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Comparing EWGSOP2 and FNIH Sarcopenia Definitions: Agreement and Three-Year Survival Prognostic Value in Older Hospitalized Adults. The GLISTEN Study.

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ABSTRACT

Background. Sarcopenia is common among older hospitalized adults but estimates vary according to definitions used. Aims of this study were to investigate the agreement between the European Working Group on Sarcopenia in Older People (EWGSOP2) and the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project criteria and to compare the predictive value of both definitions for 3-year mortality.

Methods. Analysis was performed on 610 older hospitalized patients enrolled in the GLISTEN study. Participants were categorized as sarcopenic or not sarcopenic according to EWGSOP2 and FNIH definitions separately and in a four-group variable (neither criterion positive, only EWGSOP2, only FNIH, both criteria).

Results. Sarcopenia prevalence was 22.8% and 23.9% using EWGSOP2 and FNIH criteria respectively, with a low classification agreement (Cohen's kappa statistic: 0.29). Sarcopenic participants by each definitions had higher mortality rate when compared to those not sarcopenic (both log-rank test: $p < 0.001$). Participants that met both positive criteria had the shorter survival as compared with the other three groups. Cox models showed that, after adjustment for potential confounders, only EWGSOP2 definition predicted 3-years mortality (HR 1.84; 95% C.I. 1.33-2.57). When the four-group variable was used, compared with the NO EWGSOP2/NO FNIH group, significant mortality risk was found for the EWGSOP2 (HR 2.08; 95% C.I. 1.38-3.16) and the combined EWGSOP2/FNIH group (HR 1.75; 95% C.I. 1.11-2.79).

Conclusions. Agreement between EWGSOP2 and FNIH definitions is poor. Sarcopenia on hospital admission is associated with increased risk of 3-year mortality and EWGSOP2 criteria seem to have the highest predictive value.

Key words: Sarcopenia, hospital, acute care, mortality

INTRODUCTION

The aging process is characterized by a progressive decline in skeletal muscle mass, resulting in loss of muscle strength and function, condition that has been referred to as sarcopenia (1). Sarcopenia is receiving an increasing interest in research and practice (2) due to its high prevalence, especially in nursing home or hospital setting (3), and its association with mobility impairment, disability, loss of independence, poor quality of life, hospitalization, and death (4). Furthermore, sarcopenia has been recently recognized as a specific disease entity, deserving its own ICD-10-CM code (M62.84) (5).

However, one of the major obstacles in both research and clinical practice is the lack of consensus regarding the diagnostic criteria and the methods used to assess such a condition. The most widely used definitions of sarcopenia are those proposed by the European Working Group on Sarcopenia in Older People (EWGSOP) (6) and the Foundation for the National Institutes of Health (FNIH) Sarcopenia Project (7). Despite handgrip strength and skeletal muscle mass are key features in all sarcopenia definitions, cut off values and techniques used to assess muscle mass and strength differ between definitions, resulting in a low concordance between FNIH and EWGSOP criteria (8) and, specifically, in a low positive percent agreement (PPA) where PPA was defined by Dam et al. as the proportion of participants who were categorized as having sarcopenia by both the FNIH criteria and EWGSOP divided by the number of participants who were categorized as having the condition by the second set of criteria (9). Recently, the European Working Group updated the original definition in order to incorporate the new insights collected on the condition over the last decade, and proposed a new operational definition of sarcopenia, the EWGSOP2 (10).

So far, no data are available on the agreement between the new EWGSOP2 and the FNIH sarcopenia definitions. Moreover, it is unclear whether the different sarcopenia definitions have similar associations with clinical outcomes, such as mortality. The primary objective of this report

was to investigate the agreement between EWGSOP2 and FNIH sarcopenia definitions in a sample of older patients admitted to 12 Geriatrics and Internal Medicine acute care wards in Italy, enrolled in the GLISTEN Study (11). Furthermore, we sought to compare the predictive value of both definitions towards 3-year mortality.

