Muscle Mass Index As a Predictor of Longevity in Older Adults

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Preethi Srikanthan, MD, MS,[a] Arun S. Karlamangla, MD, PhD[b]

[a]Division of Endocrinology, Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, Calif; [b]Division of Geriatrics, Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, Calif.

ABSTRACT

OBJECTIVE: Obesity (as defined by body mass index) has not been associated consistently with higher mortality in older adults. However, total body mass includes fat and muscle, which have different metabolic effects. This study was designed to test the hypothesis that greater muscle mass in older adults is associated with lower all-cause mortality.

METHODS: All-cause mortality was analyzed by the year 2004 in 3659 participants from the National Health and Nutrition Examination Survey III who were aged 55 years or more (65 years if women) at the time of the survey (1988-1994). Individuals who were underweight or died in the first 2 years of follow-up were excluded to remove frail elders from the sample. Skeletal muscle mass was measured using bioelectrical impedance, and muscle mass index was defined as muscle mass divided by height squared. Modified Poisson regression and proportional hazards regression were used to examine the relationship of muscle mass index with all-cause mortality risk and rate, respectively, adjusted for central obesity (waist hip ratio) and other significant covariates.

RESULTS: In adjusted analyses, total mortality was significantly lower in the fourth quartile of muscle mass index compared with the first quartile: adjusted risk ratio 0.81 (95% confidence interval, 0.71-0.91) and adjusted hazard ratio 0.80 (95% confidence interval, 0.66-0.97).

CONCLUSIONS: This study demonstrates the survival predication ability of relative muscle mass and highlights the need to look beyond total body mass in assessing the health of older adults.

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KEYWORDS: Mortality; Muscle

A high level of adiposity, as implied by a body mass index (BMI) more than 30 kg/m^2, is linked to abnormal glucose metabolism[1] and incidence of cardiovascular disease,[2] and is strongly associated with increased mortality in multiple prospective cohort studies.[3] In older adults, however, all-cause mortality may be lower in those who are obese than in those who are nonobese.[4] This seemingly protective role

for obesity in older ages is not due solely to confounding by weight loss in severely ill individuals at the end of life. Studies that have controlled for this possibility by excluding those with recent weight loss, those with end-stage diseases (eg, cancer), and those who died in the first few years after BMI assessment also have found that obesity is *not* associated with increased mortality in older adults.[5,6]

However, adiposity and muscle mass have opposite associations with glucose metabolism[7] and health risks,[8] and thus possibly opposite associations with mortality risk. Because old age is a time of changing balance between fat and muscle mass, total body mass (and BMI) becomes less useful in assessing the metabolic health of older adults. In contrast, waist–hip ratio, which indirectly reflects the relative abundance of central fat over peripheral fat and muscle (specifically, gluteal muscle), does have positive associations with all-cause mortality even in older

individuals.[9] A few studies also have found that muscle strength is related inversely to mortality risk in older adults.[10,11]

It has been noted that muscle mass index, defined as muscle mass divided by the square of height (analogous to BMI but with muscle mass instead of total body mass), is associated with better insulin sensitivity and lower risk of pre-diabetes or diabetes.[12] Thus, we hypothesized that muscle mass index would be associated inversely with all-cause mortality in older adults. To test this hypothesis, we examined the association of muscle mass index with all-cause mortality over 10 to 16 years in a nationally representative cohort of older adults.

MATERIALS AND METHODS

Design and Methods

The Third National Health and Nutrition Examination Survey (NHANES III) was a national survey conducted from 1988 to 1994, using a stratified, multistage, probability cluster design.[13]

We restricted our analysis to the 4321 older participants (men aged $\geq$55 years and women aged $\geq$65 years) who were not underweight (BMI >18.5 kg/m^2) or undernourished (waist circumference at least 50 cm) and did not die in the first 2 years after the NHANES examination. A higher minimum age criterion was used for women because of the later onset of cardiovascular disease[14] and longer life expectancy in women[15] relative to men. Of these 4321 eligible participants, 662 were excluded for missing the primary exposure (because of contraindications, such as implanted pacemakers and defibrillators or congestive heart failure), leaving us with a final study sample of size 3659.

