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Sarcopenia-Related Parameters and Incident Disability in Older Persons: Results From the "Invecchiare in Chianti" Study

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Background. Current operational definitions of sarcopenia are based on algorithms' simultaneous considering measures of skeletal muscle mass and muscle-specific as well as global function. We hypothesize that quantitative and qualitative sarcopenia-related parameters may not be equally predictive of incident disability, thus presenting different clinical relevance.

Methods. Data are from 922 elder adults (mean age = 73.9 years) with no activities of daily living (ADL) impairment recruited in the "Invecchiare in Chianti" study. Incident disability in ≥1 ADL defined the outcome of interest. The specific capacities of following sarcopenia-related parameters at predicting incident ADL disability were compared: residuals of skeletal muscle mass, fat-adjusted residuals of skeletal muscle mass, muscle density, ankle extension strength, ratio ankle extension strength/muscle mass, gait speed, and handgrip strength.

Results. During the follow-up (median = 9.1 years), 188 (20.4%) incident ADL disability events were reported. Adjusted models showed that only gait speed was significantly associated with the outcome in both men (per standard deviation [*SD*] = 0.23 m/s increase, hazard ratio [HR] = 0.46, 95% confidence interval [CI] = 0.33–0.63; $p < .001$) and women (per *SD* = 0.24 m/s increase, HR = 0.64, 95% CI = 0.50–0.82; $p < .001$). In women, the fat-adjusted lean mass residual (per *SD* = 4.41 increase, HR = 0.79, 95% CI = 0.65–0.96; $p = .02$) and muscle density (per *SD* = 3.60 increase, HR = 0.76, 95% CI = 0.61–0.93; $p = .01$) were the only other parameters that predicted disability. In men, several of the tested variables (except muscle mass measures) reported significant results.

Conclusions. Gender strongly influences which sarcopenia-related parameters predict disability. Gait speed was a powerful predictor of disability in both men and women, but its nonmuscle-specific nature should impose caution about its inclusion in definitions of sarcopenia.

Key Words: Skeletal muscle—Sarcopenia—Disability—Body composition—Gait speed.

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SARCOPENIA represents a major phenotypic manifestation of aging both in terms of prevalence among elder adults as well as impact over their health status (1). The definition of sarcopenia has been evolving over the last decade from a pure quantification of skeletal muscle mass (2,3) to algorithms requiring the additional assessment of function (4–7). Several operational definitions of sarcopenia propose to adopt the handgrip strength (HG) and/or the usual gait speed (UGS) as tests for measuring the qualitative component of the phenomenon and estimate the skeletal muscle production.

Recently, several reports from the Foundation for National Institutes of Health-Sarcopenia Project (FNIH-SP) were published in the *Journals of Gerontology Medical Sciences* (8–12). The aim of the FNIH-SP was to develop evidence-based diagnostic criteria for sarcopenia in the attempt of addressing the ambiguities and controversies raised by the previous definitions (13). For doing this, two FNIH-SP reports determined gender-specific cut-points for muscle weakness (as HG) (12) and low muscle mass (in terms of appendicular lean mass) (9) using a statistical approach based on Classification and Regression Tree (CaRT) models. A third report then explored the predictive value of the developed criteria for incident mobility disability and mortality (11).

In this study, we hypothesize that the various parameters, which are commonly considered in the existing operational

definitions of sarcopenia, are differently predictive of incident functional loss. In particular, a clear difference in the predictive capacity of negative health-related events may exist between quantitative and qualitative measures of the skeletal muscle (ie, those estimating the mass and the function, respectively). Therefore, to confirm and potentially extend the results of the FNIH-SP reports, we formally tested the relationships between multiple sarcopenia-related parameters and incident disability in a sample of community-dwelling men and women.

Methods

Data are from the "Invecchiare in Chianti" (InCHIANTI) study, a prospective population-based study designed by the Laboratory of Clinical Epidemiology of the Italian National Research Council of Aging (INRCA, Firenze, Italy). The InCHIANTI project has been previously described in detail (14).

