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Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia

Fulvio Lauretani,[1] Cosimo Roberto Russo,[1] Stefania Bandinelli,[1] Benedetta Bartali,[1] Chiara Cavazzini,[1] Angelo Di Iorio,[2] Anna Maria Corsi,[1] Taina Rantanen,[3] Jack M. Guralnik,[4] and Luigi Ferrucci[1,5]

[1]*Laboratory of Clinical Epidemiology, Geriatric Department, Italian National Institute of Research and Care on Aging, 50125 Florence; and* [2]*Department of Medicine and Aging, Geriatric Clinic, University of Chieti, 66013 Chieti, Italy;* [3]*Department of Health Sciences, University of Jyvaskyla, 40351 Jyvaskyla, Finland;* [4]*Laboratory of Epidemiology, Demography and Biometry, National Institute on Aging, Bethesda 20892; and* [5]*Longitudinal Studies Section, Clinical Research Branch, National Institute on Aging, Baltimore, Maryland 21224-6825*

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Lauretani, Fulvio, Cosimo Roberto Russo, Stefania Bandinelli, Benedetta Bartali, Chiara Cavazzini, Angelo Di Iorio, Anna Maria Corsi, Taina Rantanen, Jack M. Guralnik, and Luigi Ferrucci. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol* 95: 1851–1860, 2003; 10.1152/japplphysiol.00246.2003.—Sarcopenia, the reduction of muscle mass and strength that occurs with aging, is widely considered one of the major causes of disability in older persons. Surprisingly, criteria that may help a clinician to identify persons with impaired muscle function are still lacking. Using data from a large representative sample of the general population, we examined how muscle function and calf muscle area change with aging and affect mobility in men and women free of neurological conditions. We tested several putative indicators of sarcopenia, including knee extension isometric torque, handgrip, lower extremity muscle power, and calf muscle area. For each indicator, sarcopenia was considered to be present when the measure was >2 SDs below the mean. For all four measures, the prevalence of sarcopenia increased with age, both in men and women. The age-associated gradient in prevalence was maximum for muscle power and minimum for calf-muscle area. However, lower extremity muscle power was no better than knee-extension torque or handgrip in the early identification of poor mobility, defined either as walking speed <0.8 m/s or inability to walk at least 1 km without difficulty and without developing symptoms. Optimal cutoff values that can be used in the clinical practice to identify older persons with poor mobility were developed. The findings of the study lay the basis for a cost-effective, clinical marker of sarcopenia based on a measure of isometric handgrip strength. Our findings should be verified in a longitudinal study.

elderly; muscle power; strength

SARCOPENIA, AN AGE-RELATED reduction of muscle mass and strength, is considered one of the most important components in the causal pathway, leading to frailty and disability in older persons (12). Observational studies have shown that muscle mass and force reach their peak value between the second and the fourth decade of life and then decline steadily with aging (6, 13). Accordingly, the prevalence of sarcopenia is thought to increase with age (10).

Finding a valid definition is critical to translate the concept of sarcopenia from the research setting to the clinical arena and to start testing interventions. Although some definitions have been proposed (5, 21, 22), no standardized criteria for the diagnosis of sarcopenia have been established. In clinical practice, the term "sarcopenia" is often used to identify patients who appear, on qualitative inspection, to have "small" muscle mass. As a consequence, many patients at an early stage of sarcopenia are undetected. This is a major problem, because there is strong evidence that sarcopenia is a reversible cause of disability and because older persons with early sarcopenia are probably those who are most likely to benefit from interventions (9, 16, 31).

A clinical definition of sarcopenia could be particularly useful if it could be routinely obtained in medical practice and allow for early detection of the detrimental effect of reduced muscle function on physical ability. Based on limited data, it has been suggested that muscle power, which is an integrated index of force and velocity, is probably the most important muscular predictor of physical function in humans (3). However, accurate measurement of power requires complex, expensive equipment and technical skills without proof of superiority over simpler measures of muscle strength. Furthermore, because the etymology of the term sarcopenia comes from the Greek words *sarx* (meaning flesh) and *penia* (meaning loss), a definition of sarcopenia based on the reduction of muscle mass should also be considered (30).

Using data from a representative cohort of persons living in the Chianti geographic area (Tuscany, Italy),

Address for reprint requests and other correspondence: Luigi Ferrucci, Longitudinal Studies Section, Clinical Research Branch, ASTRA Unit, National Institute on Aging (NIH), Harbor Hospital, 5th Floor, 3001 S. Hanover St., Baltimore, MD 21225 (E-mail: FerrucciLu@grc.nia.nih.gov).

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we describe how isometric muscle strength, muscle power, and muscle cross-sectional area change with age, and we propose alternative definitions of sarcopenia based on these different muscular parameters. Finally, we identified the optimal cutoff values that discriminate best the early stage of reduced physical function in older persons.

MATERIALS AND METHODS

Study population. InCHIANTI is an epidemiological study of risk factors for mobility disability in old age. The InCHIANTI study population is a representative sample of the population living in Greve in Chianti and Bagno a Ripoli, two small towns located in the Chianti countryside of Tuscany, Italy. The study design and data collection have been previously described (11). Of the initial 1,453 subjects who received an in-home interview, 277 were excluded from the analyses because information on muscle function and calf muscle cross-sectional area for these participants was not available, either because they refused to come to the clinic for an examination or were too sick to be evaluated. To avoid the possible interference of neurological impairments in the measure of muscle function, participants with a diagnosis of stroke ($n = 55$), Parkinson's disease ($n = 9$), peripheral neuropathy ($n = 4$), and cognitive impairment (Mini Mental State Examination Score ≤ 21; $n = 78$) were also excluded. The final study population thus included 1,030 persons, 469 men and 561 women, dispersed over a wide age range of 20–102 yr. The study protocol was examined and approved by the Italian National Institute of Research and Care on Aging ethics committee. All participants were informed of the study procedure, purposes, and known risks, and all gave their informed consent.

Measures. After the home interview, participants received a full standardized medical and functional evaluation by, respectively, a geriatrician and an experienced physical therapist, both of whom had received special training on the assessment tools used in this study. The objective assessment of physical function was performed within 4 wk after the interview in a dedicated laboratory.

In particular, isometric muscle strength was assessed on eight muscle groups of the lower extremity by a hand-held dynamometer, by using a standard protocol (2). We measured strength with isometric dynamometry because this method could be used both in the InCHIANTI study clinic and in the participants' homes for those who could not come to the study clinic. All measures of lower extremity muscle strength were highly correlated (Pearson's correlation coefficients ranging from 0.87 to 0.92). Therefore, in the analyses presented here, we used only knee-extension torque to indicate lower extremity muscle strength.

