ORIGINAL ARTICLE

Low appendicular skeletal muscle mass (ASM) with limited mobility and poor health outcomes in middle-aged African Americans

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Abstract

Background Recent efforts to provide a consensus definition propose that sarcopenia be considered a clinical syndrome associated with the loss of both skeletal muscle mass and muscle function that occurs with aging. Validation of sarcopenia definitions that include both low muscle mass and poor muscle function is needed.

Methods In the population-based African American Health (AAH) study (N=998 at baseline/wave 1), muscle mass and mobility were evaluated in a clinical testing center in a subsample of N=319 persons (ages 52–68) at wave 4 (2004). Muscle mass was measured using dual energy x-ray absorptiometry and mobility by a 6-min walk test and 4-m gait walk

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test. Height corrected appendicular skeletal mass (ASM; 9.0 ± 1.5 in n=124 males, 8.3 ± 2.2 in n=195 females) was computed as total lean muscle mass in arms and legs (kilograms) divided by the square of height (meters). Cross-sectional and longitudinal (6-year) associations of low ASM (bottom 25 % AAH sample; <7.96 males and <7.06 females) and low ASM with limited mobility (4-m gait walk \le 1 m/s or 6-min walk \le 400 m) were examined for basic activities of daily living (ADL) difficulties, instrumental activities of daily living (IADL) difficulties, frailty, falls, and mortality (longitudinal only).

Results Low ASM with limited mobility was associated with IADL difficulties (p=.008) and frailty (p=.040) but not with ADL difficulties or falls in cross-sectional analyses; and with ADL difficulties (p=.022), IADL difficulties (p=.006), frailty (p=.039), and mortality (p=.003) but not with falls in longitudinal analyses adjusted for age and gender. Low ASM alone was marginally associated with mortality (p=.085) but not with other outcomes in cross-sectional or longitudinal analyses.

Conclusion Low ASM with limited mobility is associated with poor health outcomes among late middle-aged African Americans.

 $\begin{tabular}{ll} \textbf{Keywords} & Sarcopenia \cdot Mobility \cdot African \ Americans \cdot \\ Mortality \cdot Frailty \cdot ADLs \end{tabular}$

1 Introduction

The age-associated loss of skeletal muscle mass is well known. Estimates of severe muscle loss that represents sarcopenia range from 5 to 13 % for adults ages 60 to 70 and 11 to 50 % for those 80 or older [1]. Adverse clinical outcomes associated with sarcopenia include disability and mortality [2, 3]. While research on sarcopenia has rapidly



expanded in the past two decades, there remains no widely accepted definition. Baumgartner and colleagues' traditional definition of sarcopenia is muscle mass 2 standard deviations below a young adult referent group [4]. Researchers have studied sarcopenia extensively using this definition, but it had not been widely adopted among clinicians, industry, and regulatory agencies [5].

Recent efforts to reach a consensus definition propose that sarcopenia be considered a clinical syndrome associated with the loss of both skeletal muscle mass and muscle function that occurs with aging [5-8]. In particular, the Society on Sarcopenia, Cachexia, and Wasting Disorders (SCWD) and the European Working Group on Sarcopenia in Older People (EWGSOP) each have proposed consensus definitions for sarcopenia. The SCWD has defined sarcopenia with limited mobility as a person with a low lean appendicular skeletal mass (ASM; height corrected, 2 standard deviations below referent adult group ages 20-30), and with a gait speed walk ≤ 1 m/s or with a 6-min walk distance less than 400 m [5]. The EWGSOP defines sarcopenia as someone with a low lean ASM (same definition as SCWD) and with low muscle strength (e.g., grip strength) or physical performance (e.g., gait speed) [7]. The SCWD and EWGSOP sarcopenia definitions provide clear outcomes for clinical interventions. Validation of sarcopenia definitions that include both low muscle mass and poor muscle function is needed [6, 9] and testing should include studies with minority population samples.

The African American Health (AAH) project is a longitudinal study of a representative sample of African Americans. AAH was designed to identify factors, such as decreased muscle mass and mobility that are associated with excess disability and early decline in self-care functioning in late middle-age and older African Americans. This population has been shown to have more dysphoric symptoms [10], lower health-related quality of life [11] and excess disability [12] than US national averages. These health issues highlight the importance of examining low muscle mass and limited mobility in the AAH cohort, despite the relatively younger age of this cohort in comparison to other sarcopenia studies in older populations. We hypothesize that low muscle mass with limited mobility will be associated with poor health outcomes in AAH. We investigate crosssectional and longitudinal associations of low ASM and low ASM with limited mobility with poor outcomes.