The InCHIANTI population was recruited between September 1998 and March 2000 from residents of two towns in the Chianti geographic area (ie, Greve in Chianti and Bagno a Ripoli, Tuscany, Italy). A total of 1,155 individuals aged ≥65 years were evaluated at the baseline visit. Three, six, and nine years after the baseline visit, participants underwent repeated clinical visits. The INRCA Ethical Committee ratified the study protocol. All participants signed a written informed consent.

These analyses are conducted on 922 participants, after exclusion of 116 subjects presenting ≥1 impaired activities of daily living (ADL) at baseline, 81 died before the first follow-up assessment, and 36 lost to follow-up. Excluded participants were older (81.7 vs 73.9 years) and presented more cognitive impairment (19.1 vs 25.4 at the Mini-Mental State Examination [MMSE]), depressive symptoms (15.5 vs 12.6 at the Centre for Epidemiologic Studies-Depression [CES-D] scale), and comorbidities (3.7 vs 0.4) than those included in the analyses (all $p < .01$).

Incident Disability

Disability status of participants was measured using the ADL scale (15). It includes six functional tasks of daily living: bathing, dressing, toileting, transfer, continence, and feeding. All participants were completely autonomous in the ADLs at the baseline. Incident disability (dependent variable of interest) was defined as the incident loss of ≥1 ADL reported by the participant at one of the follow-up visits.

In the FNIH-SP reports, the primary outcome was mobility disability (ie, UGS < 0.8 m/s). In our study, we decided to use incident ADL disability events because UGS here is considered among the predictors (see in what follows), and for extending/confirming the FNIH-SP results to a more severe stage of the disabling process.

Sarcopenia-Related Parameters

At the baseline, a right leg peripheral quantitative computed tomography (pQCT) scan was performed in all participants by a recent generation device (XCT 2000; Stratec, Pforzheim, Germany) to evaluate the muscular and fat cross-sectional areas of the calf. Data were derived from a standard 2.5-mm thick transverse scan obtained at 66% of the tibial length starting from the tibiotarsal joint (ie, the region with the largest outer calf diameter and small variability across individuals) (16). Muscle density (in mg/cm^3), muscle area (in cm^2), and fat area (in cm^2) were calculated using the BonAlyse software version 3.1 (BonAlyse, Ltd., Jyväskylä, Finland). Different tissues in the analyses were separated according to different density thresholds, using the "soft tissue" algorithm: a density value of 15 mg/mm^3 was used to separate fat from muscle tissue and 180 mg/mm^3 to separate muscle from bone tissue. Muscle density represents a measure of fatty degeneration of muscle tissue (17). Two variables of muscle mass were defined by the residuals of gender-specific linear regressions predicting the dependent variable of muscle mass area (in cm^2) from (i) height (in cm), and (ii) height (in cm) and fat area (in cm^2) (3). A positive result at the (fat-adjusted) residuals indicates an individual with more muscle than what is predicted from his/her height (and fat mass).

The HG test was measured with a handheld dynamometer (hydraulic hand "BASELINE"; Smith & Nephew, Milan, Italy). As UGS, the HG has been included in algorithms defining sarcopenia to capture the qualitative component of the muscle decline (4).

Ankle extension strength (in kg) was measured with a hand-held dynamometer (Nicholas Muscle Tester, Sammon Preston Inc., Chicago, Illinois). This parameter was chosen because (i) it has been previously used to estimate muscular strength of the lower limb (18), and (ii) it measures the muscle function of the body district where the pQCT scan was conducted.

An additional qualitative parameter measuring the strength production per skeletal muscle unit (19) was defined by the ratio (rMS-MM) between the ankle extension strength and the calf muscle area (in cm^2).