Measurements: Exposures

Total skeletal muscle mass was calculated from measurements of bioelectrical impedance using the Valhalla Scientific Body Composition Analyzer 1990 B (Valhalla Scientific, San Diego, Calif), obtained after fasting for at least 6 hours (in which all fluids other than water were also restricted).[13] The bioelectrical impedance-based approach relies on the relationship between body composition and body water content, and this may be disturbed in pathologic states that increase whole body water, such as cardiac failure. Thus, participants with diagnosed congestive heart failure were excluded. The bioelectrical impedance measurement was converted to total skeletal muscle mass (in kilograms) via the

> ### CLINICAL SIGNIFICANCE
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> - Muscle mass is associated inversely with mortality risk in older adults independently of fat mass and cardiovascular and metabolic risk factors.
> - Anabolic processes that promote muscle bulk may be associated with longer survival.
> - Changes in body composition, rather than adiposity alone, should be considered when counseling older adults on preventative health behaviors.

calibration equation of Janssen et al[16]:

$$\text{skeletal muscle mass} = [0.401 \times (\text{height}^2/\text{bioelectrical impedance}) + (3.825 \times \text{sex}) - (0.071 \times \text{age})] + 5.102,$$

with height measured in centimeters, bioelectrical impedance measured in ohms, sex coded 1 for men and 0 for women, and age measured in years. Muscle mass index, the ratio of skeletal muscle mass to the square of body height, in kilograms/meters squared, was calculated, and sex-specific quartiles of muscle mass index were created.

Measurements: Outcomes

NHANES III participants were assessed for mortality over the years 1986 to 2004 by the National Center for Health Statistics Research Data Center using 3 sources of information: a probabilistic match to a National Death Index record, the Social Security Administration, and the Centers for Medicare and Medicaid Services. Participants whose deaths resulted from accidents, suicide, homicide, firearms, and war were treated as not having died and censored at the recorded time of death.

Measurements: Covariates

Age, race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican-American, and other), sex, smoking status (current, past, never), and doctor-diagnosed cancer (yes/no) were obtained from self-reports. Five-year age categories were created, from 55 to 59 years upward; the last was $\geq$95 years. Waist circumference, body height, and body weight were measured, and central obesity was defined as waist circumference >88 cm in women and >102 cm in men.[17]

Serum insulin and plasma glucose were measured from fasting blood samples (from participants who had fasted $\geq$6 hours). Plasma glucose level was measured with a hexokinase enzymatic reference method (COBAS MIRA; Roche Diagnostics, Indianapolis, Ind), and serum insulin level was measured by means of a radioimmunoassay (Pharmacia Diagnostics, Uppsala, Sweden).[13] Insulin resistance was approximated using the Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) using the following formula[18]: HOMA-IR = fasting glucose (in mmol/L) $\times$ fasting insulin (in µU/mL)/22.5.

Glycosylated hemoglobin was measured using the Primus Automated HPLC system (model CLC330 [Primus I]; Primus Corp, Kansas City, Mo).[13] Diabetes mellitus was

defined by the presence of 1 or more of the following 3 conditions[19]: (1) glycosylated hemoglobin ≥6.5%; (2) fasting glucose ≥7 mmol/L (126 mg/dL); or (3) self-report of diabetes (based on the participant's response to the question "Have you ever been told by a doctor that you have diabetes or sugar diabetes?"). Pre-diabetes was defined by the presence of glycosylated hemoglobin ≥6.0% or fasting glucose ≥5.5 mmol/L (100 mg/dL) in the absence of diabetes.

Total serum cholesterol and high-density lipoprotein cholesterol were measured using a Hitachi 737 Analyzer (Boehringer-Mannheim Diagnostics, Indianapolis, Ind).[13] Total cholesterol was categorized into 3 groups: <200 mg/dL, 200 to 240 mg/dL, and ≥240 mg/dL. High-density lipoprotein was marked as low if ≤40 mg/dL.

Serum C-reactive protein levels were measured using latex-enhanced nephelometry (Behring Nephelometer Analyzer System; Behring Diagnostics, Somerville, NJ).[13] C-reactive protein levels were categorized on the basis of clinical thresholds as <0.3 mg/dL, ≥0.3 but <1.0 mg/dL, and ≥1.0 mg/dL.

