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Consequences of applying the new EWGSOP2 guideline instead of the former EWGSOP guideline for sarcopenia case finding in older patients

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Abstract

Introduction: we examined the consequences of applying the new EWGSOP2 algorithm for sarcopenia screening instead of the former EWGSOP algorithm (EWGSOP1) in geriatric inpatients.
Methods: the dataset of our formerly published Sarcopenia in Geriatric Elderly (SAGE) study includes 144 geriatric inpatients (86 women, 58 men, mean age 80.7±5.6 years) with measurements of gait speed, handgrip strength and appendicular muscle mass by dual x-ray absorptiometry (DXA). We analysed the agreement between EWGSOP and EWGSOP2 algorithms in identifying patients as sarcopenic/non-sarcopenic. Differences in the distribution sarcopenic vs. non-sarcopenic were assessed by Chi²-test.
Results: sarcopenia prevalence according to EWGSOP1 (41 (27.7%)) was significantly higher than with EWGSOP2 (26(18.1%), $p<0.05$). The sex-specific sarcopenia prevalence was 22.1% (EWGSOP1) and 17.4% (EWGSOP2), respectively, for women (difference not significant) and 37.9% vs. 19.4% for men ($p<0.05$%). The overall agreement in classifying

subjects as sarcopenic/non-sarcopenic was 81.25% (81.4% for women, 81.0% for men). However, among the 41 sarcopenia cases identified by EWGSOP1, only 20 (48.8%) were diagnosed with sarcopenia by EWGSOP2 (9/19 w (47.4%), 11/22 m (50.0%)). Ten of 19 women (52.6%) and 11 of 22 men (50.0%) diagnosed with sarcopenia by EWGSOP1 were missed by EWGSOP2, while 6 of 15 women (40.0%) and 0 of 11 men (0.0%) were newly diagnosed.
Discussion: there is a substantial mismatch in sarcopenia case finding according to EWGSOP1 and EWGSOP2. The overall prevalence and the number of men diagnosed with sarcopenia are significantly lower in EWGSOP2. While the absolute number of women identified as sarcopenic remains relatively constant, the overlap of individual cases between the two definitions is low.

Keywords

sarcopenia, case finding, EWGSOP, EWGSOP2, older people

Key points

- The sarcopenia definition of the European Working Group on Sarcopenia in Older People (EWGSOP) is the most frequently used in research as well as the clinical setting.
- The EWGSOP2 algorithm yielded lower sensitivity but more specificity for sarcopenia case finding in older hospitalised patients.
- Concordance rates of individual cases were low between EWGSOP1 and EWGSOP2.
- Unlike EWGSOP1, EWGSOP2 defined sarcopenia did not show a significant association with malnutrition and disability.

Editor's Note: *Since this paper was accepted for publication, we have received a correction to the EWGSOP2 sarcopenia guideline, changing the cut-off point defining an abnormal for appendicular skeletal muscle (ASM) for women. This has been reviewed by the authors, who do not believe it changes the conclusion of their paper.*

Introduction

Since Irwin Rosenberg coined the term sarcopenia in 1989 [1], there has been ongoing debate on the best operational definition for sarcopenia [2]. While the early definitions [3, 4] focused on muscle mass alone, it became increasingly clear that muscle strength is more important in terms of clinical outcomes than sheer quantity [5]. Consequently, Clark and Manini suggested the term dynapenia to set more focus on muscle function [6]. Concurrently, the metabolic role of muscle beyond locomotion became increasingly evident [7]. Maintaining muscle mass is important for glucose and protein storage and to counteract low grade inflammation due to excess visceral fat leading to sarcopenic obesity [8].

Thus, the newer definitions of sarcopenia from 2010 onwards included both muscle mass and function with gait speed and grip strength as the primordial functional parameters [survey in [9]]. Today, the definition of The European Working Group on Sarcopenia in Older People (EWGSOP) [10] is the most frequently used in research as well as the clinical setting. The clinical relevance of EGSWOP-defined sarcopenia in regard to relevant outcomes like functional decline and mortality is well established [11].