METHODS

Study Design and Data Collection

Data were obtained from the Gruppo di Lavoro Italiano Sarcopenia – Trattamento E Nutrizione (GLISTEN) project, a cohort study performed in Geriatric and Internal Medicine acute care wards of 12 Italian hospitals (Monza, Turin, Ferrara, Verona, Parma, Florence, Ancona, Rome, Napoli I, Napoli II, Cagliari, Messina). Methodology of the GLISTEN project has been described in detail elsewhere (11). Briefly, the study was designed to investigate the prevalence and clinical correlates of sarcopenia in older hospitalized patients in Italy and to estimate the incidence of sarcopenia during hospital stay. All study centers obtained ethical approval from their institutions; participants signed a written informed consent. All patients consecutively admitted to the participating wards from February 2014 and May 2014 were screened for enrollment. Exclusion criteria were age younger than 65 years and patient's unwillingness to take part in the study. All patients were assessed within 2 days since hospital admission and were followed until discharge. Participants' data were collected through a standardized dedicated questionnaire including demographic characteristics, self-report functional status, cognitive, and mood assessment; medication use; incident and prevalent medical conditions; and biochemical test results. Objective measures of muscle mass (bioimpedance analysis [BIA]) and physical performance (handgrip strength and 4-m usual walking speed) were obtained at hospital admission and before discharge. Survival status was recorded up to 36 months after hospital discharge. In this study, 45 of the original 655 enrollees were excluded because of some baseline missing data, leading to a final sample of 610 persons

(mean age 80.7 ± 6.6 years, male 48.7%). Mortality data were available in 527 participants, who were therefore included in survival analyses.

Assessment of Sarcopenia

According to EWGSOP2 (10) and FNIH criteria (12), sarcopenia was defined as presence of low muscle strength plus low muscle mass assessed at hospital admission.

Muscle strength was assessed by grip strength (GS), measured using a calibrated hand-held dynamometer (JAMAR hand dynamometer Model BK-7498, Fred Sammons Inc., Brookfield, IL). According to Southampton protocol (13), three trials for each hand were performed in sitting or supine position (14), and the highest value of the strongest hand was used in the analyses. GS values below 27 kg in men and 16 kg in women were considered as abnormal according to the EWGSOP2 consensus (15). The corresponding cut-offs for the FNIH criteria were 26 kg and 16 kg for men and women, respectively (16).

Muscle mass was measured by BIA using a Quantum/S Bioelectrical Body Composition Analyzer (Akern Srl, Florence, Italy). Whole-body BIA measurements were taken with standard four-pole technique between the right wrist and ankle with the subject in a supine position using a sinusoidal current at 50 kHz frequency. Appendicular Skeletal muscle Mass (ASM) was calculated using the following equation by Sergi and colleagues (17): $ASM (Kg) = -3.964 + (0.227 \times height^2/resistance) + (0.095 \times weight) + (1.384 \times sex) + (0.064 \times reactance)$ where height is measured in centimeters, resistance and reactance in ohms, weight in kilograms; for gender, men=1 and women=0. ASM was standardized by height squared ($ASM/height^2$) and Body Mass Index (ASM/BMI) as requested by EWGSOP2 and FNIH criteria, respectively. Low appendicular muscle mass was classified as $ASM/height^2$ less than 7.0 kg/m² in men and 5.5 kg/m² in women, in line with EWGSOP2 cut-off

points (18), and as a ASM/BMI ratio lower than 0.789 in men and 0.512 in women, according to FNIH (19).

Covariates

Sociodemographic variables (age, gender, smoking habits, education) were obtained through clinical interview at hospital admission. Cognitive functioning and functional status in six basic activities of daily living (ADL) were assessed as reported elsewhere (11). Severe ADL disability was defined as the presence of difficulty in three or more activities (20). Cognitive functioning was assessed using the Short Portable Mental Status Questionnaire (SPMSQ). The total number of errors on individual test's items was added to provide the SPMSQ score (one or two errors indicate normal cognitive status; 3–4 errors indicate mild; 5–7 errors indicate moderate; and 8–10 errors indicate severe cognitive impairment) (21). Diagnoses of specific medical conditions were gathered from the participant, the attending physicians, and medical charts review; comorbidity was assessed using the Charlson Comorbidity Index (22) by adding scores assigned to specific diagnoses. Assessors recorded all drugs currently taken by the participants on admission; number of drugs taken was also calculated.