A set of blood pressure measurements was obtained during the 4-hour physical examination at the mobile examination center.[13] Hypertension was defined as mean systolic blood pressure ≥140 mm Hg, mean diastolic blood pressure ≥90 mm Hg, or self-report of hypertension.[13]

Finally, serum creatinine was measured by the modified kinetic Jaffe reaction using a Hitachi Model 737 multichannel analyzer (Boehringer Mannheim Diagnostics, Indianapolis, Ind).[13]

Statistical Analyses

We examined the risk of all-cause mortality before December 2004 by sex-specific quartiles of muscle mass index and used Poisson regression with robust estimation of standard errors to adjust for covariates. We chose to use modified Poisson regression over ordinary logistic regression because the outcome was not rare; risk of mortality in each of the muscle mass index quartiles was more than 10%. We first adjusted only for demographics (age, sex, race/ethnicity), smoking status, cancer history, and central obesity. We then added cardiovascular risk factors: inflammation (C-reactive protein), hypertension, high-density lipoprotein cholesterol, total cholesterol and serum creatinine, and glucose metabolism measures (HOMA-IR, glycosylated hemoglobin, diabetes mellitus, and pre-diabetes).

We also examined mortality rates (number of deaths per 10,000 person-months) by sex-specific quartiles of muscle mass index and used Cox proportional hazards regression (with person-time censored at December 31, 2004, for those who were still alive at that date) to adjust for the same covariates.

To address the possibility that longevity associations with muscle mass primarily reflect the cardiovascular and metabolic consequences of fat mass, we also examined mortality risk and rate as a function of total nonmuscle mass. In these analyses, we used sex-specific quartiles of nonmuscle mass index, defined as BMI minus muscle mass index, as the primary predictor, and adjusted for all the same covariates except for central obesity (a marker of truncal fat mass). To contrast the mortality associations of muscle mass index against those of BMI, we ran parallel analyses with sex-specific quartiles of BMI.

To make the results representative of the US population, we used NHANES mobile examination center weights (with robust standard error estimation), and to account for the NHANES survey design, we modeled clustering at the NHANES geographic (primary) sampling units using generalized estimating equations in the Poisson regressions and Wei and Lin's[20] approach in Cox proportional hazards regressions. SAS version 9.2 (SAS Institute Inc, Cary, NC) was used for all the analyses.

RESULTS

The complete NHANES sample that met eligibility criteria (age ≥55 years for men, ≥65 years for women; BMI >18.5 kg/m^2; waist size ≥50 cm; survived at least 2 years) included 4321 participants. The study sample that also had valid bioelectrical impedance measurements (N = 3659) was representative of the larger, complete NHANES sample (Table 1).

The sex-specific 25th, 50th, and 75th percentiles of muscle mass index, the primary predictor, were 6.2, 6.9, and 7.6 kg/m^2 in women, respectively, and 9.2, 10.0, and 10.8 kg/m^2 in men, respectively. For comparison, the sex-specific 25th, 50th, and 75th percentiles of BMI were 22.8, 25.9, and 29.6 kg/m^2 in women, respectively, and 24.4, 26.8, and 29.7 kg/m^2 in men, respectively.

The median length of follow-up in the study sample was 158 person-months (13.2 person-years), and there were 2012 deaths. The median age at death was 82.7 years; 7 individuals were aged 100 years or more at the time of death. The median age at the end of follow-up (or censoring) for those not known to have died was 80.6 years; 10 individuals were aged 100 years or more at the end of follow-up.

Unadjusted all-cause mortality risk was significantly higher in the lowest muscle mass index quartile compared with the highest muscle mass index quartile (58% compared with 41%; relative reduction of 30%) (Table 2). Unadjusted mortality rates also were significantly higher in the lowest muscle mass index quartile compared with the highest muscle mass index quartile (42.5 per 10,000 person-months compared with 27.9 per 10,000 person-months; relative reduction of 34%). However, both mortality risk and mortality rate in the third quartile were not significantly different from that in the fourth quartile (Table 2). Kaplan-Meier survival curves by muscle mass index quartiles also show higher survival in the top 2 quartiles than in the bottom 2 quartiles, but little difference between the top 2 quartiles (Figure 1).