Measures of upper extremity muscle strength were isometric shoulder adduction and handgrip. Between them, we selected the handgrip for the present analysis because the assessment of handgrip is easy, reliable, and inexpensive. Furthermore, there is strong evidence in the literature that handgrip is a strong predictor of disability and mortality (27, 28). We decided to include both measures of lower and upper extremity muscle strength because previous studies suggested that the rate of age-associated decline in muscle strength is quite different in these two anatomic regions (13). In fact, the correlation between handgrip and isometric strength of the lower extremity muscle groups was moderately high, ranging from 0.70 to 0.72. In previous studies, the intraclass correlation coefficients for duplicate measures of knee-extension isometric strength and handgrip strength were, respectively, 0.81 and 0.85 for interrater reliability and 0.79 and 0.98 for test-retest reliability (2, 25).

Lower extremity muscle power was measured in a single leg extension movement, according to the method described by Bassey and Short (4). The value of the best performance obtained over eight repetitions on the right side and eight repetitions on the left side was used in the analysis. Using this method, Bassey and Short (4) reported that the coefficient of variation for retests obtained after 1 wk was 9.4%.

Crude values of muscle power were divided by individual body weights, and the resulting values were multiplied by the gender-specific average body weight for the study population. These weight-adjusted values of muscle power are expressed in a scale that is comparable with the values directly obtained from the power rig. In exploratory analyses, we also obtained a weight-adjusted measure of muscle power using a regression approach. However, because the correlation between the measures obtained with the two different types of adjustment was 0.98 in men and 0.94 in women, only the simpler measure that does not require a regression model was used in the analysis.

A lower leg peripheral quantitative computerized tomography (pQCT) was performed in all participants by means of a recent generation device (XCT 2000, Stratec, Pforzheim, Germany) to evaluate calf muscle cross-sectional area. Data presented here were derived from standard 2.5-mm-thick transverse scans obtained at 66% of the tibia length, proximal to the anatomic marker. Previous studies demonstrated that this is the region with the largest outer calf diameter, with little variability across individuals (29). The total dose of radiation administered to the participants was <1 mrem.

The cross-sectional images obtained from the pQCT were analyzed by using the BonAlyse software (BonAlyse, Jyvaskyla, Finland; http://www.bonalyse.com). Different tissues in the analysis were separated according to different density thresholds: a density value of 35 mg/mm^3 was used to separate fat from muscle tissue, and 180 mg/mm^3 to separate muscle from bone tissue.

To assess walking ability, we collected both subjective and objective information. The subjective evaluation consisted of asking participants to estimate the maximum distance they could walk without difficulty. The interviewer provided examples of distances taken from real life. For instance, for the participants living in Greve in Chianti, 1 km was exemplified as the distance between the municipal building and the local hospital. Based on responses, we categorized participants into able or unable to walk 1 km without stopping, feeling fatigued, or developing symptoms.

To measure walking speed, two photocells connected to a recording chronometer were placed at the beginning and the end of a 4-m course established at the site clinic. Participants were instructed to stand with both feet touching the starting line and to begin walking at their usual pace after a verbal command. The time between the activation of the first and the second photocell was recorded. The average of two walks was used to compute a measure of walking speed. The coefficient of variation between duplicate trials was 5.2%, and only in 3.7% of the participants did the second measure differ by >20% from the first one. Use of aids (canes or walkers) was allowed for this test. The 4-m walk test has been used extensively in previous studies, and its concurrent and predictive validity and its sensitivity to change have been confirmed in large epidemiological studies (17, 18, 23, 24). For the purpose of this analysis, low walking speed was defined as walking slower than 0.8 m/s. After exclusion of those who where unable to walk, this value approximately identified

the lowest quintile of the speed distribution in our population.

Statistical analysis. All analyses were performed separately in men and women. Continuous variables are reported as means ± SD and categorical values as a percentage. Anthropometric characteristics were compared between age groups by using ANOVA. By analogy with the standard criteria for the diagnosis of osteoporosis and in accordance with Baumgartner et al. (5) and Melton et al. (21), the definition of sarcopenia was based on the comparison between individual muscle parameters and average values calculated in healthy, young adults. For example, in men 20–29 yr old, knee extension torque was 802.0 ± 202.6 N/dm. Therefore, all male participants with knee extension torque <396.8 N/dm (802.0 − 2 ∗ 202.6) were considered to be affected by sarcopenia. Using an analogous method, we also identified participants who could be defined as sarcopenic based on their values of handgrip, lower extremity muscle power, and calf muscle cross-sectional area. Then we calculated the prevalence of sarcopenia for each one of these four possible definitions. To study the relationship between muscle parameters and performance in mobility tasks, we computed the percentage of participants walking slower than 0.8 m/s and of those unable to walk 1 km without difficulty. Percentages were compared by using age-adjusted tests for trend obtained by logistic regression models. Furthermore, we obtained receiver operator characteristic (ROC) curves for each muscle parameter using, for reference, the two abovementioned definitions of poor mobility. In a ROC analysis, the area under the curve (AUC) estimated for each muscle parameter yields a discriminative value in the identification of a participant walking slower than 0.8 m/s and unable to walk for 1 km without difficulty. AUCs for the four muscle parameters were compared by using the De Long method implemented in the statistical software ACCUROC for Windows, version 2.5 (8, 19). From the ROC curves, we identified optimal diagnostic cut points as those yielding the best compromise between sensitivity and specificity in the identification of each of the two mobility outcomes. Finally, using logistic regression models, we obtained crude and age-adjusted odd ratios estimating the probability of poor mobility associated with having a specific muscle parameter below vs. above the optimal cutoff threshold.

RESULTS

The anthropometric characteristics of the participants are shown by age interval in Table 1. The average stature was progressively smaller with older age. This age trend was not completely explained by postural changes or reduction of the intervertebral spaces, as evidenced by the parallel changes observed in the tibia length. In both genders, body weight increased from young to middle age and declined progressively thereafter. The three measures of muscle function and the calf muscle cross-sectional area, an index of muscle mass, were progressively lower with increasing age, in both men and women (Fig. 1 and Table 2). Within each age group, men were stronger and had larger calf muscle cross-sectional areas than women, although, in the oldest-old, the magnitude of the difference was quite small. The slope of the age-associated decline was steepest for muscle power, intermediate for knee-extension torque and handgrip, and less evident for calf muscle cross-sectional area, especially in women. For example, average muscle power was 72 W in men older than 85 yr, which is only 25% of the initial 280 W observed in men 20–29 yr old. By contrast, comparing men in the two extreme age groups, knee-extension torque and handgrip were lower by ~50% and calf muscle cross-sectional area by only 20%.