Mortality

Mortality data of the original GLISTEN cohort were collected using data from the Mortality General Registry maintained by each Region. Time from the day of study enrollment to last follow up (date of death or April 26, 2017) was considered as temporal function in our study. No information on cause of death were collected.

Statistical analysis

Prevalence of sarcopenia was assessed using each algorithm; concordance between the two definitions was visually assessed with a mosaic plot of frequencies and quantitatively evaluated with Cohen's kappa coefficients. Kappa values, that is a measure of agreement corrected to take into account the amount of concordance due to chance, varies between 0 and 1 and can be interpreted as follows: 0-0.39 indicating minimal agreement, 0.40–0.59 as weak, 0.60–0.79 as moderate, ≥ 0.80 as strong agreement (23)

A combination definition was also considered (neither criterion positive, only EWGSOP2 criterion positive, only FNIH criterion positive, both criteria).

Baseline characteristics were compared across the sarcopenia groups. Continuous variables distribution was visually inspected through histograms and normal qq-plot. Continuous data with approximately normal distribution were described as mean \pm standard deviation and compared by t-test and one-way ANOVA. Median [interquartile range, IQR] and, accordingly, the Mann–Whitney U and Kruskal–Wallis tests, were used when the distribution deviated substantially from normal. Categorical variables were summarized in terms of percentages and were compared by using the Pearson's chi squared test or the Fisher's exact test, as appropriate.

Crude mortality rates were estimated, and Kaplan–Meier curves were fitted to explore survival probabilities. The log-rank test and Cox regression analysis were used to assess the effect of sarcopenia on 3-year mortality. Three Cox models were hierarchically fitted: unadjusted, age and gender adjusted, and adjusted for other potential confounders (i.e. age, gender, SPMSQ, severe ADL disability, Charlson Comorbidity Index).

All analyses were done using Stata version 13 (StataCorp, College Station, TX) and statistical significance was set at 0.05.

RESULTS

Participants' baseline characteristics

One hundred thirty-nine participants (22.8%) and 146 (23.9%) met EWGSOP2 and FNIH criteria, respectively. Baseline characteristics of participants according to the presence of sarcopenia, defined by each criterion separately, are presented in Table 1. Compared with participants without sarcopenia, those diagnosed with sarcopenia according to EWGSOP2 definition were significantly older ($p < 0.001$), had lower BMI ($p < 0.001$), greater prevalence of weight loss in the previous 6 months ($p < 0.001$) and severe ADL disability ($p = 0.032$). Using FNIH definition, no significant age difference was found between sarcopenic and the non-sarcopenic counterpart; sarcopenic participants had higher BMI ($p < 0.001$), greater prevalence of severe ADL disability ($p < 0.001$), diabetes ($p = 0.030$), chronic obstructive pulmonary disease ($p = 0.004$), higher number of errors at SPSMQ test ($p = 0.024$), higher Charlson Index score ($p = 0.031$) and a greater number of medications ($p = 0.045$).

Agreement between EWGSOP2 and FNIH definitions

Figure 1 shows agreement between the 2 sarcopenia definitions: out of the 220 participants who were classified as sarcopenic by at least one definition, agreement was obtained in only 65 (10.7%), whereas 12.1% were classified as sarcopenic by EWGSOP2 but not FNIH criterion and 13.3% as sarcopenic by FNIH but not EWGSOP2 criterion. Cohen's kappa coefficient was 0.29.

Compared to those deemed as non-sarcopenic by both definitions and those identified as sarcopenic by one but not the other, participants with agreement sarcopenia status were older, had greater prevalence of male, smokers and severe ADL disability (Table 2).

Predictive value of EWGSOP2 and FNIH definitions

During a median follow-up time of 30.1 months, 178 participants (33.8% of the 527 in whom survival status could be ascertained) died. As shown in Figures 2, participants with sarcopenia by

EWGSOP2 (2a) and FNIH (2b) definitions had higher mortality rate when compared with those without sarcopenia (log-rank test: $p < 0.001$ for both definitions). Participants with agreement on sarcopenia status (Figure 2c) had the shorter survival as compared with the other three groups.