In the fully adjusted models, mortality in the third and fourth highest quartiles of muscle mass index was significantly lower than in the bottom quartile but not different from each other. Also, mortality in the second muscle mass

Table 1 Descriptive Statistics: Median (Interquartile Range) or Percentage*

	Analytic Sample (N = 3659)	Total NHANES III Sample (N = 4321)†
Age (y)	69.0 (64.0-75.0)	69.0 (64.0-75.0)
Gender: male	57.2%	56.9%
Race/ethnicity		
Non-Hispanic white	85.2%	84.6%
Non-Hispanic black	07.4%	07.7%
Mexican-American	02.1%	02.3%
Other	05.3%	05.4%
BMI (kg/m^2)	26.4 (23.8-29.7)	26.5 (23.8-29.8)
Waist circumference (cm)	97.8 (89.4-105.5)	97.8 (89.4-105.9)
Smoking status		
Past	43.2%	43.5%
Current	14.8%	15.1%
Serum creatinine (mg/dL)	1.1 (1.0-1.3)	1.1 (1.0-1.3)
Glycosylated hemoglobin (%)	5.5 (5.2-5.9)	5.6 (5.2-5.9)
HOMA-IR	2.2 (1.6-3.5)	2.3 (1.6-3.5)
Pre-diabetes	36.1%	35.8%
Diabetes	17.5%	18.6%
Hypertension	61.4%	62.9%
Serum CRP (mg/dL)	0.21 (0.21-0.44)	0.21 (0.21-0.44)
HDL cholesterol (mg/dL)	47 (39-58)	47 (39-58)
Serum cholesterol (mg/dL)	219 (193-246)	219 (193-246)
Cancer	7.8%	7.9%
Mortality by December 2004	48.0%	50.3%

For definitions of generalized obesity, central obesity, pre-diabetes, diabetes, see the "Materials and Methods" section.

BMI = body mass index; CRP = C-reactive protein; HDL = high-density lipoprotein; HOMA-IR = Homeostasis Model Assessment of Insulin Resistance; NHANES III = Third National Health and Nutrition Examination Survey.

*Descriptive statistics computed with observations weighted by NHANES Mobile Exam Center weights.

†Those in the NHANES III sample who were aged ≥55 years (male) or 65 years (female), not underweight or undernourished, who survived at least 2 years after the NHANES examination.

index quartile was not different from that in the bottom (reference) quartile (Table 2). Compared with the lowest quartile of muscle mass index, the mortality risk ratio for the third quartile was 0.84 (95% confidence interval [CI], 0.74-0.94) when adjusted only for demographics, smoking, cancer, and central obesity; 0.80 (95% CI, 0.70-0.92) after additional adjustment for cardiovascular risk factors and serum creatinine; and 0.81 (95% CI, 0.70-0.94) in the fully adjusted model (which also included glucose metabolism measures) of Table 2. Likewise, the mortality hazard ratio for the third quartile compared with the bottom quartile of muscle mass index was 0.78 (95% CI, 0.66-0.93) adjusted for demographics, smoking, cancer, and central obesity; 0.73 (95% CI, 0.60-0.87) with additional adjustment for cardiovascular risk factors and serum creatinine; and 0.74 (95% CI, 0.60-0.90) in the fully adjusted model of Table 2.

In contrast, mortality risk (likewise, mortality rate) remained essentially unchanged from the lowest to the highest sex-specific quartile of nonmuscle mass index: 49.6% in the highest to 49.1% in the lowest, P for mortality risk trend .8 (likewise, 35.6 per 10,000 person-months in the highest to 33.5 per 10,000 person-months in the lowest; P for mortality rate trend .7) (Table 3). In the fully adjusted models (adjusted for all the same covariates as before except central obesity), mortality was not significantly different across quartiles of nonmuscle mass index; adjusted mortality risk ratio for the highest compared with the lowest quartile was 0.96 (95% CI, 0.83-1.11; P for trend across quartiles .5); adjusted mortality hazard ratio was 0.84 (95% CI, 0.67-1.10; P for trend across quartiles .1) (Table 3).