Table 1. *Variables related to body size of the InCHIANTI study participants, according to gender and age strata*

Age, yr	*n*	Height, cm	Weight, kg	Tibial Length, mm
		Men		
20–29	25	175.9 ± 7.2	76.3 ± 13.4	391.6 ± 30.7
30–39	25	175.1 ± 5.9	79.5 ± 11.2	391.0 ± 20.2
40–49	27	171.1 ± 7.3	83.1 ± 12.5	376.5 ± 21.1
50–64	43	171.6 ± 6.7	80.5 ± 11.0	382.6 ± 23.4
65–74	230	166.9 ± 6.9	76.6 ± 11.1	372.7 ± 21.9
75–85	97	164.5 ± 7.2	72.9 ± 12.1	371.8 ± 23.6
85+	22	159.1 ± 9.5	62.9 ± 7.0	356.6 ± 18.6
ANOVA		$P < 0.0001$	$P < 0.0001$	$P < 0.0001$
		Women		
20–29	22	163.7 ± 6.3	60.9 ± 8.4	362.1 ± 22.9
30–39	31	161.4 ± 5.8	61.4 ± 10.4	356.3 ± 20.5
40–49	26	159.6 ± 5.8	65.6 ± 11.4	348.8 ± 17.9
50–64	58	157.9 ± 6.0	67.5 ± 10.9	352.1 ± 23.7
65–74	255	154.9 ± 6.4	67.2 ± 11.4	346.9 ± 22.2
75–85	134	151.3 ± 7.0	63.1 ± 11.3	340.5 ± 20.9
85+	35	148.4 ± 6.7	59.3 ± 9.8	341.7 ± 18.9
ANOVA		$P < 0.0001$	$P < 0.0001$	$P < 0.0001$

Values are means ± SD; *n*, no. of subjects. ANOVA was used for the comparison of mean values across age groups, within each gender.

Given the early drop in muscle power over the life span, we hypothesized that the measure of muscle power could be used to identify an impaired muscle function at an early stage. By analogy with the criteria used for the clinical diagnosis of osteoporosis, we obtained four possible definitions of sarcopenia based on a T-score lower than −2 for each of the four muscle parameters shown in Fig. 1. Figure 2 reports the percentages of men and women in each age group who were considered sarcopenic based on the four different muscle variables. Regardless of the muscle parameter used for the definition, the prevalence of sarcopenia increased with age. Interestingly, within each age group, the percentage of participants with a T-score below −2 was higher in women than in men for knee-extension torque and lower extremity muscle power and, conversely, was higher in men than in women for handgrip and calf muscle area. The high percentages of participants defined as sarcopenic based on low muscle power were striking. Above 50 yr of age, almost all women and >70% of men have a T-score below −2. The percentages were much lower for the criterion based on calf muscle area and intermediate for knee-extension torque and handgrip.

Walking speed measures over a 4-m course declined progressively with age, and, in both men and women, the magnitude of decline per year increased with age, showing a clear curvilinear trajectory (Fig. 3*B*). In

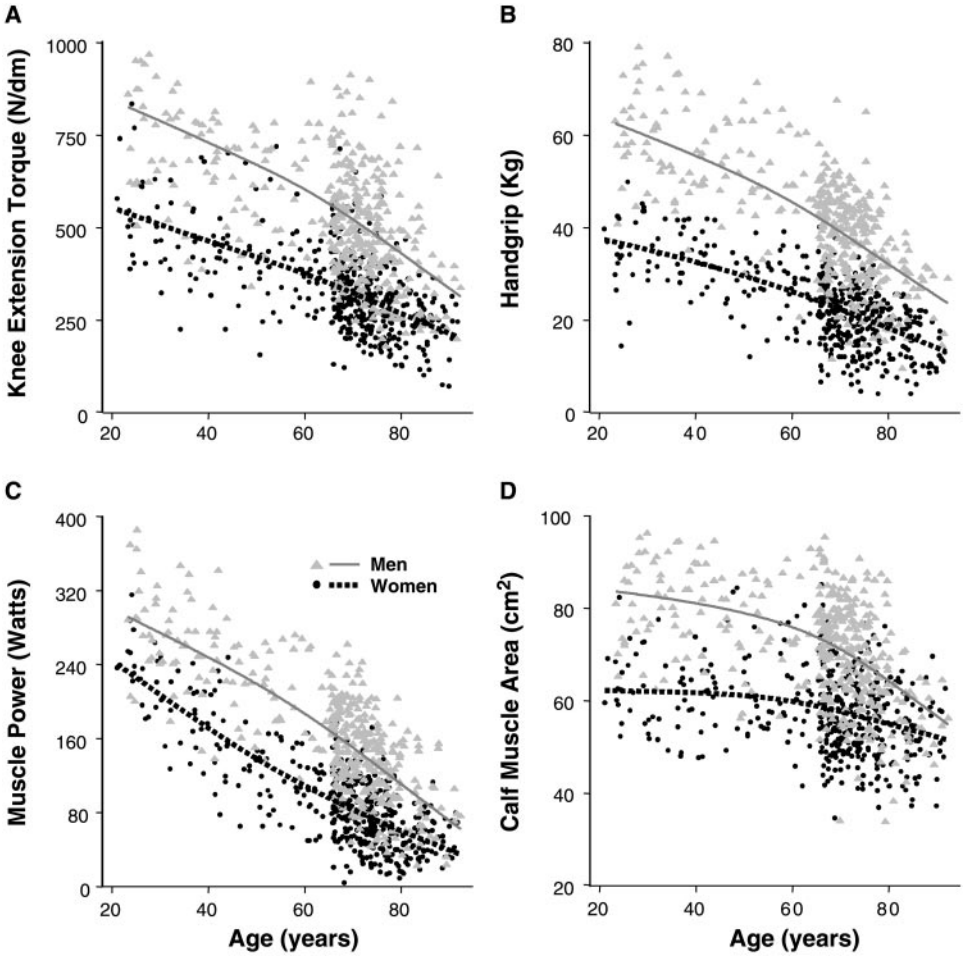

Fig. 1. The relationships between age and knee-extension torque (*A*), handgrip (*B*), weight-specific lower extremity muscle power (*C*), and calf muscle cross-sectional area (*D*) in men (triangles) and women (circles) who participated in the InCHIANTI study are illustrated by scatter plots and summarized by using smoothing splines.

parallel, the percentage of participants who reported to be unable to walk for 1 km without stopping increased with age and, within each age group, was higher in women than in men (Fig. 3*A*).

Table 3 reports the percentages of men and women with poor mobility, defined as walking speed <0.8 m/s and inability to walk 1 km without difficulty, according to quintiles of the four muscle parameters. Regardless

Table 2. *Mean values and 95% confidence intervals for knee-extension torque, handgrip, muscle power, and calf muscle area in the InCHIANTI study participants, according to gender and age strata*