UGS was defined as the best performance (time in seconds) of two 4-meter walks at usual pace. In the FNIH-SP reports, the UGS was mainly used to define the study outcome, and not as a predictor. In our study, we included the UGS among our independent variables of interest simply because it has been indicated in all the previous consensus papers on sarcopenia as an ideal marker for assessing the skeletal muscle function (4–7).

Other Measures

Covariates included sociodemographic variables (ie, age, gender, study site, current smoking), MMSE (20), CES-D scale (21), sedentary behavior, clinical conditions, and Instrumental ADL (IADL) (22). In this study, we defined

as "sedentary" those participants who had performed no physical activity, spent most of the time sitting, or rarely had a short walk (or other nondemanding physical activity) in the past year according to an interviewer-administered questionnaire (23). The following diseases (based on self-reported history, clinical documentation, and medication use, as well as prestandardized criteria derived from the Women's Health and Aging Study protocol) (24) were considered: cancer, coronary artery disease, dementia, diabetes, hypertension, osteoarthritis, Parkinson's disease, peripheral artery disease, respiratory disease, and stroke.

Statistical Analysis

All the analyses were stratified according to gender given the significant differences in muscle function and body composition between men and women. Differences in proportions and means of variables according to incident ADL disability were assessed by using chi-square and analysis of variance statistics, respectively. Variables showing a significant difference ($p < .05$) at the univariate analyses were considered as covariates of the subsequent adjusted models. Receiver Operating Characteristic (ROC) curve analyses were computed to estimate the predictive value of the independent variables of interest (ie, sarcopenia-related parameters) for incident ADL disability through the evaluation of the Areas Under the Curves (AUC). Cox proportional hazard models with the Efron's approximation method of handling ties (25) were used to evaluate the relationship of sarcopenia-related parameters with incident ADL disability. The proportional hazard assumption of the models was graphically explored and confirmed by Schoenfeld residuals tests (all p values > .1). The linear relationship assumption between the sarcopenia-related variables and the studied outcome was validated by use of quadratic terms. Time was censored to the last contact date (for participants not experiencing an event) or to the date of the visit at which ADL impairment was first detected (for participants presenting the outcome of interest). Hazard ratios (HR) and 95% confidence intervals (95% CIs) are reported. In order to allow a direct comparison between the sarcopenia-related parameters, risks are shown per standard deviation (*SD*) increase. The IADL variable was used as an additional covariate of the adjusted models to exclude that our findings could be differently explained by initial signs of the disabling cascade (not adequately taken into account by the selection criterion of ADL independence).

A $p < .05$ was chosen for statistical significance. Statistical analyses were conducted with SPSS Statistics 20.0 for Mac (IBM Corporation, Armonk, New York) and Stata/SE 12.0 for Mac (College Station, Texas).

Results

Main characteristics of the sample ($n = 922$) are described in Table 1. Mean age of participants was 73.9 (*SD* = 6.7) years, and women were more prevalent than men (57.0% vs 43.0%). The most prevalent diseases (in descending order were): hypertension (58.4%), diabetes (10.5%), osteoarthritis (9.7%), peripheral artery disease (9.0%), coronary heart disease (6.7%). During the study follow-up (median 9.1 years, interquartile range 7.0–9.3 years), 188 (20.4%) events of incident ADL disability were reported.

The ROC curves analyses (Table 2) showed that all the AUCs for the variables of interest, except for height residuals, were able to significantly discriminate women at risk of developing ADL disability (all AUCs > 0.65, all p-values < .001). In men, nonstatistically significant results were additionally obtained for height residuals and only a borderline significance was reported for muscle density. The UGS was the variable most strongly discriminating the risk of ADL disability in both men (AUC = 0.738, 95% CI = 0.662–0.814) and women (AUC = 0.752, 95% CI = 0.693–0.811).