There was a small and statistically nonsignificant decline in mortality risk (50.5% to 45.9%, P for trend .2) and mortality rate (36.1 per 10,000 person-months to 31.2 per 10,000 person-months, P for trend .09) from the lowest to the highest quartile of BMI (Table 4). BMI associations with mortality risk and rate remained statistically nonsignificant in the fully adjusted models (after adjusting for all covariates except

Table 2 Unadjusted and Adjusted All-cause Mortality Risk (% Mortality by December 2004) and Rate (Number of Deaths per 10,000 Person-Months) as a Function of Sex-specific Quartiles of Muscle Mass Index

	Muscle Mass Index Lowest Quartile	Muscle Mass Index Second Quartile	Muscle Mass Index Third Quartile	Muscle Mass Index Highest Quartile	P for Trend*
Absolute risk (%)	58.0	51.9	41.3	40.8	<.0001
Adjusted relative risk (risk ratio)†	ref	0.97 (0.85-1.10)	0.81 (0.70-0.94)	0.81 (0.71-0.91)	.0003
Absolute rate (per 10,000 person-mo)	42.5	36.4	27.4	27.9	<.0001
Adjusted relative rate (hazard ratio)†	ref	0.94 (0.76-1.16)	0.74 (0.60-0.90)	0.80 (0.66-0.97)	.006

Adjusted effect sizes presented as point estimate (95% confidence interval).

*P value for linear trend across the 4 quartiles. Muscle mass index (skeletal muscle mass divided by height-squared); quartile cut-points: 6.2, 6.9, and 7.6 kg/m^2 for women and 9.2, 10.0, and 10.8 kg/m^2 for men.

†Adjusted for age (in half-decade categories); sex; race; central obesity; current smoking; past smoking; cancer (yes/no); C-reactive protein categories: <0.3, 0.3-1.0, and ≥1.0 mg/dL; hypertension; low high-density lipoprotein cholesterol (≤40 mg/dL); total cholesterol (categorized as <200, 200-240, and ≥240 mg/dL); HOMA-IR (log-transformed); glycosylated hemoglobin (log-transformed); diabetes; pre-diabetes; and serum creatinine.
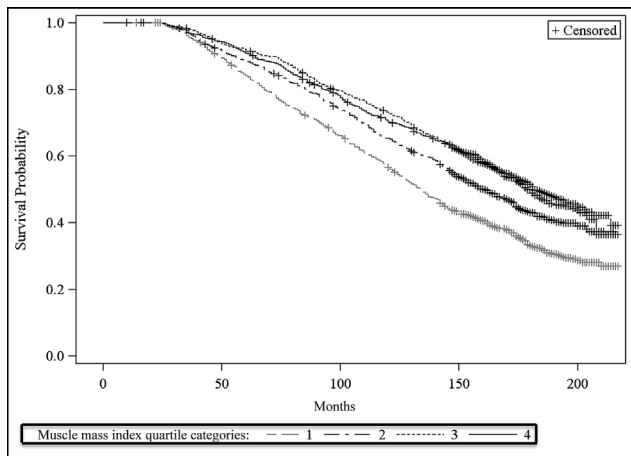
Figure 1   Kaplan-Meier curves for survival by sex-specific quartiles of muscle mass index. Muscle mass index quartile category cut-points: 6.2, 6.9, and 7.6 kg/m^2 for women, and 9.2, 10.0, and 10.8 kg/m^2 for men.

central obesity): The adjusted mortality risk ratio for the highest compared with the lowest quartile of BMI was 0.92 (95% CI, 0.80-1.10; *P* for trend across the quartiles .12), and the adjusted mortality hazard ratio for the highest compared with the lowest quartile of BMI was 0.85 (95% CI, 0.69-1.40; *P* for trend across the quartiles .25) (**Table 4**).

DISCUSSION

As hypothesized, in older Americans, muscle mass relative to body height was associated inversely with all-cause mortality over a 10- to 16-year follow-up. This inverse relationship was not explained by traditional cardiovascular risk factors (dyslipidemia, hypertension, and inflammation) or glucose dysregulation (pre-diabetes, diabetes, insulin resistance, and dysglycemia), suggesting that relative muscle mass is an independent prognostic marker for survival in older adults.

Traditional cardiovascular risk factors and glucose dysregulation are linked to the development of atherosclerotic

vascular disease and reduced cardiac output,[21,22] which in turn lead to reduced blood flow to skeletal muscle, and thus, potentially, to reduced muscle mass.[23] The cardiovascular risk factors and markers of glucose dysregulation and inflammation in this study may not have completely captured the extent of subclinical cardiovascular disease, and the independent prognostic ability of relative muscle mass may be a reflection of the mortality risks conferred by subclinical cardiovascular disease in older adults.

