777	4.66	0.95
≤7.74	314,802	73,276	3.12	0.95
≤7.99	546,818	135,141	3.31	0.90
≤8.24	877,267	164,973	2.52	0.90
≤8.49	1,404,328	243,044	2.32§	0.85
≤8.74	2,103,479	317,333	2.02	0.81
≤8.99	2,887,116	394,151	1.83	0.78
≤9.24	4,091,933	481,209	1.58	0.75
≤9.49	5,042,845	553,381	1.47	0.72
≤9.74	5,255,704	555,975	1.42	0.74
≤9.99	6,445,389	691,872	1.44	0.61
≤10.24	7,580,687	781,090	1.38	0.53
≤10.49	8,571,582	871,328	1.36	0.39
≤10.74	9,518,009	927,245	1.30	0.30§
≤10.99	9,712,979	927,245	1.28	0.31
≤11.24	10,469,597	950,107	1.22	0.29
≤11.49	11,218,951	955,195	1.14	0.35
≤11.74	11,835,470	972,652	1.10	0.34
≤11.99	12,432,060	975,678	1.05	0.48
≤12.24	12,730,743	985,422	1.04	0.49
≤12.49	13,140,018	991,511	1.01	0.72
≤12.74	13,336,668	993,443	1.00	1.09
≥12.75	13,649,602	1,019,011		

* Equations: sensitivity = cumulative frequency at risk/total at risk; specificity = 1 − (total not-at-risk cumulative frequency/total not at risk); L_{pos} = sensitivity/1 − specificity; L_{neg} = 1 − sensitivity/specificity.

† SMI, skeletal muscle index; L_{pos}, likelihood ratio for positive result; L_{neg}, likelihood ratio for negative result.

‡ The numbers of subjects at risk and not at risk are weighted sample sizes.

§ Value represents the L_{pos} or L_{neg} value selected to denote the SMI cutpoint.

muscle mass [whole-body muscle = (1.17 × appendicular muscle) − 1.01] and explains 96 percent of the between-subject variation in whole-body muscle (31). It is important to note that the skeletal muscle cutpoints determined in this study are similar to the arbitrary cutpoints determined in previous studies (8, 9, 32). For example, using the 2 standard deviations below the young adult mean, Baumgartner et al. (8) used cutoff values of 8.1 kg/m^2 in men and 5.9 kg/m^2 in women to define sarcopenia (*note*: these values were converted from appendicular to whole-body muscle using a published algorithm (31)). These values are similar to the high-risk sarcopenia cutpoints calculated in the present study of 8.50 kg/m^2 in men and 5.75 kg/m^2 in women. However, the sarcopenia cutpoints calculated in the present study predict physical disability to a better degree than do the –2 standard deviation values. Using the NHANES III data, we determined that the odds ratios for physical disability in older men and women with SMI values 2 standard deviations or more below the young adult mean (<8.48 kg/m^2 in men, <6.06 kg/m^2 in women) were 1.61 and 1.66, respectively, by comparison with older men and women having SMI values above the –2 standard deviation cutpoint (data not shown). These odds ratios are considerably smaller than those for the older adults whose SMI values fell within the high-risk categories determined from receiver operating characteristics analysis in the current study.

It is important to note that our cutpoints were for physical disability (difficulty performing activities of daily living). It is possible that the SMI cutpoints would have been different had we assessed the relation between SMI and functional impairment (limitations in mobility such as walking). It is also possible that other characteristics such as age and chronic disease status could substantially alter the association between SMI and physical disability. Future studies are needed to determine whether or not different sarcopenia cutpoints are required for different population subgroups.

We were unable to identify a single cutpoint that was associated with a high likelihood of correctly identifying subjects both with and without physical disability. For both men and women, two cutpoints were identified, one with a large likelihood ratio for positive results (L_{pos}) and one with a low likelihood ratio for negative results (L_{neg}). This allowed classification of subjects with a high likelihood of physical disability (values below L_{pos}), subjects with a moderately

TABLE 4. Summary of results, Third National Health and Nutrition Examination Survey, 1988–1994

Range of values (kg/m²)†	% of population‡	% disabled§	Odds ratios for disability	95% CI¶	All ages		Aged 60–74 years		Aged ≥75 years	
					Adjusted odds ratios for disability#	95% CI	Adjusted odds ratios for disability#	95% CI	Adjusted odds ratios for disability#	95% CI
Women										
≤5.75	9.4	25.8	2.98*	1.93, 4.61	3.31*	1.91, 5.73	5.73*	2.46, 13.36	2.61*	1.32, 5.18
5.76–6.75	21.9	14.1	1.37	0.98, 1.90	1.41	0.97, 2.04	1.51	0.82, 2.77	1.23	0.78, 1.94
≥6.76	68.7	10.8	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Men										
≤8.50	11.2	14.8	6.96*	3.72, 13.05	4.71*	2.28, 9.74	5.44*	2.05, 14.42	3.25*	1.17, 9.02
8.51–10.75	53.1	8.1	3.49	1.95, 6.25	3.65	1.92, 6.94	5.33	1.94, 14.67	2.73	0.96, 7.78
≥10.76	35.7	2.8	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent

* Significant trend ($p < 0.05$) for increasing odds ratios with increased grades of sarcopenia.
† Ranges were determined using likelihood odds ratios for positive and negative test results (tables 2 and 3).
‡ Percentage of total subject pool within skeletal muscle index range.
§ Percentage of subjects within skeletal muscle index range that were disabled.
¶ CI, confidence interval.
# Odds ratios were adjusted for age, race, smoking status, alcohol intake, comorbidity, and body fat.

increased likelihood of physical disability (values between L_{pos} and L_{neg}), and subjects with a low likelihood of physical disability (values above L_{neg}). For example, in men SMI values of ≤8.50 kg/m² were associated with a relatively high frequency of true positives, and SMI values of ≤10.75 kg/m² were associated with a relatively low frequency of true negatives. Subsequent analysis revealed that men with SMI values of ≤8.50 kg/m² (high risk) were about seven times as likely to have physical disability by comparison with men having SMI values of ≤10.76 kg/m² (low risk), whereas men with SMI values between 8.51 and 10.75 kg/m² (moderately increased risk) were only 3.5 times as likely to have physical disability by comparison with men having SMI values of ≥10.76 kg/m².