2 Methods

2.1 Participants

Previous papers have described the AAH study sampling and recruitment procedures in detail [11, 12]. In brief, AAH

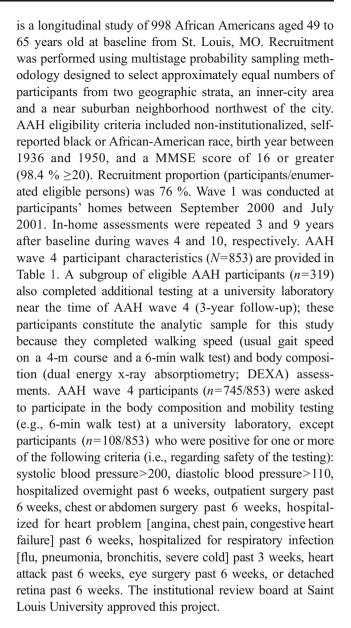


Table 1 Wave 4 AAH participants (N=853)

Characteristics	Completed AAH wave 4 in-home interview and assessments
Age (mean±SD)	59.17±4.4
Male (%)	37.4
Years of education (mean±SD)	12.48 ± 3.0
Annual household income below 20,000 (%)	40.3
City area (%)	45.0
Self-rated health: fair or poor (%)	36.5
Body mass index (mean±SD)	31.42 ± 7.3



2.2 Measures

2.2.1 Gait speed

Gait speed was measured using a standardized 4-m course with tape markers at the starting point, at 4 m, and at 6 m in a hallway with linoleum flooring. Participants were directed to wear flat, comfortable walking shoes, to start at the beginning marker when instructed "Begin," and to walk all the way to the 6-m marker "at your usual speed, just as if you were walking down the street to go to the store." The average gait speed (m/s) was computed for two trials. Average times of ≤ 1 m/s were scored as 1 and > 1 m/s scored as 0.

2.2.2 Six-minute walk test

A 6-min walk test was done using an unimpeded 90-ft hallway path and a standardized protocol in which participants were instructed to walk as far as possible in the allotted time [13]. Total 6-min walk distances of <400 m were scored as 1 and ≥400 m were scored as 0.

2.2.3 Limited mobility

Participants were classified as positive for limited mobility if gait speed=1, 6-min walk total distance=1, or both=1.

2.2.4 ASM, low ASM, sarcopenia, low ASM with limited mobility, and sarcopenia with limited mobility

Muscle mass was measured using DEXA (Hologic QDR 4500W; Hologic, Inc., Bedford, MA). ASM corrected for height $(9.0\pm1.5 \text{ in } n=124 \text{ males and } 8.3\pm2.2 \text{ in } n=195$ females) was computed as total lean muscle mass in arms and legs (kilograms) divided by the square of height (meters squared). Low ASM corrected for height was categorized as positive for the bottom 25 % in the AAH sample (<7.96 for males and <7.06 for females). Sarcopenia was defined according to height (meters squared) corrected ASM (kilograms) two standard deviations below an adult group ages 20–30 as <6.40 for males and <5.50 for females [4]. Low ASM with limited mobility was classified as positive for participants with both low ASM (bottom 25 %) and limited mobility, and sarcopenia with limited mobility was classified as positive for those meeting both criteria as well. The low ASM (bottom 25 %) cutoff was chosen because the 4 % prevalence of sarcopenia in the analytic sample (N=319) for AAH wave 4 is too small (i.e., statistical power is too low) to investigate the associations of sarcopenia and sarcopenia with limited mobility with poor health outcomes after 6 years. Additional cutoffs (20 %, 15 %, 10 %, and sarcopenia) for low ASM and low ASM with limited mobility are reported for 6-year mortality to illustrate that low ASM with limited mobility is a robust predictor of mortality even when statistical power is low.

2.2.5 AAH baseline (wave 4) characteristics

Baseline characteristics included age (years), sex (male/female), education (years), residence (inner-city versus near suburban neighborhood in St. Louis, MO), self-rated health (fair or poor versus excellent, very good, or good), annual household income (<20,000 per year versus ≥20,000 per year), and BMI (kilograms/meters squared).