Estimates derived from the Cox proportional hazard models (Table 3) showed that sarcopenic participants, regardless of the definition used, were more likely to die compared to non-sarcopenic individuals (model 1); nevertheless, after adjusting for potential confounders (model 3), the results were confirmed only for EWGSOP2 sarcopenic participants (HR 1.84; 95% C.I. 1.33-2.57). Furthermore, when the four-grouping variable was used, a similar significant mortality risk was found for the EWGSOP2 group and for the combined EWGSOP2/FNIH group (HR 2.08; 95% C.I. 1.38-3.16) and HR 1.75; 95% C.I. 1.11-2.79 respectively) compared to the NO EWGSOP2/NO FNIH group.

DISCUSSION

This study, performed in a cohort of older patients admitted to Geriatric and Internal Medicine acute care wards, showed that agreement between EWGSOP2 and FNIH definitions on the identification of sarcopenic patients is poor, therefore the two definitions cannot be used interchangeably. Both sarcopenia definitions were associated with increased 3-year mortality, although the EWGSOP2 seemed to have the best predictive value in terms of mortality.

Agreement between EWGSOP2 and FNIH definitions

Previous reports in which the original EWGSOP was compared to FNIH sarcopenia definition showed that the prevalence of such condition varied substantially when different diagnostic criteria were used (8, 9, 24). Agreement was not improved in our study, where sarcopenia prevalence was

similar among EWGSOP2 and FNIH definitions but, more importantly, the overlap between the two definitions was low (kappa statistics = 0.29).

EWGSOP2 and FNIH definitions have similar conceptual frameworks and both include measures of lean mass and strength. As previously explained by Dam and Colleagues (9), we believe that the lack of agreement between these two criteria is mainly explained by differences in the categorization of low muscle mass. On one hand, EWGSOP2 criteria recommend the utilization of ASM adjusted for height or ASM (12), on the other, FNIH criteria recommend to use ASM adjusted for BMI as first choice (10). As a result of that categorization, subjects identified as sarcopenic by EWGSOP2 criteria in the present study had lower average BMI, no case of obesity, higher prevalence of underweight (23.7%, data not shown), and higher rates of reported weight loss in the last 6 months, compared to those identified with FNIH criteria. Conversely, sarcopenic patients according to FNIH definition were characterized by high prevalence of obesity (31%, data not shown) and diabetes, with a negligible prevalence of underweight (2.7%, data not shown). As already commented, FNIH criteria seems to identify participants that, despite having high lean mass and high BMI, are functionally more impaired because are unable to generate enough muscular strength relative to their body mass (condition conceptualized as sarcopenic obesity) (9). EWGSOP2, as well as EWGSOP criteria, instead, seem to catch malnourished patients and, possibly, might include cachectic patients as previously investigated in the same sample (11).

Predictive value of EWGSOP2 and FNIH definitions

Previous prospective studies have evaluated the validity of the original EWGSOP and FNIH criteria for predicting mortality in several settings (4, 25-27), including acute care wards (24, 28). Only one recent report, instead, has examined the predictive value of the new EWGSOP2 sarcopenia definition in terms of mortality in a group of community-dwelling older persons (29). In all these cohorts, sarcopenia was associated with a high risk of all-cause mortality. Our study confirmed the

association between FNIH sarcopenia definition and mortality, and, for the first time, recognized the predictive value of the EWGSOP2 criteria applied in a hospital setting.

Cox regression analyses showed that sarcopenia, according to both definitions, represents an independent risk factor for mortality, even though statistical significance was reduced for FNIH definition after adjusting for comorbidity, cognitive status and disability. Furthermore, when the two definitions were combined, generating a four-group variable, only EWGSOP2 and EWGSOP2/FNIH combined group showed a significant independent risk of mortality. Although generalization of these findings should obviously be done with caution given the relatively small number of patients, our results suggest that EWGSOP2 might predict mortality better than FNIH definition in acutely hospitalized sarcopenic patients. However, the main finding that should be highlighted is that using each definition, we lost a share of sarcopenic subjects that are at increased risk mortality.

Clinical research has to progress in order to overcoming the discrepancy between sarcopenia definitions, and our study strongly supports the need not only of reaching general consensus in the criteria and cut-off values for sarcopenia to enable a comparison between studies, but, above all, to identify all the individuals at risk of complication related to sarcopenia.