Age, yr	*n*	Knee-Extension Torque, N/dm	Handgrip, kg	Muscle Power, W	Calf Muscle Area, cm^2
			Men		
20–29	25	802.0(722.5–881.4)	61.1(57.0–65.2)	279.5(256.4–302.6)	83.3(78.9–87.8)
30–39	25	766.9(677.2–856.6)	56.4(52.2–60.7)	255.8(237.2–274.3)	81.3(77.8–84.9)
40–49	27	643.4(598.1–688.6)	53.2(48.7–57.6)	240.7(221.0–260.4)	78.5(74.5–82.5)
50–64	43	656.5(603.3–713.6)	49.1(45.3–52.9)	196.3(179.5–213.2)	76.1(72.8–79.4)
65–74	230	524.5(505.7–543.2)	39.2(37.9–40.5)	150.6(144.6–156.6)	72.2(70.7–73.6)
75–85	97	453.8(423.7–484.0)	31.8(29.7–33.9)	111.8(103.6–120.0)	64.8(62.5–67.2)
85+	22	320.4(270.9–370.0)	27.1(22.8–31.3)	71.8(55.2–88.4)	57.6(54.6–60.6)
ANOVA		$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$
			Women		
20–29	22	552.0(500.5–603.5)	35.6(32.0–39.1)	233.5(217.8–249.1)	62.6(58.5–66.7)
30–39	31	455.9(413.6–498.2)	34.3(32.3–36.3)	180.3(164.6–196.1)	59.3(56.4–62.1)
40–49	26	427.9(387.8–467.9)	31.8(29.5–34.1)	146.4(127.0–165.8)	63.1(59.5–66.7)
50–64	58	386.6(360.9–412.3)	27.1(25.3–29.0)	107.0(98.1–115.9)	60.0(58.8–62.2)
65–74	255	327.4(315.2–339.6)	22.2(21.2–23.2)	83.0(78.7–87.2)	57.5(56.4–58.6)
75–85	134	269.7(254.9–284.6)	19.3(17.9–20.7)	59.9(54.7–65.0)	54.7(53.1–56.3)
85+	35	237.0(211.1–263.0)	14.5(12.9–16.2)	55.2(47.7–62.7)	53.2(50.7–56.7)
ANOVA		$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$

Values are means with 95% confidence intervals in parentheses; *n*, no. of subjects. ANOVA was used for the comparison of mean values across age groups, within each gender.

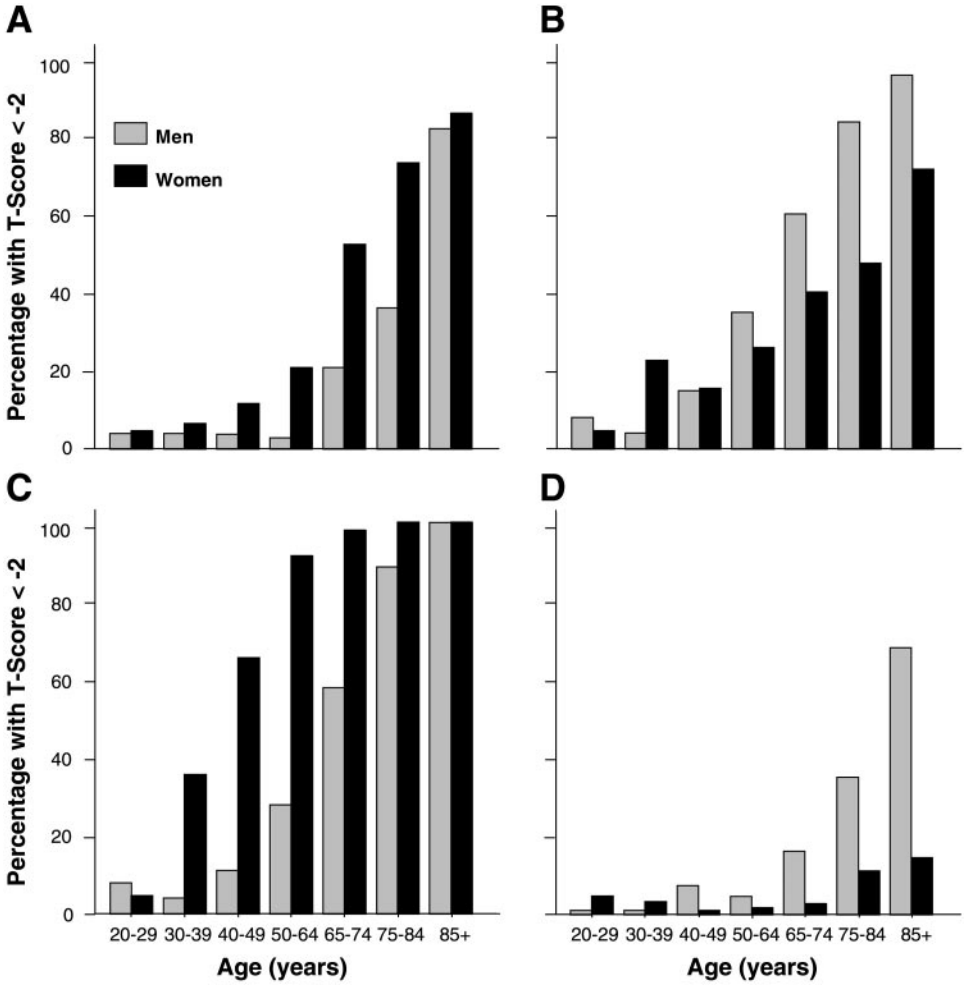

Fig. 2. Percentage of InCHIANTI participants with a T-score value less than −2 for knee-extension torque (*A*), handgrip (*B*), weight-specific lower extremity muscle power (*C*), and calf cross-sectional area (*D*), according to gender and age group.

of the definition used for poor mobility, the percentage of participants with poor mobility declines progressively from the lowest to the highest quintile of knee-extension torque, handgrip, and lower extremity muscle power. The percent values are quite similar in analogous quintiles across the three parameters. For example, the percentages of men walking slower than 0.8 m/s in the first quintiles of knee-extension torque, handgrip, and lower extremity muscle power are, respectively, 29.2, 34.5, and 29.0% and become 6.0, 7.0, and 5.5% in the highest quintiles. On the contrary, the relationship between calf muscle area and both definitions of poor mobility is weak and less consistent across the quintiles.

In further analyses, we used the ROC method to statistically compare the discriminating power of each of the four continuous muscle measures in the identification of persons with poor mobility. The results of these analyses are shown in Fig. 4. Each curve was obtained by recursively selecting all possible diagnostic thresholds within the range of the specific muscle variable and plotting for each of these thresholds the true positive rate (sensitivity, *y*-axis) vs. the false positive rate (1-specificity, *x*-axis) in the identification of participants with poor mobility. In Fig. 4*A*, we defined poor mobility as a walking speed <0.8 m/s, whereas in Fig. 4*B*, poor mobility was defined as inability to walk at least 1 km without difficulty and without developing symptoms. The AUC and its 95% confidence interval express the discriminating power of each test. In both men and women and for the two definitions of poor mobility, results were highly consistent. The AUCs for knee-extension torque, handgrip, and lower extremity muscle power were nearly superimposed and never statistically different, although lower extremity muscle power showed a slightly higher discriminating power in the identification of women walking slower than 0.8 m/s. Furthermore, the AUCs for calf muscle area were substantially smaller and always statistically different from those calculated for the other three muscle variables ($P < 0.01$). Among the cutoff values explored in the ROC curves, we selected optimal diagnostic cut points as those yielding the highest sensitivity and specificity in the identification of participants with poor mobility (Table 4). Then, using logistic regression models, we estimated the odds ratio (OR) for poor mobility associated with having, respectively, knee-extension torque, handgrip, lower extremity muscle power, and calf muscle area below vs. above the optimal cut point. The analysis is shown in Table 4, for