In September 2018, thw EWGSOP published a revised version of this guideline (known as EWGSOP2), which introduced fundamental changes both conceptually and regarding the diagnostic algorithm [12]. Briefly, sarcopenia is hereafter classified as a disease ('muscle failure', ICD-10-CM M62.84) and no longer a geriatric syndrome. The primordial role of gait speed in diagnosing sarcopenia has been reduced to discriminating severe from less severe sarcopenia while cut-offs for hand grip strength and muscle mass where reset [12]. These changes likely will affect case finding in clinical practice.

The aim of our study was to examine the impact of choosing the former (here called EWGSOP1) or the recent diagnostic guideline (EWGSOP2) for sarcopenia case finding in a geriatric care unit. What is the level of agreement in classifying individual subjects as sarcopenic/non-sarcopenic? Is there a difference in sarcopenia prevalence between the two methods? Are both types of sarcopenia equally associated with comorbidity (osteoporosis), functionality (Barthel index) and nutritional state (mini nutritional assessment (MNA))?

We tried to answer these questions by retrospectively applying both algorithms to the population of the SAGE study, [13] which focused on issues of measurement accuracy in determining muscle mass. The study provided a sample of 144 geriatric inpatients with dual X-ray absorptiometry (DXA) measurements of muscle mass as well as hand grip strength, gait speed and some additional functional and nutritive parameters.

Methods

The study design of the SAGE study was described elsewhere [13, 14]. Briefly, between 2013 and 2017 144 geriatric

inpatients were recruited at the department of geriatric medicine, Paracelsus Medical University Salzburg. The lower age limit was 70 years. Exclusion criteria were critical or terminal illness, advanced dementia or delirium, complete or partial amputation of one or more limbs and indwelling electrical devices such as pacemakers (the latter because bioimpedance analysis in comparison to DXA was part of the study protocol) [13]. All patients gave written informed consent. The study was approved by the local ethics committee of the state of Salzburg and performed in accordance with the Declaration of Helsinki.

Gait speed was measured over a distance of 5 m. Hand grip strength was determined by using a dynamometer (JAMAR hydraulic hand dynamometer). Low gait speed was defined by ≤0.8 m/s. Low hand grip strength was defined according to EWGSOP1 [10] as <30 kg for men and <20 kg for women and according to EWGSOP2 [12] as <27 kg and <16 kg, respectively.

The Hologic Discovery A was used for all DXA scans. For the EWGSOP1 algorithm, we applied appendicular skeletal muscle mass (ASMM) adjusted for height2 using the DXA based thresholds established by Baumgartner [15]: ASMMI $< 5.5\ kg/m^2$ for women and $<7.26\ kg/m^2$ for men. The cut offs refer to 2 standard deviations below the mean of a young reference population (non-Hispanic white men and women aged 18–40 years) participating in the Rosetta Study [3]. For EWGSOP2 cut-offs were set at ASMMI $< 6\ kg/m^2$ for women and $<7\ kg/m^2$ for men [15]. Diagnosis of osteoporosis was made according to the WHO definition [16]. BMD measurements were performed at three sites in the same session and with same DXA device (see above): lumbar spine (L2-L4), total hip and femoral neck. A T-score of ≤−2.5 standard deviation (SD) at any location was considered diagnostic of osteoporosis.

Statistical analysis was performed with SPSS 24. Descriptive variables are presented as mean ± standard deviation (±SD). Significance of differences between EWGSOP1 and EWGSOP2 were determined by Mann Whitney *U* test for not normally distributed parameters (Barthel index, MNA) and chi-square test for contingency tables. A *P*-value < 0.05 was considered significant.

Results

Properties of the study sample and baseline characteristics have been described elsewhere [13, 14]. Briefly, the study population consisted of 144 geriatric inpatients (86 women, 58 men) with a mean age of 80.7 ± 5.6 years.

The number of DXA measurements needed to find one sarcopenia case was higher for EWGSOP1 (2.80) than for EWGSOP2 (1.65, $P = 0.005$). The screening algorithms´ sensitivity and specificity (Sens, Spec), positive and negative predictive value (PPV, NPV) for predicting low muscle mass were (EWGSOP1, EWGSOP2): Sens 83.7% vs. 41.9%, Spec 22.1% vs. 79.3%, PPV 35.7% vs. 60.5%, NPV 72.4% vs. 64.4%.