Strength and limitations

Our study has several strengths. It is a large, multicenter, prospective cohort study involving Geriatric and Internal Medicine hospital units, thus providing easily generalizable information from the “real-world”. Second, we explored the association between sarcopenia and mortality, which has been rarely investigated in a hospital setting. Third, this is the first study that investigated the predictive value of EWGSOP2 sarcopenia definition and compared EWGSOP2 and FNIH criteria in a hospital setting: thus, our results are of current interest for researchers and major relevance for clinicians.

Nevertheless, in interpreting these findings, some limitations should be considered. First, we estimated appendicular muscle mass by BIA using Sergi equation instead of dual energy X-ray absorptiometry (DEXA), the technique that is recognized as the gold standard for the assessment of muscle mass. BIA measures are affected by the hydration status of patients, which admittedly change very rapidly in geriatric patients; nevertheless, this technique is inexpensive, easy to use, readily reproducible, and appropriate for bedridden patients, being therefore considered as an acceptable alternative to DEXA in a hospital setting (30).

Second, as previously described (11), the assessment of sarcopenia in acutely ill older patients might be affected by a transient impairment in muscle strength, unrelated to sarcopenia, but due to the systemic effect of the acute disease responsible for hospital admission, leading to a potential overestimation of the condition. Third, we cannot exclude that the association between sarcopenia and mortality is related to residual confounding, because data on some potential confounders (including admission diagnoses) were not collected. Fourth, this study was conducted on a cohort of hospitalized older people, therefore generalization of results to community dwelling or institutionalized older people is not possible. In this regard, further researches are needed to confirm the association between the two sarcopenia's phenotypes and mortality in these populations.

Finally, the evaluation of the prognostic utility of sarcopenia definition should include additional important clinical endpoints, including functional status and disability, not assessed in our work.

In summary, in this sample of Italian hospitalized geriatric patients, the agreement between EWGSOP2 and FNIH definitions was low, suggesting that these criteria cannot be used interchangeably. Diagnosis of sarcopenia on hospital admission was associated with increased risk of 3-year mortality and EWGSOP2 criteria seemed to have the best predictive value in terms of mortality. Future research is needed to examine consistency of sarcopenia definitions and their clinical implications, and to overcome the discrepancy between current diagnostic criteria, in order to identify all the individuals at risk for complications related to sarcopenia.

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Conflicts of interest

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References

1. Rosenberg IH. Sarcopenia: origins and clinical relevance. *J Nutr.* 1997;127:990S-991S.
2. Beudart C, McCloskey E, Bruyere O, *et al.* Sarcopenia in daily practice: assessment and management. *BMC Geriatr.* 2016;16:170. DOI: 10.1186/s12877-016-0349-4.
3. Cruz-Jentoft AJ, Landi F, Schneider SM, *et al.* Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age Ageing.* 2014;43:748-759. DOI: 10.1093/ageing/afu115.
4. Bianchi L, Ferrucci L, Cherubini A, *et al.* The Predictive Value of the EWGSOP Definition of Sarcopenia: Results From the InCHIANTI Study. *J Gerontol A Biol Sci Med Sci.* 2016;71:259-264. DOI: 10.1093/gerona/glv129.
5. Anker SD, Morley JE, von Haehling S. Welcome to the ICD-10 code for sarcopenia. *J Cachexia Sarcopenia Muscle.* 2016;7:512-514. DOI: 10.1002/jcsm.12147.
6. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, *et al.* Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing.* 2010;39:412-423. DOI: 10.1093/ageing/afq034.
7. Studenski SA, Peters KW, Alley DE, *et al.* The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. *J Gerontol A Biol Sci Med Sci.* 2014;69:547-558. DOI: 10.1093/gerona/glu010.
8. Boetto E, Bianchi L, Andolfo FM, Maietti E, Volpato S. Prevalence and clinical correlates of sarcopenia in institutionalized older people: cross-sectional study of a nursing home population. *Journal of Gerontology and Geriatrics.* 2019;67:32-38.
9. Dam TT, Peters KW, Fragala M, *et al.* An evidence-based comparison of operational criteria for the presence of sarcopenia. *J Gerontol A Biol Sci Med Sci.* 2014;69:584-590. DOI: 10.1093/gerona/glu013.