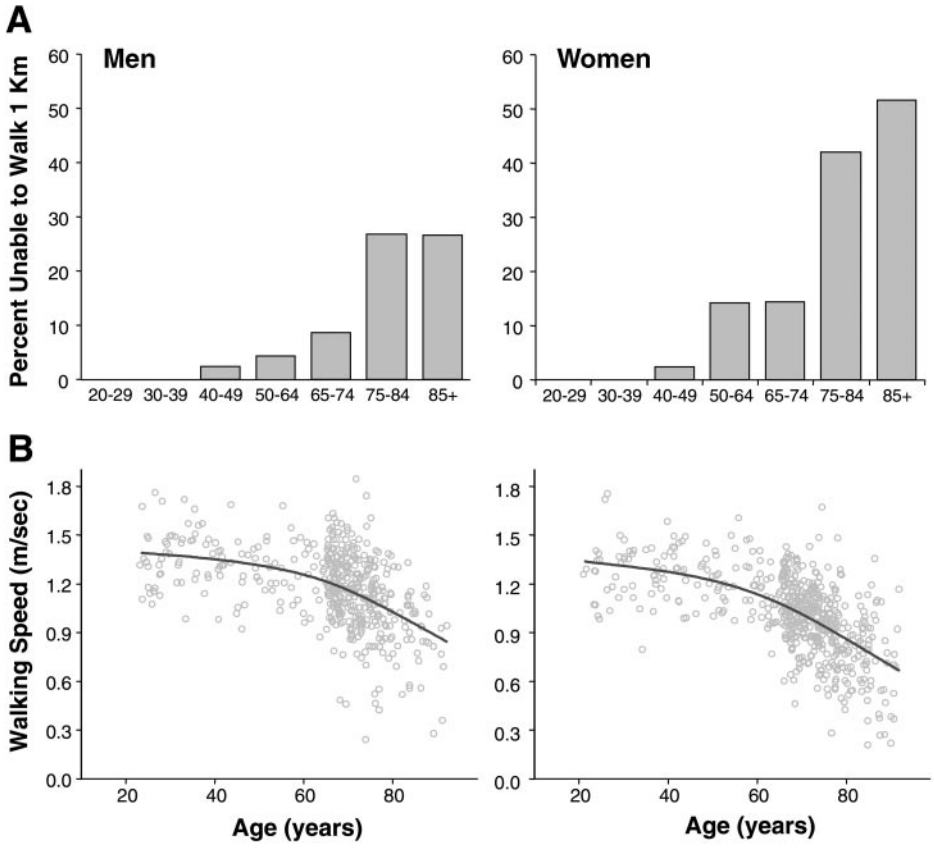

Fig. 3. Age-related differences in walking ability. *A*: percentage of men and women who reported being unable to walk 1 km without stopping and without developing symptoms, according to age groups. *B*: relationship between age and measured walking speed (over a 4-m course) in men and women in the form of scatter plots, with the relationship summarized by using smoothing splines.

the two definitions of mobility, separately in men and women. In the unadjusted models, all four muscle tests were strongly associated with both walking slower than 0.8 m/s and inability to walk 1 km. The association was always statistically significant, except for calf muscle area predicting women unable to walk 1 km. After adjusting for age, the OR values became substantially smaller, but those for knee-extension torque, handgrip, and lower extremity muscle power remained statistically significant. In contrast, calf muscle area remained a significant predictor of walking slower than 0.8 m/s only in men and was no longer associated with the ability to walk 1 km in men and women. In both genders, lower extremity muscle power was the strongest predictor of walking slower than 0.8 m/s, whereas knee-extension torque was the strongest predictor of being unable to walk 1 km. However, when the OR values for knee-extension torque, handgrip, and lower extremity muscle power were formally compared, they were not statistically different, and, in fact, the 95% confidence intervals were largely superimposed. Finally, OR values for calf muscle area were statistically smaller than those calculated for the other three muscle parameters, except for the prediction of men walking slower than 0.8 m/s.

To test the hypothesis that calf muscle area is associated with functional outcomes, independent of age and measures of strength (or power), we added muscle cross-sectional area as a covariate in the models shown in Table 4. Interestingly, muscle cross-sectional area was a significant predictor of walking at a speed >0.8 m/s, independent of knee-extension torque, handgrip, and muscle power, in men but not in women. Neither in men nor women was muscle cross-sectional area an independent predictor of the self-reported ability to walk for 1 km (data not shown).

DISCUSSION

Confirming previous reports, this study demonstrates that isometric muscle strength and muscle power decline considerably with aging. Furthermore, we showed that, independent of age and in both genders, low muscle strength and power are strongly associated with two complementary definitions of poor mobility. On the contrary, calf muscle cross-sectional area, an indicator of muscle mass, shows only a moderate decline with aging, and a small calf muscle cross-sectional area is a weak and inconsistent predictor of mobility limitations.

Similar to other authors (3), we found that the percent per year drop in muscle power is substantially larger than the per year drop in isometric strength. Based on this observation, the same authors recommended that muscle power be the method of choice for the early detection of patients with sarcopenia. Indeed, in our study population, the estimated prevalence of sarcopenia based on "low muscle power T-score" was much higher than the prevalence estimated by using definitions based on isometric strength and calf muscle

Table 3. *Percentage of men and women walking slower than 0.8 m/s and unable to walk 1 km without difficulty, according to quintiles of knee-extension torque, handgrip, weight-specific lower extremity muscle power, and calf muscle area*

Quintiles	Men	Walking speed <0.8 m/s, %	Unable to walk 1 km, %	Women	Walking speed <0.8 m/s, %	Unable to walk 1 km, %
			Knee-extension torque			
1	<395.4 N/dm	29.2	19.5	<240.3 N/dm	58.2	26.9
2	395.4–485.7 N/dm	17.5	2.9	240.3–291.0 N/dm	33.7	17.2
3	485.8–575.7 N/dm	13.6	5.6	291.1–349.1 N/dm	28.0	11.6
4	575.8–697.0 N/dm	7.2	3.3	349.2–385.2 N/dm	18.0	9.8
5	>697.0 N/dm	6.0	0.0	>385.2 N/dm	9.2	5.5
			Handgrip			
1	<29.5 kg	34.5	18.9	<15.0 kg	43.6	25.1
2	29.5–37.4 kg	19.8	6.6	15.0–20.5 kg	29.7	19.2
3	37.5–44.0 kg	7.4	4.3	20.6–24.7 kg	37.4	12.6
4	44.1–51.0 kg	7.3	1.1	24.8–30.0 kg	18.8	11.0
5	>51.0 kg	7.0	1.0	>30.0 kg	7.7	2.4
			Lower extremity muscle power			
1	<102.2 W	29.0	19.9	<49.0 W	61.0	28.6
2	102.2–141.8 W	22.5	8.5	49.0–71.1 W	39.0	18.6
3	141.9–170.1 W	10.8	8.0	71.2–94.4 W	25.7	13.7
4	170.2–214.3 W	8.7	4.8	94.5–124.4 W	17.6	8.2
5	>214.3 W	5.5	0.0	>124.4 W	11.3	5.1
			Calf muscle area			
1	<6,112.0 mm^2	21.1	6.2	<4,970 mm^2	32.7	14.6
2	6,112–6,925 mm^2	12.2	7.2	4,970–5,455 mm^2	26.7	12.0
3	6,926–7,575 mm^2	9.6	3.4	5,456–5,945 mm^2	27.9	10.5
4	7,576–8,233 mm^2	17.8	2.7	5,946–6,463 mm^2	26.9	13.5
5	>8,233 mm^2	11.3	1.8	>6,463 mm^2	22.6	16.3

cross-sectional area. However, many persons with a low muscle power T-score showed no evidence of mobility limitations. In fact, in a ROC analysis, knee-extension torque, handgrip, and lower extremity muscle power showed similar good discriminating value in the identification of poor mobility, defined either as walking speed <0.8 m/s or inability to walk 1 km without difficulty. Based on these findings, we suggest that the handgrip should be the measure of choice used for the screening of sarcopenia in clinical geriatric practice.