In the women, we observed a "J"-shaped relation between SMI and physical disability (figure 1). The incidence of physical disability was increased in women with both low and very high SMI values. The increased physical disability risk in women with very high SMI values may have in part reflected the increased fat mass and obesity in these subjects. Fat mass is an independent predictor of physical disability (21, 22), and fat mass was considerably higher (39.2 kg vs. 28.1 kg) in women with very high SMI values (≥9.00 kg/m²) than in women with moderately high SMI values (6.75–8.99 kg/m²). The women with very high SMI values were also quite obese, while the women with moderately high SMI values were only moderately overweight (body mass index of 37.5 vs. 28.4 kg/m²). Previous studies have shown that there is not increased risk or likelihood for functional limitations in older women until a high level of obesity (body mass index of ≥35.0 kg/m²) is reached (33, 34). In addition to fat mass and obesity level, other undetermined factors may have played a role in elevating the likelihood of physical disability in the women with very high SMI values.

In this study, the SMI cutpoints for predicting physical disability were considerably higher in men than in women. The reason for this gender difference is unclear. Sarcopenia, as determined from the SMI cutpoints, was also a stronger predictor of physical disability in men than in women. For example, the adjusted odds ratios for disability for the men and women in the high-risk SMI categories were 4.71 and 3.31, respectively. This observation is consistent with that of Visser et al. (35), who report that mid-thigh muscle size is more strongly associated with lower extremity performance in older men than women in the Health, Aging, and Body Composition Study. These authors also report that fat mass is a better predictor of lower extremity performance in older women than men (35), which is also consistent with our findings as very high SMI values, which were associated with a high fat mass, were associated with increased physical disability in women but not men (figure 1). The implication of these observations is that interventions aimed at improving function and decreasing physical disability through changes in body composition may need to have a different emphasis in older men and women.

Based on the findings reported here, we conclude that approximately 10 percent of the older American population is considerably more likely to have physical disability and that approximately 35 percent of the older American population is somewhat more likely to have physical disability in relation to a low SMI. These numbers confirm that low muscle mass has an impact on the health and well-being of a considerable number of older Americans. Given the health-care costs associated with physical disability (36, 37), these findings also suggest that sarcopenia imposes a significant economic burden on the US health-care system.

The NHANES III subjects were a representative sample of the noninstitutionalized US population. Therefore, our results can be applied to most Americans aged 60 years or above. However, because NHANES III was conducted among the noninstitutionalized population and because the NHANES III participants who were physically unable to make it to the mobile examination center were not included in our analysis (bioelectrical impedance analysis measures

were not obtained in these subjects), the prevalences of sarcopenia and physical disability in the entire elderly population is likely higher than what is reported here. Further, it is possible that the relation between muscle mass and physical disability in institutionalized subjects is different from that reported here.

Our study has other limitations that warrant recognition. First, the cross-sectional nature of this study precludes definitive causal inferences about the relation between sarcopenia and physical disability. Although no longitudinal studies report that sarcopenia causes physical disability, muscular strength, which is in large measure determined by muscle mass in older adults (38), is predictive of physical disability in longitudinal studies (7, 39). Second, many of the variables examined in NHANES III, including the physical disability measures, were based on self-report, and the reliability of self-reported physical function in older persons is only about 85 percent (40). Finally, we used bioelectrical impedance analysis to estimate muscle mass. Previous studies have noted inaccuracies when using bioelectrical impedance analysis to assess lean body mass in the elderly, which may in part be caused by changes in the hydration of lean mass and the cylindrical shape of the appendicular muscles (41, 42). However, the skeletal muscle bioelectrical impedance analysis equation used in the current study was developed in a heterogeneous sample (11) that varied widely in age (18–86 years) and muscle mass. Further, in that sample (11), age explained only an additional 1–2 percent of the variance in muscle mass that was not already explained by body mass index measures. Another limitation of the bioelectrical impedance analysis method is that the standard error of the estimate for predicting muscle mass in both genders is 9 percent (11). Thus, because imprecision biases the results toward the null hypothesis, we likely underestimated the true odds ratios for sarcopenia. Further, the magnitude of the bioelectrical impedance analysis measurement error suggests that it may not be precise enough for the clinical setting. The feasibility of using bioelectrical impedance analysis or other techniques to estimate SMI in the clinical setting needs to be addressed in future studies.

In conclusion, our study presents disability-related sarcopenia cutpoints for older men and women. Using these cutpoints, we demonstrated that SMI is a strong independent predictor of physical disability. Future applications of these cutpoints include the comparison of morbidity and mortality risk in older persons with normal muscle mass with those having sarcopenia, the determination and comparison of sarcopenia prevalences at the population level, and the estimation of health-care costs attributable to sarcopenia. These and other applications should lead to an improved understanding of the public health impact of sarcopenia.

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