Table 3 presents results from Cox proportional hazard models. In women, only UGS (HR = 0.64, 95% CI = 0.50–0.82; $p < .001$), muscle density (HR = 0.76, 95% CI = 0.61–0.93; $p = .01$), and fat-adjusted residuals (HR = 0.79, 95% CI = 0.64–0.96; $p = .02$) were associated with incident ADL disability, independently of potential confounders. Differently, although UGS remained the strongest predictor of incident ADL disability (HR = 0.46, 95% CI = 0.33–0.63; $p < .001$), rMS-MM ($p = .009$), muscle density ($p = .01$), ankle extension strength ($p = .04$), and HG ($p = .04$) also reported significant results in men. In order to exclude that our findings were affected by early manifestations of the disabling process, Cox proportional hazard models were further adjusted for the number of impaired IADL (Model 3). Consistent results were reported for both men and women.

Age-adjusted exploratory models having all the skeletal muscle parameters simultaneously tested were performed. UGS was the only independent variable showing a significant relationship with incident ADL disability both in men (HR = 0.53, 95% CI = 0.36–0.78; $p = .002$) and in women (HR = 0.63, 95% CI = 0.48–0.82; $p = .001$). Significant results were also obtained for fat-adjusted residuals in women only (HR = 0.72, 95% CI = 0.57–0.91; $p = .006$).

Findings remained substantially unaltered after exclusion of participants with dementia ($n = 22$) and/or Parkinson's disease ($n = 12$) from analyses, conditions that more than others may cause disability through a direct process not mediated by sarcopenia (Supplementary Table 1).

Discussion

In this study, we formally compared the predictive value of multiple sarcopenia-related parameters for incident ADL disability in a sample of community-dwelling older men and women. The UGS confirms to be the strongest predictor of disability, independently of gender and potential confounders. On the other hand, it is noteworthy for the lack of significant results obtained for skeletal muscle mass. The

Table 1. Characteristics of the Sample Stratified by Gender According to Incident ADL Disability

	Women (n = 526)			Men (n = 396)		
	No Incident ADL Disability (n = 405)	Incident ADL Disability (n = 121)	p	No Incident ADL Disability (n = 329)	Incident ADL Disability (n = 67)	p
Age (years)	72.5 ± 5.7	81.1 ± 6.8	<.001	72.1 ± 5.6	77.8 ± 7.3	<.001
Site (Bagno a Ripoli)	50.6	57.9	.18	52.9	46.3	.35
Current smoking	9.6	4.1	.06	21.3	23.9	.64
Mini-Mental State Examination	25.6 ± 3.0	23.0 ± 4.1	<.001	26.3 ± 2.5	23.9 ± 4.6	<.001
CES-D	14.2 ± 9.0	18.5 ± 8.5	<.001	8.7 ± 6.4	12.0 ± 8.8	.001
Sedentary behavior	14.9	44.6	<.001	5.2	18.2	<.001
Cancer	7.9	2.5	.04	4.0	1.5	.32
Coronary heart disease	4.2	5.8	.46	8.2	16.4	.04
Dementia	1.0	8.3	<.001	1.2	6.0	.01
Diabetes	8.9	9.9	.73	12.5	11.9	.91
History of stroke	3.7	7.4	.08	4.0	14.9	<.001
Hypertension	58.5	68.6	.05	53.2	64.2	.10
Osteoarthritis	12.3	17.4	.16	3.6	9.0	.06
Parkinson's disease	—	5.0	<.001	0.9	4.5	.03
Peripheral artery disease	4.9	9.9	.04	11.2	20.9	.03
Respiratory disease	1.0	0.8	.87	12.8	20.9	.08
Impaired IADL (/8)	0.3 ± 0.8	1.6 ± 2.0	<.001	0.1 ± 0.5	0.9 ± 1.9	<.001
Residuals	0.10 ± 8.84	–0.34 ± 10.21	.68	0.59 ± 7.41	1.10 ± 8.14	.13
Fat-adjusted residuals	0.36 ± 4.14	–1.46 ± 4.97	<.001	0.31 ± 3.64	0.47 ± 2.60	.14
Muscle density (mg/cm^3)	71.1 ± 3.4	69.1 ± 3.9	<.001	71.51 ± 3.32	70.60 ± 3.70	.07
Ankle extension strength (kg)	28.3 ± 8.3	23.3 ± 7.3	<.001	38.6 ± 9.4	33.8 ± 10.9	.001
rMS-MM (kg/cm^2)	0.45 ± 0.15	0.38 ± 0.13	<.001	0.50 ± 0.14	0.43 ± 0.13	.003
HG (kg)	23.4 ± 7.1	18.4 ± 7.3	<.001	40.2 ± 9.8	32.3 ± 8.9	<.001
UGS (m/s)	1.06 ± 0.21	0.80 ± 0.25	<.001	1.20 ± 0.21	0.99 ± 0.22	<.001