Alternately, factors that lead to better than average relative muscle mass, such as genetic predisposition and a consistently active lifestyle over the life-course, also are likely to increase cardiorespiratory fitness, a major predictor of improved survival.[24] The survival prediction ability of relative muscle mass may simply reflect the protective role of cardiorespiratory fitness. Finally, a potential causal pathway from muscle mass to longevity is through the role of muscle as a reliable protein reserve, which is vital in protecting an individual after a prolonged illness.[25]

Even if there are no causal links between muscle mass and longevity, this study definitively demonstrates that muscle mass relative to body height has independent predictive ability for all-cause mortality in older adults. This is the first study to establish this in a large, nationally representative cohort. Previous studies have uncovered associations between muscle function (strength, power, speed) and mortality, but have failed to find associations between muscle bulk and mortality.[10,11,26,27] With a few exceptions, prior studies were small or in select populations.[28-31] In a younger (50-64 years at baseline) Danish cohort, Bigaard et al[32] noted an inverse association between skeletal muscle mass and mortality. Our study extends the findings of Bigaard et al to an older, nationally representative cohort from the United States.

Increasingly, it is being recognized that total body mass is an inadequate marker of prognosis in older adults,[4-6] although it is still standard clinical practice to counsel patients regarding their BMI. A recent meta-analysis noted that although older adults (≥65 years) with BMI ≥35 kg/m^2 (grade 2 or 3 obesity) indeed had increased mortality

Table 3   Unadjusted and Adjusted All-cause Mortality Risk (% Mortality by December 2004) and Rate (Number of Deaths per 10,000 Person-Months) as a Function of Sex-specific Quartiles of Nonmuscle Mass Index

	Nonmuscle Mass Index Lowest Quartile	Nonmuscle Mass Index Second Quartile	Nonmuscle Mass Index Third Quartile	Nonmuscle Mass Index Highest Quartile	*P* for Trend*
Absolute risk (%)	49.6	44.9	48.6	49.1	.8
Adjusted relative risk (risk ratio)†	ref	0.94 (0.83-1.05)	0.91 (0.79-1.05)	0.96 (0.83-1.11)	.5
Absolute rate (per 10,000 person-mo)	35.6	30.7	33.9	33.5	.7
Adjusted relative rate (hazard ratio)†	ref	0.87 (0.71-1.10)	0.84 (0.68-1.00)	0.84 (0.67-1.10)	.1

Adjusted effect sizes presented as point estimate (95% confidence interval).

P value for linear trend across the 4 quartiles. Nonmuscle mass index quartile cut-points: 16.5, 19.2, and 22.2 kg/m^2 for women and 14.7, 16.8, and 19.1 kg/m^2 for men.

†Adjusted for age (in half-decade categories); sex; race; current smoking; past smoking; cancer (yes/no); C-reactive protein categories: <0.3, 0.3-1.0, and ≥1.0 mg/dL; hypertension; low high-density lipoprotein cholesterol (≤40 mg/dL); total cholesterol (categorized as <200, 200-240, and ≥240 mg/dL); HOMA-IR (log-transformed); glycosylated hemoglobin (log-transformed); diabetes; pre-diabetes; and serum creatinine.

Table 4 Unadjusted and Adjusted All-cause Mortality Risk (% Mortality by December 2004) and Rate (Number of Deaths per 10,000 Person-Months) as a Function of Sex-specific Quartiles of Body Mass Index

	BMI Lowest Quartile	BMI Second Quartile	BMI Third Quartile	BMI Highest Quartile	P for Trend*
Absolute risk (%)	50.5	48.0	47.6	45.9	.2
Adjusted relative risk (risk ratio)†	ref	0.99 (0.89-1.10)	0.91 (0.80-1.00)	0.92 (0.80-1.10)	.12
Absolute rate (per 10,000 person-mo)	36.1	33.4	32.9	31.2	.09
Adjusted relative rate (hazard ratio)†	ref	1.0 (0.84-1.20)	0.86 (0.71-1.30)	0.85 (0.69-1.40)	.25

Adjusted effect sizes presented as point estimate (95% confidence interval).