Aging and muscles. Despite extensive research efforts, the mechanism responsible for the age-associated decline in muscle mass and strength has not been completely elucidated. An age-associated decline in muscle mass certainly plays an important role (5). Recent studies suggest that changes in the amount and type of skeletal muscle proteins occur as well, caused by a number of multiple mechanisms (1, 15, 35), and may explain the age-associated reduction of muscle strength per unit muscle mass described by some authors (15). Interestingly, resistance exercise training enhances muscle protein synthesis and improves muscle protein quality and, therefore, may counteract the progression of age-associated sarcopenia (36, 37).

Muscles and physical function. The relationship between muscle function and physical disability has been previously examined by Ploutz-Snyder et al. (26), who searched for functionally relevant thresholds in the ratio of isometric leg extension peak torque to body weight [strength/weight (STR/WT)] that best discriminated the ability to perform three functional ambulatory tasks (26). They found that individuals with a STR/WT <3.0 $N \cdot m \cdot kg^{-1}$ were at a substantial higher risk for impaired function in chair rise, gait speed, and stair ascent and descent. In our study, the best threshold in STR/WT that discriminated the ability to walk at a speed >0.8 m/s was 4.7. The difference between the two studies is likely to be attributable to differences in the functional outcomes. In fact, the ability to walk faster than 0.8 m/s pertains to the higher portion of the functional spectrum, and a STR/WT of 4.5 is very similar to 4.2–4.5 identified by Ploutz-Snyder et al. (26) as the best threshold for "optimal functioning."

Although several authors have used a definition of sarcopenia based on muscle mass (5, 21, 22), our findings suggest that measures of muscle mass should be complemented with measures of strength. This is consistent with recent data demonstrating that muscle strength, but not muscle mass, is independently associated with lower extremity performance (34). In addition, this is in accordance with research suggesting that the mechanical force produced per volumetric unit of muscle tissue declines with aging in humans (32) and with preclinical data, which demonstrate that the tension developed by a single-muscle fiber depends on the age of the experimental animal (7).

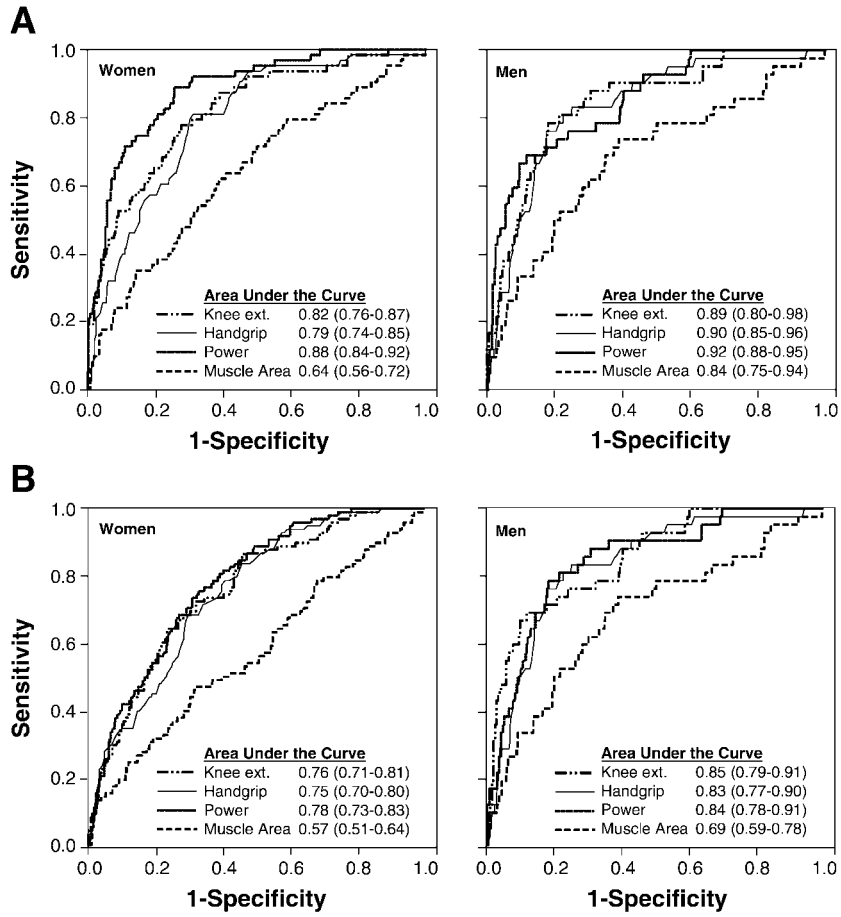

Fig. 4. Receiver operator characteristic curve plots compare how different measures of muscle mass/function allow the identification of participants with mobility problems. Each curve is created by *1*) selecting a cutoff threshold within the muscle measure range of values; *2*) plotting for that specific threshold value the sensitivity and 1-specificity for the identification of participants walking slower than 0.8 m/s (*A*) and unable to walk without difficulty for 1 km (*B*); and *3*) repeating *steps 1* and *2* for all possible cutoff thresholds within the range of the muscle measure. The area under the curve (AUC) expresses the overall discriminative value for that muscle measure and is reported on the *bottom* of each panel. Curves for different muscle measures are superimposed to enhance their visual comparison. The AUC for knee extension torque, handgrip, and lower extremity muscle power are statistically different ($P < 0.001$) from the AUC for calf muscle area.

Our findings concerning the age effect on calf muscle cross-sectional area (used as a proxy measure of muscle mass) and muscle strength are highly consistent with those obtained by using other measures of body composition. Janssen et al. (20) showed that the slopes of the regression lines between age and dual-energy X-ray absorptiometry-derived skeletal muscle mass were significantly greater in men than in women, suggesting that the age-associated decline in skeletal muscle is steeper in men than in women.