2.2.6 Disability

Disability was measured using activities of daily living (ADL) and instrumental activities of daily living (IADL) scales. ADLs included seven items (bathing, dressing, eating, transferring bed or chair, walking across a room, getting outside, and using toilet) from the Second Longitudinal Study of Aging (LSOA-II) [14]. ADL difficulties were scored as the total number of these tasks for which respondents reported difficulty performing the task. IADLs included eight items (preparing meals, shopping for groceries, managing money, making phone calls, doing light housework, doing heavy housework, getting to places outside walking distance, and managing medications) from LSOA-II [14] and Lawton and Brody [15]. IADL difficulties were scored as the total number of tasks for which the respondent reported difficulty performing the task.

2.2.7 Frailty

Frailty was measured using the FRAIL scale, which includes five components: fatigue, resistance, ambulation, illnesses, and loss of weight [16, 17]. FRAIL scores range from 0 to 5 (i.e., 1 point for each component; 0=best to 5= worst) and represent frail (3-5), pre-frail (1-2), and robust (0) health status. Fatigue was measured by asking respondents how much time during the past 4 weeks they felt tired with responses of "all of the time" or "most of the time" scored 1 point. Resistance was assessed by asking participants if they had any difficulty walking up 10 steps alone without resting and without aids, and ambulation by asking if they had any difficulty walking several hundred yards alone and without aids; "yes" responses were each scored as 1 point. Illnesses was scored 1 for respondents who reported 5 or more illnesses out of 11 illnesses. Loss of weight was scored 1 for respondents with a weight decline of 5 % or greater within the past 12 months based on selfreport. Falls were based on self-reports to the question, "Have you fallen down in the last year"; responses of "yes" were coded as 1 and "no" as 0.



2.2.8 Mortality

Mortality up to 6 years after AAH wave 4 was determined by proxy report as part of the annual AAH follow-up interview and tracing via local databases (e.g., obituaries); data were coded 1 for decedents and 0 for survivors.

2.3 Data analysis

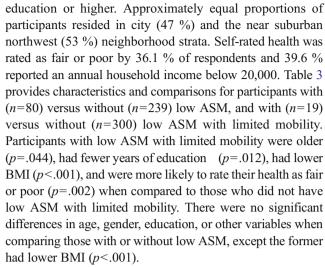
Data were analyzed using IBM SPSS Statistics, version 20.0 (Somers, NY). Descriptive statistics are reported as means±standard deviations (SD) or percentages (Tables 1, 4, and 5). *T* tests for continuous variables and chi-square tests for categorical variables were used to compare characteristics of study groups (Tables 2 and 3). Binary logistic regressions adjusted for age and gender were used to investigate the associations of low ASM, low ASM with limited mobility and sarcopenia with 6-year mortality (Table 6). ANCOVA with adjustments for age and gender for continuous variables and chi-square for categorical variables were used to compare cross-sectional and longitudinal outcomes for low ASM (bottom 25 %) and for low ASM with limited mobility groups with poor health outcomes, including ADLs, IADLs, frailty, and falls (Table 7).

3 Results

AAH participant (n=319) characteristics at wave 4 were similar for those who completed the body composition and mobility assessments versus those who completed only the in-home interview (n=534), except the latter had slightly fewer years of education (Table 2). Eligible wave 4 AAH participants' (n=319) average age was 59.2±4.4, 61.1 % were female, and the majority (76.7 %) had a high school

Table 2 Wave 4 AAH participants who completed or did not complete DEXA at wave 4

Characteristics	Completed DEXA N=319	Did not complete DEXA N=534	P value
Age (mean±SD)	59.17±4.4	59.16±4.4	.976
Male (%)	38.9	36.5	.492
Years of education (mean±SD)	12.75 ± 3.0	12.32±2.9	.039
Annual household income below 20,000 (%)	39.6	40.7	.768
City area (%)	47.0	43.8	.363
Self-rated health: fair or poor (%)	36.1	36.7	.848
Body mass index (mean±SD)	31.83±7.2	31.16+7.3	.207



ASM was 9.03 ± 1.5 for males and 8.33 ± 2.2 for females. The values for low ASM in AAH were <7.96 for males and <7.06 for females and, overall, 6 % (n=19) of subjects had low ASM with limited mobility. ASM values for sarcopenia were <6.40 for males and <5.50 for females with prevalence rates of 4.1 % (n=13) and 1.3 % (n=4) for sarcopenia and sarcopenia with limited mobility, respectively. Limited mobility was present in 25.1 % (n=80) of AAH participants. As shown in Table 4, approximately 75 % of participants with low ASM, across different cut points for low ASM (bottom 25 %, bottom 20 %, bottom 15 %, bottom 10 %, and sarcopenia), did not have limited mobility. Among those with limited mobility in the AAH sample shown in Table 5, there were only 5 % (n=4/80) with sarcopenia.