Figure 1 shows the case finding process following the two different algorithms step by step. Sarcopenia prevalence according to the EWGSOP1 algorithm ($n = 41$, 27.7%) was significantly higher than with EWGSOP2 ($n = 26$, 18.1%, $P < 0.05$). The sex specific sarcopenia prevalence was 22.1% (EWGSOP1) and 17.4% (EWGSOP2) respectively for women (difference not significant) and 37.9% vs. 19.4% for men ($P < 0.05$%). There was a significant

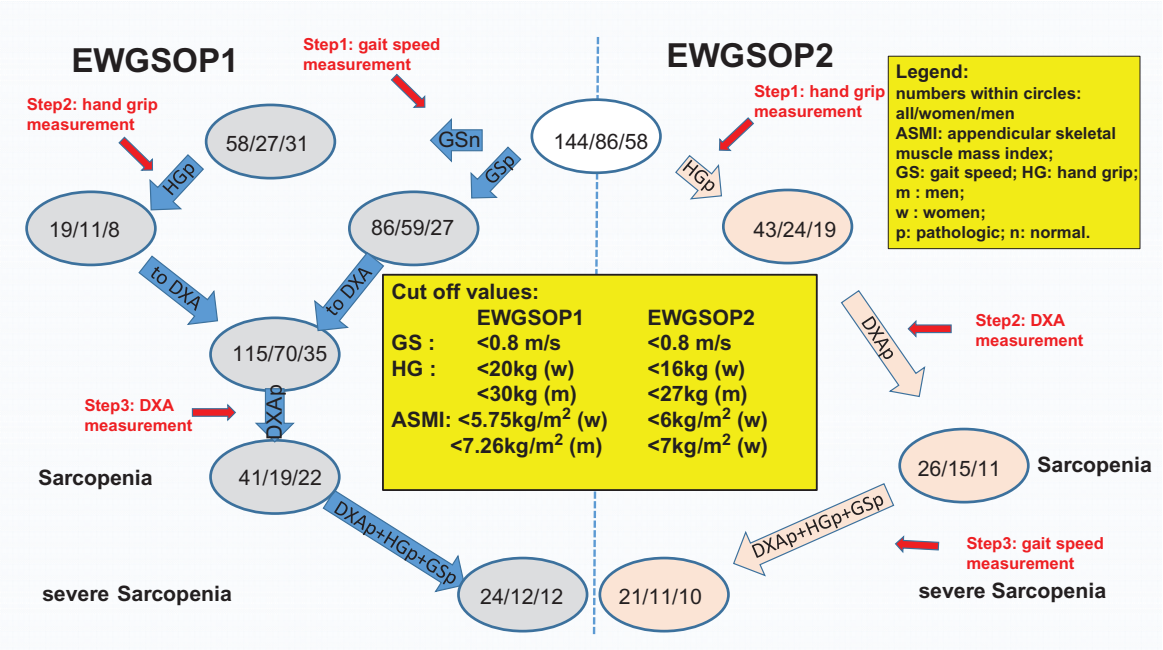

Figure 1 Sarcopenia case finding according to EWGSOP1 and EWGSOP 2.

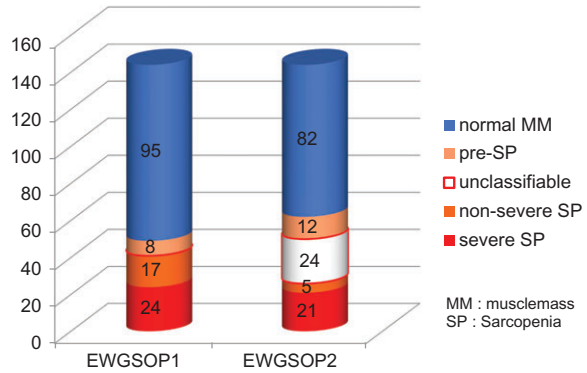

Figure 2 Conceptual stages of sarcopenia. Note that in EWGSOP2 24 subjects with normal hand grip but pathologic gait speed couldn't be ascribed to one conceptual stage of sarcpenia (white with red frame).