Table 4. *Optimal cutoff values for the various muscle parameters in the identification of participants walking slower than 0.8 m/s and unable to walk for 1 km without difficulty*

	Participants Walking Slower Than 0.8 m/s			Participants Unable to Walk Without Difficulty for 1 km		
	Optimal cutoff value*	OR at the optimal cutoff†	Age-adjusted OR at the optimal cutoff	Optimal cutoff value	OR at the optimal cutoff‡	Age-adjusted OR at the optimal cutoff
			Men			
Knee-extension torque, N/dm	390.9	25.5(7.2–90.8)	11.7(3.1–44.5)	435.0	14.36(6.96–29.61)	7.83(3.62–16.94)
Handgrip, kg	30.3	16.5(5.3–51.8)	6.9(2.1–23.3)	32.8	11.68(5.75–23.72)	5.93(2.77–12.67)
Muscle power, W	101.0	28.3(7.9–100.9)	11.9(3.1–45.9)	119.9	11.00(5.47–22.13)	5.13(2.39–11.02)
Calf muscle area, mm^2	6,304.6	12.5(4.0–39.1)	4.8(1.4–16.8)	6,881.9	3.69(1.91–7.11)	1.42(0.66–3.04)
			Women			
Knee-extension torque, N/dm	266.4	7.8(4.3–14.3)	3.7(1.9–7.1)	287.0	5.53(3.43–8.90)	2.95(1.76–4.93)
Handgrip, kg	19.3	5.7(3.2–10.1)	2.7(1.4–5.0)	20.5	3.49(2.20–5.55)	1.79(1.08–2.97)
Muscle power, W	59.1	15.0(7.8–28.9)	7.7(3.9–15.5)	70.03	4.81(3.00–7.72)	2.43(1.45–4.05)
Calf muscle area, mm^2	5,497.0	2.4(1.4–4.1)	1.5(0.8–2.8)	5,666.6	1.45(0.93–2.28)	0.93(0.57–1.53)

The odds ratios (OR) and age-adjusted OR for walking slower than 0.8 m/s and being unable to walk without difficulty for 1 km were estimated for each muscular parameter by comparing participants below and above optimal cutoff values. *Optimal cutoff values were identified in the receiver operator characteristic curve as the value yielding the highest sensitivity and specificity. †Risk of walking slower than 0.8 m/s was associated with having the specific muscle parameter below compared with above the optimal cutoff value. ‡Risk of being unable to walk without difficulty for 1 km was associated with having the specific muscle parameter below compared with above the optimal cutoff value.

This finding is explained only in part by a larger absolute decline in men who have a greater amount of muscles at baseline. In fact, the percent differences in calf muscle cross-sectional area between subsequent age groups were similar in men and women aged <65 yr. However, 75- to 84-yr-old men and women in the study had, respectively, 10.2 and 4.9% lower muscle area compared with participants of the same gender who were 65–74 yr old. Analogously, the percent differences in calf muscle area comparing 85+-yr-old vs. 75- to 84-yr-old participants were 11.2% in men and 2.7% in women.

In our study, measures of isometric strength obtained from both the upper and lower extremities were similar in their relationship with poor mobility, which specifically explores lower extremity function. This finding suggests that sarcopenia is a condition generalized to the whole body, further supporting the appropriateness of using the handgrip for screening purposes. An extensive literature review showed that handgrip strength is cross-sectionally associated with disability and predicts future disability as long as 25 yr before the development of the disability outcome (14, 28, 29). However, no previous study has attempted to identify the diagnostic threshold in handgrip strength that best discriminates subjects with mobility limitations. Our findings suggest that a good approximation to be used in clinical practice is 30 kg in men and 20 kg in women. Providing support for our findings, both for men and women, the optimal discriminating thresholds identified for two very different functional outcomes (walking at a speed <0.8 m/s and self-reported inability to walk for 1 km) were quite similar. Use of the handgrip strength for screening purposes is appealing because testing handgrip strength is easy, rapid, and relatively inexpensive. However, some potential problems intrinsic to this method should be considered. Handgrip is probably appropriate to monitor the effectiveness of systemic treatments, both pharmacological and nonpharmacological, aimed at improving muscle strength. However, exercise interventions may have a differential impact on different muscle groups and should be monitored with appropriate regional measures. Furthermore, in patients affected by rheumatoid arthritis, hand osteoarthritis, or carpal tunnel syndrome, grip strength may not be strongly correlated with global muscle function. Because these conditions are relatively highly prevalent and sometimes difficult to detect in older persons, the results of handgrip tests should be interpreted with caution in older persons.

Study limitations. Some limitations of this study should be pointed out. Both the self-reported and the performance-based measures of mobility limitation used in our study are probably sensitive enough to identify persons who experience even a mild reduction of mobility. We selected these measures in our analysis because one major reason for screening for "poor muscles" is to identify persons who just entered the early stage of the disablement process, those in whom interventions are most likely to be effective. However, our findings may not apply for measures that capture more advanced stages of disability, such as measures of mobility that directly reflect ability in the basic daily activities (i.e., ability to climb stairs or to rise from a chair). This is probably the reason that explains the difference between our findings and those reported by Ploutz-Snyder et al. (26).

In our study, we measured muscle strength by a hand-held isometric dynamometry. Although a preliminary pilot study demonstrated that our method provided reliable measures over a wide range of strength, other methods of assessing strength, such as isokinetic dynamometry, allow more precise and reliable assessments. However, these methods are unlikely to be applied in large epidemiological studies, especially in frail, older participants who are unable to come to the study clinic and should be evaluated in their homes.

In our study, we used a pQCT to assess calf-muscle area as an indicator of muscle mass. Because of the small dimensions of our equipment, we could not measure larger muscle masses. Furthermore, to minimize the amount of radiation administered to the participants, we performed a single-slice scan. Because of these limitations, our findings on muscle mass should be considered with caution, and we cannot exclude the hypothesis that, using multislice computed tomography measures of large muscle groups or whole body measure of lean body mass, we may have obtained different findings. However, supporting our results, previous reports have shown that high body fatness, as estimated by total-body dual-energy X-ray absorptiometry scans, but not low fat-free mass, predicts disability in older men and women (33).

Finally, the results shown in this paper were obtained from a cross-sectional survey. A gold-standard definition of sarcopenia that could be recommended for diagnosis in routine clinical practice would require the demonstration of its predictive value on subsequent adverse outcomes. This further validation requires the analysis of prospective data that are not available at this stage for the InCHIANTI study.

Conclusions. Despite the limitations, our findings indicate that a standard quantitative diagnosis of sarcopenia may be an extremely useful component in the assessment of middle-aged and older patients. Because the screening of sarcopenia can be performed by using handgrip, this simple, rapid, and inexpensive method should be introduced in the routine clinical assessment of geriatric patients.