Forty-seven subjects (14.7 %) were deceased and 272 were alive at the end of the 6-year follow-up period. Notably, low ASM with adjustments for age and gender did not predict mortality, adjusted odds ratio (AOR) 1.80 (95 % Confidence Interval [CI], 0.9–3.5), p=.085. Using different cut points for low ASM (20 %, 15 %, 10 %, and sarcopenia) did not yield any statistically significant associations for ASM alone and mortality (Table 6). On the other hand, low ASM with limited mobility was associated with mortality up to 6 years later, AOR 4.56 (95 % CI, 1.7–12.8). As shown in Table 6, the association between low ASM with limited mobility and mortality was present for all ASM cut points except sarcopenia (although power was low to find a significant association with sarcopenia, and the point estimate for the OR was 4.35).

Cross-sectionally (wave 4) low ASM with limited mobility was associated with having more IADL disabilities and with being frail or pre-frail, but not with ADL disabilities or falls (see Table 7). In a 6-year follow-up period, low ASM with limited mobility was associated with having more ADL and IADL disabilities and being pre-frail or frail, but not with falls. Low ASM was not associated with any cross-sectional or longitudinal outcomes.



Table 3 Characteristics for N=319 AAH participants who completed muscle mass and mobility assessments at wave 4

Characteristics	Low ASM			Low ASM with limited mobility		
	Yes (n=80)	No (n=239)	P value	Yes (n=19)	No (n=300)	P value
Age (mean±SD)	59.66±4.7	59.01±4.3	.271	61.58±5.1	59.02±4.3	.044
Male (%)	38.8	38.9	.979	26.3	39.7	.247
Years of education (mean±SD)	12.55 ± 3.6	12.82 ± 2.8	.537	10.58 ± 3.5	12.89 ± 3.0	.012
Annual household income below 20,000 (%)	42.5	31.4	.070	52.6	33.0	.080
City area (%)	45.0	47.7	.675	36.8	47.7	.359
Self-rated health: fair or poor (%)	40.0	34.7	.395	68.4	34.0	.002
Body mass index (mean±SD)	24.29 ± 3.5	33.15 ± 6.0	<.001	24.82 ± 4.0	31.31 ± 6.6	<.001

Low ASM represents participants in the bottom 25 % of study sample

4 Discussion

Prevalence rates for sarcopenia reported in the literature for older adults ages 60-70 range from 5 to 13 % [1]. The prevalence of sarcopenia was 4 % and sarcopenia with limited mobility was 1.3 % in AAH and, in general, these rates may be considered low based on known prevalence rates for older adult cohorts. Nonetheless, the variation in rates observed across prevalence studies for sarcopenia is impacted by a number of factors, including differences in populations studied, differences in the methods used to assess muscle mass (e.g., DEXA versus bioelectrical impedance), and the availability of normative values from a young healthy referent group that are used to calculate sarcopenia rates [18]. In AAH, the low sarcopenia and sarcopenia with limited mobility prevalence rates, in part, may be due to each of these factors. First, the AAH cohort includes a late middle-aged population (ages 53–68 at wave 4; 84.4 %<age 65), where as many prevalence studies focus on adults ages 60 and above [5, 7]. Second, muscle mass was measured using DEXA and could differ with other methods such as computed tomography, magnetic resonance imagery, ultrasound, or bioelectrical impedance. Third, the relatively low

Table 4 Appendicular skeletal mass (ASM) in AAH

ASM	Low ASM without limited mobility
Bottom 25 % (<7.96 males and <7.06 females)	76.3 % (<i>n</i> =61/80)
Bottom 20 % (<7.75 males and <6.75 females)	76.9 % (n=50/65)
Bottom 15 % (<7.50 males and <6.50 females)	74.5 % (<i>n</i> =35/47)
Bottom 10 % (<6.71 males and <6.16 females)	77.4 % (24/31)
Sarcopenia (<6.40 males and <5.50 females)	69.2 % (9/13)

ASM calculated total lean muscle mass in arms and legs (kilograms) divided by the square of height (meters squared). Sarcopenia defined as ASM values that are two standard deviations below an adult referent group ages 20–30.