10. Cruz-Jentoft AJ, Bahat G, Bauer J, *et al.* Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2018. DOI: 10.1093/ageing/afy169.
11. Bianchi L, Abete P, Bellelli G, *et al.* Prevalence and Clinical Correlates of Sarcopenia, Identified According to the EWGSOP Definition and Diagnostic Algorithm, in Hospitalized Older People: The GLISTEN Study. *J Gerontol A Biol Sci Med Sci*. 2017;72:1575-1581. DOI: 10.1093/gerona/glw343.
12. Correa-de-Araujo R, Hadley E. Skeletal muscle function deficit: a new terminology to embrace the evolving concepts of sarcopenia and age-related muscle dysfunction. *J Gerontol A Biol Sci Med Sci*. 2014;69:591-594. DOI: 10.1093/gerona/glt208.
13. Roberts HC, Denison HJ, Martin HJ, *et al.* A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. *Age Ageing*. 2011;40:423-429. DOI: 10.1093/ageing/afr051.
14. Govoni B MG, Maietti E, *et al.* Hand grip strength assessment in older people: is the supine position valid and reliable? *European Geriatric Medicine*. 2019. DOI: 10.1007/s41999-019-00226-9.
15. Dodds RM, Syddall HE, Cooper R, *et al.* Grip strength across the life course: normative data from twelve British studies. *PLoS One*. 2014;9:e113637. DOI: 10.1371/journal.pone.0113637.
16. Alley DE, Shardell MD, Peters KW, *et al.* Grip strength cutpoints for the identification of clinically relevant weakness. *J Gerontol A Biol Sci Med Sci*. 2014;69:559-566. DOI: 10.1093/gerona/glu011.
17. Sergi G, De Rui M, Veronese N, *et al.* Assessing appendicular skeletal muscle mass with bioelectrical impedance analysis in free-living Caucasian older adults. *Clin Nutr*. 2015;34:667-673. DOI: 10.1016/j.clnu.2014.07.010.
18. Gould H, Brennan SL, Kotowicz MA, Nicholson GC, Pasco JA. Total and appendicular lean mass reference ranges for Australian men and women: the Geelong osteoporosis study. *Calcif Tissue Int*. 2014;94:363-372. DOI: 10.1007/s00223-013-9830-7.

19. Cawthon PM, Peters KW, Shardell MD, *et al.* Cutpoints for low appendicular lean mass that identify older adults with clinically significant weakness. *J Gerontol A Biol Sci Med Sci.* 2014;69:567-575. DOI: 10.1093/gerona/glu023.
20. Ferrucci L, Guralnik JM, Pahor M, Corti MC, Havlik RJ. Hospital diagnoses, Medicare charges, and nursing home admissions in the year when older persons become severely disabled. *JAMA.* 1997;277:728-734.
21. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *J Am Geriatr Soc.* 1975;23:433-441.
22. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol.* 1992;45:613-619.
23. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med (Zagreb).* 2012;22:276-282.
24. Sipers W, de Blois W, Schols J, van Loon LJC, Verdijk LB. Sarcopenia Is Related to Mortality in the Acutely Hospitalized Geriatric Patient. *J Nutr Health Aging.* 2019;23:128-137. DOI: 10.1007/s12603-018-1134-1.
25. Hirani V, Blyth F, Naganathan V, *et al.* Sarcopenia Is Associated With Incident Disability, Institutionalization, and Mortality in Community-Dwelling Older Men: The Concord Health and Ageing in Men Project. *J Am Med Dir Assoc.* 2015;16:607-613. DOI: 10.1016/j.jamda.2015.02.006.
26. De Buyser SL, Petrovic M, Taes YE, *et al.* Validation of the FNIH sarcopenia criteria and SOF frailty index as predictors of long-term mortality in ambulatory older men. *Age Ageing.* 2016;45:602-608. DOI: 10.1093/ageing/afw071.
27. Beaudart C, Zaaria M, Pasleau F, Reginster JY, Bruyere O. Health Outcomes of Sarcopenia: A Systematic Review and Meta-Analysis. *PLoS One.* 2017;12:e0169548. DOI: 10.1371/journal.pone.0169548.