Notes: Results are presented as percentages, or mean ± standard deviations. ADL = activities of daily living; CES-D = Center for Epidemiologic Studies-Depression scale; HG = handgrip strength; IADL = instrumental activities of daily living; rMS-MM = ratio ankle extension strength/muscle mass area; UGS = usual gait speed.

Table 2. Gender-Stratified Areas Under the Receiver Operating Characteristic Curves of Sarcopenia-Related Parameters for Incident ADL Disability

	Women (n = 526)	Men (n = 396)
Residuals	0.532 (0.460–0.603)	0.570 (0.468–0.671)
	p = .39	p = .15
Fat-adjusted residuals	0.681 (0.613–0.749)	0.598 (0.503–0.693)
	p < .001	p = .04
Muscle density (mg/cm^3)	0.683 (0.620–0.745)	0.586 (0.490–0.682)
	p < .001	p = .08
Ankle extension strength (kg)	0.694 (0.629–0.758)	0.640 (0.546–0.734)
	p < .001	p = .004
Ratio ankle extension strength/muscle mass area (kg/cm^2)	0.658 (0.591–0.725)	0.624 (0.530–0.718)
	p < .001	p = .01
Handgrip strength (kg)	0.672 (0.606–0.737)	0.716 (0.638–0.795)
	p < .001	p < .001
Usual gait speed (m/s)	0.752 (0.693–0.811)	0.738 (0.662–0.814)
	p < .001	p < .001

Notes: ADL = activities of daily living. Residuals and fat-adjusted residuals are residuals of gender-specific linear regressions predicting the dependent variable (muscle mass area, cm^2) from height (cm), and from height (cm) and fat area (cm^2), respectively.

only body composition measures showing consistent (but weaker) results were fat-adjusted residuals (in women) and muscle density (in both men and women).

In the FNIH-SP reports, HG was chosen as the variable measuring the muscle function component of sarcopenia. A CaRT analysis model was used for identifying the gender-specific cut-points of HG for predicting mobility disability (12). Differently, for the muscle mass component, multiple body composition parameters were included in the CaRT analysis model for identifying the best predictor (and its optimal threshold of risk) of the studied outcome (9). Differently, in our study, we have conducted a comparison across multiple variables without differentiating which dimension of sarcopenia they were specifically assessing.

Table 3. Results (hazard ratios and 95% confidence intervals) From Cox Proportional Hazard Models Predicting Incident ADL Disability From Sarcopenia-Related Parameters (per SD increase)