AAH prevalence rates also may be related to the healthy young adult norms used to define sarcopenia. Indeed, the EWGSOP [7, p. 417] recently noted that, "More research is urgently needed in order to obtain good reference values for populations around the world."

Baumgartner et al. [4] originally operationalized sarcopenia as height corrected muscle mass that is 2 standard deviations below an appropriate healthy younger referent group. However, current consensus is that poor muscle mass and poor muscle function (strength or performance) are both recognized as important for sarcopenia [5–7]. The rationale for expanding the definition of sarcopenia to include poor muscle function is that the association of low muscle mass with strength is inconsistent and non-linear [5, 7]. The clinical usefulness of sarcopenia defined only as low muscle mass has not been realized nor has it been widely adapted by clinicians. In particular, the SWCD has proposed defining sarcopenia as sarcopenia with limited mobility in an effort to develop a universally acceptable definition and, also, to provide a definition that can be utilized in clinical trials [5]. Thus, function (strength or performance) is now widely recognized as a critical component for defining sarcopenia. In this study,

Table 5 Limited mobility and appendicular skeletal mass (ASM) in AAH

ASM	Limited mobility with low ASM
Bottom 25 % (<7.96 males and <7.06 females)	23.8 % (n=19/80)
Bottom 20 % (<7.75 males and <6.75 females)	18.8 % (<i>n</i> =15/80)
Bottom 15 % (<7.50 males and <6.50 females)	15.0 % (<i>n</i> =12/80)
Bottom 10 % (<6.71 males and <6.16 females)	8.8 % (<i>n</i> =7/80)
Sarcopenia (<6.40 males and <5.50 females)	5.0 % (n=4/80)

ASM calculated total lean muscle mass in arms and legs (kilograms) divided by the square of height (meters squared). Sarcopenia defined as ASM values that are two standard deviations below an adult referent group ages 20–30.



Table 6 Mortality, ASM, ASM with limited mobility, and sarcopenia in AAH

ASM	Logistic regression for 6-year mortality			
	AOR (95 % CI) ^a	P value		
ASM bottom 25 % (<7.96 males and <7.06 females)	1.80 (0.9–3.5)	.085		
ASM bottom 20 % (<7.75 males and <6.75 females)	1.60 (0.8–3.3)	.198		
ASM bottom 15 % (<7.50 males and<6.50 females)	1.51 (0.7–3.4)	.322		
ASM bottom 10 % (<6.71 males and <6.16 females)	1.50 (0.6–3.9)	.414		
Sarcopenia (<6.40 males and<5.50 females)	2.49 (0.7–8.7)	.155		
Low ASM with limited mobility				
ASM bottom 25 % (<7.96 males and <7.06 females) with limited mobility	4.56 (1.7–12.8)	.003		
ASM bottom 20 % (<7.75 males and <6.75 females) with limited mobility	4.28 (1.4–13.1)	.011		
ASM bottom 15 % (<7.50 males and <6.50 females) with limited mobility	4.35 (1.3–14.8)	.019		
ASM bottom 10 % (<6.71 males and <6.16 females) with limited mobility	7.61 (1.6–36.7)	.011		
Sarcopenia (<6.40 males and<5.50 females) with limited mobility	4.35 (0.6–33.2)	.157		

ASM calculated total lean muscle mass in arms and legs (kilograms) divided by the square of height (meters squared). Sarcopenia defined as ASM values that are two standard deviations below an adult referent group ages 20–30

we demonstrated that low muscle mass (defined as bottom 25 % of study sample) and mobility deficits (i.e., poor function) are robust correlates of poor health outcomes in a community sample of late middle-age African Americans.

Low ASM with limited mobility demonstrated both concurrent and predictive validity for poor health outcomes in the AAH cohort. Cross-sectional analyses demonstrated that the low ASM with limited mobility was associated with IADL disability and frailty. Importantly, this study showed that low ASM with limited mobility is a significant predictor of mortality, and is associated with ADL disability, IADL disability, and frailty status at 6-year follow-up. On the other hand, low ASM alone was only marginally associated with mortality and not with any other study outcomes. Low muscle mass alone does not adequately capture the geriatric syndrome of sarcopenia [19].