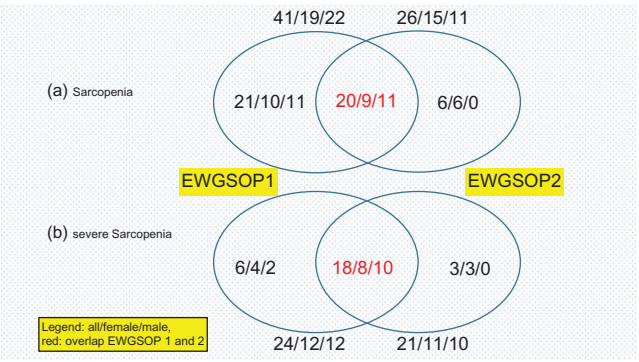

Figure 3 Concordance of individual cases identified by EWGSOP1 and EWGSOP 2.

difference in gender specific sarcopenia prevalence in EWGSOP1 ($P < 0.05$) but not in EWGSOP2 ($P = 0.816$).

When applying the conceptual stages of sarcopenia from the original EWGSOP paper [9], there were 8 (EWGSOP1) and 12 (EWGSOP2) subjects respectively with normal functional tests and decreased muscle mass (corresponding to the conceptual stage of presarcopenia from first EWGSOP paper, Figure 2). The overall agreement in classifying subjects as sarcopenic/non-sarcopenic was 81.25% (81.4% for women, 81.0% for men). Yet, only 20 of the 41 sarcopenia cases identified by EWGSOP1 (48.8%) were diagnosed with sarcopenia by EWGSOP2. 10 of 19 women (52.6%) and 11 of 22 men (50.0%) diagnosed with sarcopenia by EWGSOP1 were missed by EWGSOP2, while 6 of 15 women (40.0%) and 0 of 11 men (0.0%) were newly diagnosed (Figure 3a).

Regarding severe sarcopenia, 24 vs. 21 cases were identified using EWGSOP1 and two criteria, respectively. There was important overlap: 18 subjects were classified severely sarcopenic by both definitions (Figure 3b). The percentage of severe sarcopenic among sarcopenic subjects was 58.8% by EWGSOP1 and 80.8% by EWGSOP2.

Both definitions showed a significant difference in absolute values of MNA-SF (EWGSOP1: 9.39 + 2.42 vs. 11.15 + 2.10, $P < 0.001$; EWGSOP2:9.46 + 2.41 vs. 10.91 + 2.24, $P < 0.01$) and Barthel index (EWGSOP1:63.29 ± 21.14 vs. 72.52 + 20.16, $P < 0.05$; EWGSOP2:60.96 + 24.30 vs. 10.91 + 2.24, $P < 0.05$) between sarcopenic and non-sarcopenic subjects (Mann–Whitney *U*-test). However, when using thresholds for diagnosis of malnutrition (MNA < 17) and ADL-dependency (Barthel index < 70), these conditions were associated with sarcopenia ($P < 0.05$) by EWGSOP1, but not by EWGSOP2 criteria (Chi^2-test). Both definitions yielded a significant association of sarcopenia and osteoporosis ($P < 0.01$).

Discussion

The lower number of DXA measurements needed to detect a case of sarcopenia with the EWGSOP2 algorithm presents an advantage in terms of availability and costs. Yet, the EWGSOP2 algorithm yields fewer cases, mainly by identifying fewer men as sarcopenic. The lower prevalence rate for men (prevalence dropped by 50%) was foreseeable given that both hand grip and DXA threshold have been lowered in the new guideline. In women, where the hand grip limit was lowered while the muscle mass limit was heightened, there was no significant effect on prevalence (22.1% EWGSOP1, 17.4% EWGSOP2). There was no gender difference in sarcopenia prevalence by EWGSOP2, while prevalence among males was significantly higher by EWGSOP1. The latter is consistent with the findings of Gariballa *et al.* who also described higher sarcopenia prevalence in male than female acute hospital patients [17]. Prevalence rates for both models were within the (wide) range of published data for older people in different settings (11-50% according to Morley [18], 1-33% according to the ISI [19]). Compared to our 27.7% (EWGSOP1) and 18.1% (EWGSOP2), Martone *et al.* [20] found a 34.7% (EWGSOP1) prevalence of sarcopenia at hospital admission among 655 acute care patients. While mean age (81 years) was substantially the same as in our study, the higher sarcopenia prevalence found by Martone could be explained by different methology, cut-offs and the inclusion of patients from both acute internal medicine and geriatric wards.