	Women (n = 526)			Men (n = 396)		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Residuals	0.92 (0.76–1.12)	1.03 (0.82–1.29)	1.03 (0.82–1.29)	1.03 (0.81–1.29)	1.14 (0.88–1.48)	1.11 (0.85–1.44)
Fat-adjusted residuals	0.80 (0.68–0.93)†	0.79 (0.64–0.96)*	0.78 (0.64–0.96)*	1.10 (0.89–1.36)	1.06 (0.81–1.38)	1.07 (0.82–1.39)
Muscle density (mg/cm^3)	0.77 (0.63–0.93)†	0.76 (0.61–0.93)*	0.77 (0.62–0.95)*	0.81 (0.64–1.02)	0.73 (0.57–0.93)*	0.77 (0.60–0.99)*
Ankle extension strength (kg)	0.82 (0.62–1.09)	0.99 (0.75–1.30)	1.00 (0.76–1.32)	0.73 (0.53–1.01)	0.70 (0.49–0.98)*	0.70 (0.50–0.98)*
Ratio ankle extension strength/ muscle mass area (kg/cm^2)	0.92 (0.71–1.20)	1.01 (0.75–1.35)	1.02 (0.76–1.36)	0.69 (0.49–0.96)*	0.61 (0.42–0.89)†	0.64 (0.45–0.92)*
Handgrip strength (kg)	0.65 (0.50–0.84)†	0.89 (0.66–1.18)	0.91 (0.68–1.22)	0.63 (0.46–0.85)†	0.70 (0.50–0.99)*	0.71 (0.50–1.00)
Usual gait speed (m/s)	0.52 (0.43–0.64)‡	0.64 (0.50–0.82)‡	0.65 (0.50–0.84)†	0.44 (0.33–0.58)‡	0.46 (0.33–0.63)‡	0.51 (0.37–0.72)‡

Notes: Gender-specific standard deviations. *Women*: residuals = 9.16244; fat-adjusted residuals = 4.40731; muscle density = 3.596 mg/cm^3; ankle extension strength = 8.35476; ratio ankle extension strength/muscle mass area = 0.15361; handgrip strength = 7.487 kg; usual gait speed = 0.24076 m/s. *Men*: residuals = 7.51069; fat-adjusted residuals = 3.50264; muscle density = 3.322 mg/cm^3; ankle extension strength = 9.79286; ratio ankle extension strength/muscle mass area = 0.14200; handgrip strength = 10.112 kg; usual gait speed = 0.23008 m/s. Model 1: adjusted for age; Model 2: adjusted for Model 1 + MMSE, CES-D, sedentary behavior, cancer, coronary artery disease, dementia, history of stroke, hypertension, Parkinson's disease, peripheral artery disease; Model 3: adjusted for Model 2 + IADL. CES-D = Center for Epidemiologic Studies-Depression scale; IADL = instrumental activities of daily living; MMSE = Mini-Mental State Examination; *SD* = standard deviation.

*p < .05; †p < .01; ‡p < .001.

Our variables were standardized using the same unit (ie, one *SD* increase) to conduct fair comparisons across them and allow a hierarchization of the resulting predictive values. Such approach helped us at better highlighting how different are the two dimensions of sarcopenia in terms of clinical relevance. In fact, a novel finding of our analyses resides in the gender differences we documented. In men, the risk of incident disability was mainly reported for measures of muscle strength. Because men are stronger than women, it is possible that the wider distribution of strength results might provide the opportunity to better capture/classify the heterogeneous risk profile of the individual. Conversely, in women, the only sarcopenia-related parameters (besides UGS) reporting a significant association with incident disability were the muscle density and fat-adjusted residual variables. Such findings are consistent with previous evidence suggesting that the adipose tissue inclusion in the definition of sarcopenia provides a better estimate of the risk for negative health-related events (3,26), probably because transforming the index into a marker of muscle quality. At the same time, the adjustment for adipose tissue may better take into account the gender differences in the body composition profile, thus leading to a more accurate estimate of the risk.

Overall, these results may suggest that different sarcopenia-related pathophysiological mechanisms underlie the disabling process in men and women. Because in the FNIH-SP reports, the HG was *a priori* selected to define the qualitative domain (ie, function) of sarcopenia, a formal comparison of this parameter with the others (especially the quantitative variables) was not conducted. Further studies should confirm that, when sarcopenia-related parameters are used to predict negative events, men and women present different (i) profiles (ie, more strength-related for men, and body composition-related for women), and (ii) thresholds of risk (ie, higher cut-points for men compared with women).