Table 7 Cross-sectional and longitudinal outcomes for low ASM and low ASM with limited mobility

Cross-sectional outcomes ^a Low ASM			P value Low ASM with limited mob		limited mobility	P value
	Yes $(n=80)$	No $(n=239)$		Yes $(n=19)$	No $(n=300)$	
ADLs (0-7) (mean±SD)	0.49 ± 1.7	$0.83\!\pm\!1.8$.097	0.79 ± 1.6	0.74 ± 1.6	.970
IADLs (0–8) (mean±SD)	1.09 ± 1.6	$0.97 \!\pm\! 1.7$.641	2.11 ± 2.2	0.93 ± 1.7	.008
FRAIL scale (%)			.511			.040
Robust	51.3	48.5		21.1	51.0	
Pre-frail	42.3	40.6		63.2	39.6	
Frail	6.4	10.9		15.8	9.4	
Fallen in past year (%)	25.0	31.0	.311	26.3	29.7	.756
6-year follow-up outcomes ^a	Low ASM		P value	Low ASM with	limited mobility	P value
	Yes $(n=52)$	No $(n=185)$		Yes $(n=8)$	No $(n=229)$	
ADLs (0–7) (mean±SD)	$0.83 \!\pm\! 1.6$	0.94 ± 1.9	.651	2.00 ± 2.4	$0.87 \!\pm\! 1.8$.022
IADLs (0–8) (mean±SD)	1.04 ± 1.8	0.95 ± 1.7	.689	2.88 ± 3.3	0.90 ± 1.6	.006
FRAIL scale (%)			.677			.039
Robust	49.0	53.5		25.0	53.5	
Pre-frail	35.3	28.8		25.0	30.5	
Frail	15.7	17.6		50.0	16.0	
Fallen in past year (%)	40.4	28.3	.095	50.0	30.3	.235

ADLs denote difficulties with basic activities of daily living difficulties and IADLs denote difficulties with instrumental activities of daily living ^a Analyses adjusted for age and gender



^a Analyses adjusted for age and gender

Muscle loss due to the clinical syndrome of sarcopenia is steadily progressive and primarily results in the loss of muscle strength [6]. It is believed that reduced muscle mass and the associated loss of strength may lead to poor outcomes, including functional limitations, disability, and mortality [6]. Studies have shown that low muscle mass is associated with disability [2, 20] and mortality [21] but the causes of disability and mortality are complex and multifactorial. Recent consensus definitions for sarcopenia, including the SCWD and EWG-SOP recommendations, argue for assessments to include measures of both muscle mass and muscle function. The results of this study show that in the AAH cohort, low muscle mass alone is not associated with clinical outcomes, but low muscle mass and reduced mobility together are associated with disability, frailty, and mortality. Another recent study has found that mortality among nursing home residents is associated with sarcopenia. when defined according the EWGSOP recommendations [3].

Low muscle mass may lead to reduced mobility. Mobility impairment alone is strongly associated with disability and mortality [22–25]. Only low muscle mass and mobility impairment were associated with clinical outcomes in this study. Further research is needed to establish that improved mobility resulting from therapy for sarcopenia can reduce disability and predict positive outcomes [5].

This study has limitations. The AAH cohort is a late middle-aged population (ages 59±4; minimum 53, maximum 68) so the prevalences of sarcopenia (4 %; height corrected ASM 2 standard deviations below adult referent group) and sarcopenia with limited mobility (1.3 %) were low. Consequently, statistical power was not sufficient to examine study outcomes (i.e., disability, frailty, falls, and mortality) using the exact SCWD definition [5] for sarcopenia with limited mobility, and the analytic models bordered on over-fitting. Also, this measurement approach requires in-center assessments (e.g., DEXA, 6-min walk); the Short Portable Sarcopenia Measure [26] combines a measure reflecting muscle mass with measures of muscle function, does not require in-center assessments, and appears to be an excellent measure for assessments in the field.

This study provides preliminary evidence for a robust association between low ASM with limited mobility and poor health outcomes in a population-based sample of late middle-age African Americans, a group that has been shown to have excess health problems when compared to US national averages [10–12]. We have shown that low ASM with limited mobility, but not low ASM alone, is associated with ADL disability, IADL disability, frailty, and mortality among late middle-age African Americans. Further research is needed to investigate these issues among other minority and non-minority samples. In particular, validity studies using the exact SCWD consensus definition for sarcopenia and sarcopenia with limited mobility are needed in both late

middle-age and older populations among diverse population samples.

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Conflict of interest The authors declare that they have no conflict of interest.

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