28. Vetrano DL, Landi F, Volpato S, *et al.* Association of sarcopenia with short- and long-term mortality in older adults admitted to acute care wards: results from the CRIME study. *J Gerontol A Biol Sci Med Sci.* 2014;69:1154-1161. DOI: 10.1093/gerona/glu034.
29. Locquet M, Beaudart C, Petermans J, Reginster JY, Bruyere O. EWGSOP2 Versus EWGSOP1: Impact on the Prevalence of Sarcopenia and Its Major Health Consequences. *J Am Med Dir Assoc.* 2019;20:384-385. DOI: 10.1016/j.jamda.2018.11.027.
30. Wang JG, Zhang Y, Chen HE, *et al.* Comparison of two bioelectrical impedance analysis devices with dual energy X-ray absorptiometry and magnetic resonance imaging in the estimation of body composition. *J Strength Cond Res.* 2013;27:236-243. DOI: 10.1519/JSC.0b013e31824f2040.

Table 1. Selected general characteristics of study participants according to definition and presence of sarcopenia

	EWGSOP2			FNIH		
	No Sarcopenia	Sarcopenia	<i>p</i>	No Sarcopenia	Sarcopenia	<i>p</i>
N (%)	471 (77.2)	139 (22.8)		464 (76.1)	146 (23.9)	
Age, mean \pm SD	80.2 \pm 6.5	82.4 \pm 6.8	<.001	80.6 \pm 6.5	80.9 \pm 6.9	.627
Male sex (%)	44.2	64.0	<.001	42.9	67.1	<.001
BMI, mean \pm SD	27.6 \pm 4.9	22.5 \pm 3.1	<.001	25.8 \pm 4.8	28.2 \pm 5.4	<.001
Weight loss (%)	39.2	56.1	<.001	43.1	43.1	.987
Smokers (former/current) (%)	45.5	54.0	.079	44.3	57.3	.006
Education (years), median [IQR]	5 [5, 8]	5 [5, 8]	.477	5 [5, 8]	5 [5, 8]	.195
Severe ADL disability (%)	21.4	30.2	.032	20.0	34.2	<.001
SPMSQ, median [IQR]	2 [1, 3]	2 [1, 4]	.068	2 [1, 4]	2 [1, 4]	.024
Hypertension (%)	77.1	71.2	.158	75.0	78.1	.449
Congestive heart failure (%)	16.4	19.4	.397	16.8	17.8	.780
Coronary heart disease (%)	25.5	30.9	.206	27.2	25.3	.656
Diabetes (%)	30.8	23.7	.108	26.9	36.3	.030

COPD, n (%)	26.5	26.6	.985	23.7	35.6	.004
Osteoporosis, n (%)	14.9	21.6	.060	16.8	15.1	.200
Chronic kidney disease, n (%)	21.9	23.7	.641	22.2	22.6	.918
Charlson Comorbidity Index, median [IQR]	3 [1, 5]	3 [2, 5]	.517	3 [1, 4]	3 [2, 5]	.031
Number of drugs, mean \pm SD	6.1 \pm 2.9	6.1 \pm 2.7	.837	5.9 \pm 2.9	6.5 \pm 2.7	.045

Notes. EWGSOP2= European Working Group on Sarcopenia in Older People 2; FNIH= Foundation for the National Institutes of Health; p = p-value; SD= standard deviation; BMI= Body Mass Index; ADL= Activities of Daily Living; SPMSQ= Short Portable Mental Status Questionnaire; IQR= interquartile range; COPD= chronic obstructive pulmonary disease; p-values refer to: t-test for age, BMI and number of drugs, Wilcoxon-Mann-Whitney for SPMSQ, education and Charlson Comorbidity Index, Chi-squared test for categorical variables.