Not surprisingly, the UGS was the strongest predictor of incident disability. This parameter has been repeatedly indicated as a novel "vital sign" for elder adults and an estimation of the "biological age" of the individual (27). Thus, it may easily be argued that it is limitative to think at the UGS as a mere marker of skeletal muscle function. For this reason, its use in the operative definitions of specific conditions (such as sarcopenia) should be cautiously considered. For example, an effective intervention targeting sarcopenia may provide negative results if the outcome includes a measure of UGS. In fact, slow walkers due to factors other than sarcopenia may not benefit from the hypothetical skeletal muscle-specific treatment. Our results may suggest that UGS should be better used as a screening tool (possibly with gender-specific cut-points) rather than as a diagnostic instrument for sarcopenia. For this latter task, muscle specific parameters should better be adopted (as proposed in the FNIH-SP reports).

The interpretation of results from studies adopting a multidimensional variable of interest is often difficult and special caution is required in the analysis of its single components. The implicit assumption that the different constituting factors might equally contribute to the risk determination may easily remain unmet. In the field of sarcopenia, it seems more likely that the risk profile is not due to the poor quantitative component of the skeletal muscle, but to its qualitative loss (ie, muscle density). However, it cannot be excluded that there might be a small population in who the muscle atrophy is so severe to lead to functional consequences. These particularly frail individuals are unlikely to be living in the community, but might rather be identified in clinical populations.

The ability to generate muscular force seems particularly important in our results. Such aspect may largely affect the implementation of skeletal muscle assessment in the clinical routine. In this context, it is noteworthy what happened in

the field of osteoporosis (ie, the age-related bone decline). At the beginning, imaging techniques for the assessment of bone mineral density were developed and implemented. Today, more comprehensive and informative tools (eg, the FRAX (28) algorithm), which do not even require the bone mineral density assessment, are increasingly adopted for determining the need of specific treatment. By stating this, it is important to underline the difference between the predictive capacity of a variable and its representativeness for the targeted clinical condition. From our analyses, we have here proposed a hierarchical order of several sarcopenia-related variables in the prediction of incident disability. However, this does not automatically imply that the most statistically significant variables are also those better capturing the sarcopenia phenomenon. In fact, the ideal definition of sarcopenia should rely on the variable capacity to accurately perceive the age-related muscle decline, and not only to identify individuals at risk of developing an *a priori* and arbitrary decided health-related outcome.

Our study presents limitations worth to be mentioned. The body composition parameters were determined using pQCT. Although the pQCT technology is increasingly used in research and has shown to be highly reproducible for the assessment of body composition parameters, other techniques might have provided different results. Moreover, although more limited in accuracy compared with computed tomography or magnetic resonance imaging (commonly considered as gold standard methods for muscle mass assessment) (4,29), it still provides a clear differentiation of body composition compartments and assesses muscle quality (30). Some of our results may have been affected by limited statistical power due to the gender stratification and multiple adjustments. However, the analytical approach has still allowed fair comparisons among the markers. Finally, we cannot exclude that third factors not considered in these analyses might differently explain our findings.

In conclusion, our study demonstrates heterogeneous predictive values for incident disability across multiple skeletal muscle parameters commonly used to operationally define sarcopenia. Gender-specific pathophysiological mechanisms underlying the sarcopenia condition are possible and may require adaptations in the operationalization of the diagnostic criteria. UGS is the strongest independent predictor of incident disability among the usually sarcopenia-related parameters. Given the strong results obtained for UGS and its nonmuscle-specific nature, the use of this parameter in the definition of sarcopenia should be cautiously considered. Our findings may hopefully support discussions and studies about the best way to approach sarcopenia in older persons.

Supplementary Material

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/

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