BMI = body mass index (weight in kilograms divided by height squared); quartile cut-points: 22.8, 25.9, and 29.6 kg/m² for women, and 24.4, 26.8, and 29.7 kg/m² for men.

*P value for linear trend across the 4 quartiles.

†Adjusted for age (in half-decade categories); sex; race; current smoking; past smoking; cancer (yes/no); C-reactive protein categories: <0.3, 0.3-1.0, and ≥1.0 mg/dL; hypertension; low high-density lipoprotein cholesterol (≤40 mg/dL); total cholesterol (categorized as <200, 200-240, and ≥240 mg/dL); HOMA-IR (log-transformed); glycosylated hemoglobin (log-transformed); diabetes; pre-diabetes; and serum creatinine.

relative to normal-weight adults (BMI, 18.5-25 kg/m²), older adults with grade 1 obesity (30≤BMI<35 kg/m²) were *not* at increased mortality risk, and overweight older adults (25≤BMI<30 kg/m²) actually had lower mortality.[33] This is in sharp contrast to the declines in mortality across the quartiles of relative muscle mass, documented in this study in a national cohort, pointing to the potential usefulness of muscle mass in the assessment of prognosis in older adults. It should be noted that bioelectrical impedance is easily measured in a physician's office (using a device that looks like, and takes up as much space as, a weighing scale with 2 grip handles and costs a few hundred dollars) and can be quickly converted to muscle mass index for routine assessment of relative muscle mass in a busy clinical practice.

Study Limitations

First, as discussed earlier, a cause and effect relationship between muscle mass and survival cannot be established by a prospective cohort study. However, the value of muscle mass index as an independent predictor can be established, given the national representativeness and size of the cohort.

Second, we used bioelectrical impedance to estimate muscle mass. It has been suggested that age-related hydrostatic disturbances affect the validity of bioelectrical impedance measurements in older age groups.[34] However, the bioelectrical impedance to muscle mass conversion equation we used has been validated against a magnetic resonance imaging-based gold standard in a multiethnic sample of adults aged 18 to 86 years.[16] Although the bioelectrical impedance measurements in NHANES III were performed after at least a 6-hour fast (in which all fluids other than water also were restricted), large-volume water consumption during the fast could have caused errors in muscle mass estimates. Finally, dual x-ray absorptiometry-based measures of fat-free mass also are subject to error when there is alteration of total body water.[35] Further, dual x-ray absorptiometry estimates total muscle mass from 2-dimensinoal projected images without regard to muscle composition. Lipid infiltration of muscle, which is common with obesity, sedentary lifestyles, and aging,[36-38] leads to overestimation of effective muscle mass by dual x-ray absorptiometry. Unlike dual x-ray absorptiometry, bioelectrical impedance, because it relies on conductivity, does not count intramuscular fat (which does not conduct electricity) as muscle. Therefore, bioelectrical impedance may provide a more accurate measurement of functioning muscle mass, in addition to being less invasive, less expensive, easier to use, and faster than the other 3 main techniques commonly used to measure skeletal muscle mass (dual x-ray absorptiometry, computed tomography, and magnetic resonance imaging).

Third, individuals with high relative muscle mass may have low relative fat mass, and the latter may be the root cause for their improved survival. This potential confound is of concern when muscle mass is indexed to body weight (because increases in fat mass translate to reductions in the muscle mass fraction of body weight) but is less relevant for muscle mass indexed to body height, the approach we adopted. We also controlled for clinical measures of central obesity in all analyses. In addition, we examined total nonmuscle mass as a predictor and found no associations of nonmuscle mass with survival. However, bone is heavier than fat, and thus nonmuscle mass is a poor surrogate for fat mass. Thus, more direct measures of fat mass, using dual x-ray absorptiometry or whole body/abdominal computed tomography, will be required to confirm our findings regarding the mortality prediction ability of fat mass in older adults.

CONCLUSIONS

This study establishes the independent survival prediction ability of muscle mass as measured by bioelectrical impedance in older adults, using data from a large, nationally representative cohort. This is in sharp contrast to BMI, whose association with mortality in older adults is inconsistent, at best. We conclude that measurement of muscle mass relative to body height should be added to the toolbox of clinicians caring for older adults. Future research should determine the type and duration of exercise interventions that improve muscle mass and potentially increase survival in well, older adults.

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