The high sensitivity and low specificity of the EWGSOP1 algorithm in our population are contrary to the findings of Locquet *et al.* in a cohort of 306 healthy community dwelling older people [21], implying that the EWGSOP1 screening algorithm performs differently in different populations. As with frailty, it might be appropriate to use different tools for different purposes in the future [22]. In our study, the functional testing according to EWGSOP2 yields lower sensitivity and higher specificity for low muscle mass than following the EWGSOP1 algorithm. Thus, given that the EWGSOP follow up-paper states that sarcopenia is underdiagnosed and undertreated [12], the EWGSOP2 algorithm might not be suitable as a case finding instrument in high prevalence settings like nursing homes or hospitals [19].

Noteworthy, the new algorithm doesn't fit with the conceptual stages of sarcopenia published in the first EWGSOP guideline [9], because the subgroup of patients with decreased muscle mass, normal hand grip and low gait speed is sarcopenic according to the concept but not according to the EWGSOP2 algorithm. It seems problematic to miss out on this subgroup that represented 16.7% of our study population (Figure 2), while recent guidelines [12, 23] point out, that with regard to the potential reversibility of early stages, intervention should take place earlier.

There was substantial mismatch concerning the individuals identified as sarcopenic dependent on the applied algorithm. While this appears less of a concern in epidemiologic issues, it clearly matters in the clinical setting. Poor concordance rates between different diagnostic tools for sarcopenia have been described previously [24, 25] presenting a problem in clinical decision making and hampering comparability of scientific evidence. The huge impact of the sarcopenia definition employed on the prediction of clinical outcomes has been exemplarily demonstrated by Bischoff-Ferrari [26]. The causative link established for EWGSOP1 sarcopenia to multiple clinical outcomes [11] can´t be taken for given in EWGSOP2-defined collectives without further validation.

The overlap of identified cases of severe sarcopenia was, however, important with 18 subjects (out of 21 and 24 respectively) matching both definitions. This suggests that the most compromised subjects are reliably detected by both concepts. However, a prevalence of > 80% of severe sarcopenia among those classified as sarcopenic by EWGSOP2 makes the distinction between less and more severe cases questionable.

Both definitions displayed a striking association between sarcopenia and osteoporosis. This is in line with the growing body of evidence on muscle-bone interactions [27]. The association of malnutrition [28, 29] and functional decline [14, 29] with sarcopenia is also well established. Both the EWGSOP1 and EWGSOP2 sarcopenics had lower MNA-SF and Barthel index, but only the former had a significantly higher percentage of individuals classified as malnourished and ADL-dependent.

The strength of the study is to examine the consequences of the guidelines shift not in terms of epidemiological or prospective research considerations but in the clinical setting, where individual treatment decisions are based on the case finding process. This is especially relevant with regard to the 'call to action' included in the EWGSOP2 paper soliciting a broad clinical application of the concept. The limitations of this approach are also evident: our study collective is representative of inpatients of a geriatric clinic in central Europe and does not permit any conclusions about the performance of EWGSOP2 in other settings. It was a retrospective monocentric study relying on a preexisting dataset, that could not be adapted to the purpose of this study. Thus, it was not possible to include a pre-screening with the SARC-F tool [30]. The sample size is small and allows only for building hypotheses regarding the impact of the new definition to be confirmed in later prospective studies.

Conclusion

In the clinical setting, EWGSOP2 might present an advantage in cost effectiveness, because fewer DXA measurements are needed to establish a case of sarcopenia. Sensitivity, however, seems lower with the new algorithm, especially in men. In a clinical sample of geriatric inpatients the concordance rate for diagnosing individuals diagnosed with sarcopenia is low. To what extent the new algorithm is better at identifying patients with adverse outcomes and prone to intervention remains to be established.

Postscript: The correction of the appendicular muscle mass index threshold for women extinguishes the 6 newly found cases of sarcopenia according to EWGSOP2 and reduces the number of women diagnosed with sarcopenia to 9/86 (10.5%). While this improves classification agreement between EWGSOP1 and 2 in women to 88.4%, it makes case finding by the new definition even more restrictive.

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