Table 2. Selected general characteristics of study participants according to four sarcopenia groups

	Sarcopenia				<i>p</i>
	EWGSOP2	NO	YES	NO	
	FNIH	NO	NO	YES	
N (%)		390 (63.9)	74 (12.1)	81 (13.3)	65 (10.7)
Age, mean \pm SD		80.4 \pm 6.4	81.8 \pm 7.0	79.2 \pm 6.7	83.1 \pm 6.6
Male sex (%)		40.8	54.1	60.5	75.4
BMI, mean \pm SD		26.7 \pm 4.5	21.1 \pm 2.8	31.6 \pm 4.6	24.0 \pm 2.8
Weight loss (%)		39.7	60.8	37.0	50.8
Smokers (former/current) (%)		43.8	47.3	53.8	61.9
Education (years), median [IQR]		5 [5, 8]	5 [5, 8]	5 [4, 8]	5 [5, 8]
Severe ADL disability (%)		20.0	20.3	28.4	41.5
SPMSQ, median [IQR]		2 [1, 3]	2 [1, 4]	2 [1, 4]	2 [1, 5]
Hypertension (%)		75.6	71.6	84.0	70.8
Congestive heart failure (%)		16.7	17.6	14.8	21.5
Coronary heart disease (%)		25.7	35.1	24.7	26.2
Diabetes (%)		28.2	20.3	43.2	27.7
COPD, n (%)		24.4	20.3	37.0	33.9

Osteoporosis, n (%)	15.4	24.3	12.4	18.5	.183
Chronic kidney disease, n (%)	21.8	24.3	22.2	23.1	.968
Charlson Comorbidity Index, median [IQR]	3 [1, 4]	3 [2, 4]	3 [2, 5]	3 [1, 4]	.164
Number of drugs, mean \pm SD	5.9 \pm 2.9	5.9 \pm 2.8	6.7 \pm 2.9	6.3 \pm 2.6	.198

Notes. EWGSOP2= European Working Group on Sarcopenia in Older People 2; FNIH= Foundation for the National Institutes of Health; p = p-value; SD= standard deviation; BMI= Body Mass Index; ADL= Activities of Daily Living; SPMSQ= Short Portable Mental Status Questionnaire; IQR= interquartile range; COPD= chronic obstructive pulmonary disease; p-values refer to: ANOVA for age and number of drugs, Kruskal Wallis for BMI, SPMSQ, education and Charlson Comorbidity Index, Chi-squared test for categorical variables.

Table 3. Association between Each Sarcopenia definition and Mortality According to Cox Regression Models Adjusted for Potential Confounders

		Model 1	Model 2	Model 3
Mortality Rate				
100 person-year		HR	HR	HR
		(95% CI)	(95% CI)	(95% CI)
EWGSOP2				
No sarcopenia	12.9	1	1	1
		-	-	-
Sarcopenia	29.9	2.24	1.87	1.84
		(1.64-3.07)	(1.35-2.59)	(1.33-2.57)
FNIH				
No sarcopenia	14.0	1	1	1
		-	-	-
Sarcopenia	23.8	1.66	1.54	1.26
		(1.20-2.30)	(1.11-2.15)	(0.89-1.79)
Combined sarcopenia definition				
NO EWGSOP2/ NO FNIH	11.9	1	1	1
		-	-	-

YES EWGSOP2/ NO FNIH	28.5	2.33 (1.56-3.48)	1.98 (1.32-2.99)	2.08 (1.38-3.16)
NO EWGSOP2/ YES FNIH	18.7	1.55 (1.00-2.41)	1.56 (1.00-2.44)	1.25 (0.79-1.98)
YES EWGSOP2/ YES FNIH	31.8	2.55 (1.66-3.92)	2.11 (1.34-3.29)	1.75 (1.11-2.79)

Notes. . EWGSOP2= European Working Group on Sarcopenia in Older People 2; FNIH= Foundation for the National Institutes of Health; Model 1= unadjusted; Model 2= age and gender adjusted; Model 3= adjusted for age, gender, Short Portable Mental Status Questionnaire, severe Activities of Daily Living disability, Charlson Comorbidity Index; HR= Hazard Ratio; CI= confidence interval

Figure legends

Figure 1. Agreement between EWGSOP2 and FNIH definitions

Figure 2. Kaplan-Meier survival estimates according to sarcopenia definitions

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Figure 1

		No	Yes
FNIH	No	390 (63.9%)	74 (12.1%)
	Yes	81 (13.3%)	65 (10.7%)
		EWGSOP2	

Figure 2