DISCLOSURES

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REFERENCES

1. **Balagopal P, Rooyackers OE, Adey DB, Ades PA, and Nair KS.** Effects of aging on in vivo synthesis of skeletal muscle

myosin heavy-chain and sarcoplasmic protein in humans. *Am J Physiol Endocrinol Metab* 273: E790–E800, 1997.
2. **Bandinelli S, Benvenuti E, Del Lungo I, Baccini M, Benvenuti F, Di Iorio A, and Ferrucci L.** Measuring muscular strength of the lower limbs by hand-held dynamometer: a standard protocol. *Aging Clin Exp Res* 11: 287–293, 1999.
3. **Bassey EJ, Fiatarone MA, O'Neill EF, Kelly M, Evans WJ, and Lipsitz LA.** Leg extensor power and functional performance in very old men and women. *Clin Sci* 82: 321–327, 1992.
4. **Bassey EJ and Short AH.** A new method for measuring power output in a single leg extension: feasibility, reliability and validity. *Eur J Appl Physiol* 60: 385–390, 1990.
5. **Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, Garry PJ, and Lindeman RD.** Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol* 147: 755–763, 1998.
6. **Clement FJ.** Longitudinal and cross-sectional assessments of age changes in physical strength as related to sex, social class, and mental ability. *J Gerontol* 29: 423–429, 1974.
7. **Delbono O.** Molecular mechanisms and therapeutics of the deficit in specific force in ageing skeletal muscle. *Biogerontology* 3: 265–270, 2002.
8. **DeLong ER, DeLong DM, and Clarke-Pearson DL.** Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 44: 837–845, 1988.
9. **Evans W.** Functional and metabolic consequences of sarcopenia. *J Nutr* 127: 998S–1003S, 1997.
10. **Evans WJ.** What is sarcopenia? *J Gerontol A Biol Sci Med Sci* 50: 5–8, 1995.
11. **Ferrucci L, Bandinelli S, Benvenuti E, Di Iorio A, Macchi C, Harris TB, and Guralnik JM.** Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. *J Am Geriatr Soc* 48: 1618–1625, 2000.
12. **Fried LP and Guralnik JM.** Disability in older adults: evidence regarding significance, etiology, and risk. *J Am Geriatr Soc* 45: 92–100, 1997.
13. **Frontera WR, Hughes VA, Lutz KJ, and Evans WJ.** A cross-sectional study of muscle strength and mass in 45- to 78-yr-old men and women. *J Appl Physiol* 71: 644–650, 1991.
14. **Giampaoli S, Ferrucci L, Cecchi F, Lo Noce C, Poce A, Dima F, Santaquilani A, Vescio MF, and Menotti A.** Handgrip strength predicts incident disability in non-disabled older men. *Age Ageing* 28: 283–288, 1999.
15. **Greenlund LJ and Nair KS.** Sarcopenia–consequences, mechanisms, and potential therapies. *Mech Ageing Dev* 124: 287–299, 2003.
16. **Guralnik JM, Ferrucci L, Balfour JL, Volpato S, and Di Iorio A.** Progressive versus catastrophic loss of the ability to walk: implications for the prevention of mobility loss. *J Am Geriatr Soc* 49: 1463–1470, 2001.
17. **Guralnik JM, Ferrucci L, Pieper CF, Leveille SG, Markides KS, Ostir GV, Studenski S, Berkman LF, and Wallace RB.** Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. *J Gerontol A Biol Sci Med Sci* 55: M221–M231, 2000.
18. **Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, and Wallace RB.** Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med* 332: 556–561, 1995.
19. **Hanley JA and McNeil BJ.** The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 143: 29–36, 1982.
20. **Janssen I, Heymsfield SB, Wang ZM, and Ross R.** Skeletal muscle mass and distribution in 468 men and women aged 18–88 yr. *J Appl Physiol* 89: 81–88, 2000.
21. **Melton LJ III, Khosla S, Crowson CS, O'Connor MK, O'Fallon WM, and Riggs BL.** Epidemiology of sarcopenia. *J Am Geriatr Soc* 48: 625–630, 2000.
22. **Melton LJ 3rd, Khosla S, and Riggs BL.** Epidemiology of sarcopenia. *Mayo Clin Proc* 75, *Suppl*: S10–S12, 2000.
23. **Ostir GV, Volpato S, Fried LP, Chaves P, and Guralnik JM.** Reliability and sensitivity to change assessed for a summary measure of lower body function: results from the Women's Health and Aging Study. *J Clin Epidemiol* 55: 916–921, 2002.
24. **Penninx BW, Ferrucci L, Leveille SG, Rantanen T, Pahor M, and Guralnik JM.** Lower extremity performance in nondisabled older persons as a predictor of subsequent hospitalization. *J Gerontol A Biol Sci Med Sci* 55: M691–M697, 2000.
25. **Peolsson A, Hedlund R, and Oberg B.** Intra- and inter-tester reliability and reference values for hand strength. *J Rehabil Med* 33: 36–41, 2001.
26. **Ploutz-Snyder LL, Manini T, Ploutz-Snyder RJ, and Wolf DA.** Functionally relevant thresholds of quadriceps femoris strength. *J Gerontol A Biol Sci Med Sci* 57: B144–B152, 2002.
27. **Rantanen T, Guralnik JM, Foley D, Masaki K, Leveille S, Curb JD, and White L.** Midlife hand grip strength as a predictor of old age disability. *JAMA* 281: 558–560, 1999.
28. **Rantanen T, Masaki K, Foley D, Izmirlian G, White L, and Guralnik JM.** Grip strength changes over 27 yr in Japanese-American men. *J Appl Physiol* 85: 2047–2053, 1998.
29. **Rittweger J, Beller G, Ehrig J, Jung C, Koch U, Ramolla J, Schmidt F, Newitt D, Majumdar S, Schiessl H, and Felsenberg D.** Bone-muscle strength indices for the human lower leg. *Bone* 27: 319–326, 2000.
30. **Rosenberg IH.** Sarcopenia: origins and clinical relevance. *J Nutr* 127: 990S–991S, 1997.
31. **Roth SM, Ferrell RF, and Hurley BF.** Strength training for the prevention and treatment of sarcopenia. *J Nutr Health Aging* 4: 143–155, 2000.
32. **Thompson LV and Brown M.** Age-related changes in contractile properties of single skeletal fibers from the soleus muscle. *J Appl Physiol* 86: 881–886, 1999.
33. **Visser M, Langlois J, Guralnik JM, Cauley JA, Kronmal RA, Robbins J, Williamson JD, and Harris TB.** High body fatness, but not low fat-free mass, predicts disability in older men and women: the Cardiovascular Health Study. *Am J Clin Nutr* 68: 584–590, 1998.
34. **Visser M, Newman AB, Nevitt MC, Kritchevsky SB, Stamm EB, Goodpaster BH, and Harris TB.** Reexamining the sarcopenia hypothesis. Muscle mass versus muscle strength. Health, Aging, and Body Composition Study Research Group. *Ann NY Acad Sci* 904: 456–461, 2000.
35. **Welle S, Thornton C, Jozefowicz R, and Statt M.** Myofibrillar protein synthesis in young and old men. *Am J Physiol Endocrinol Metab* 264: E693–E698, 1993.
36. **Yarasheski KE, Pak-Loduca J, Hasten DL, Obert KA, Brown MB, and Sinacore DR.** Resistance exercise training increases mixed muscle protein synthesis rate in frail women and men ≥76 yr old. *Am J Physiol Endocrinol Metab* 277: E118–E125, 1999.
37. **Yarasheski KE, Zachwieja JJ, and Bier DM.** Acute effects of resistance exercise on muscle protein synthesis rate in young and elderly men and women. *Am J Physiol Endocrinol Metab* 265: E210–E214, 1993.