New versus old guidelines for sarcopenia classification: What is the impact on prevalence and health outcomes?

Fanny Petermann-Rocha[1,2], Minghao Chen[2], Stuart R Gray[2], Frederick K Ho[1†], Jill P Pell[1†] and Carlos Celis-Morales[2†]

[1]Institute of Health and Wellbeing, University of Glasgow, Glasgow, G12 8RZ, UK.

[2]British Heart Foundation Glasgow Cardiovascular Research Centre, Institute of Cardiovascular and Medical Science, University of Glasgow, Glasgow, G12 8TA, UK

[†]FH, CC-M and JPP contributed equally to this work and are joint senior authors

Corresponding author

Dr Carlos Celis-Morales

BHF Glasgow Cardiovascular Research Centre

Institute of Cardiovascular and Medical Sciences

College of Medical, Veterinary and Life Sciences

University of Glasgow

Glasgow, G12 8TA

United Kingdom

Tel: + 44 141 3304201

Email: Carlos.Celis@glasgow.ac.uk

Key Points

- In 2018, the European Working Group on Sarcopenia in Older people established a new operational definition and new cut-off points for sarcopenia (EWGSOP2). This new guideline suggests that low muscle strength more than low muscle mass is the principal determinant of sarcopenia.
- We identified that the EWGSOP2 recognised fewer people as having sarcopenia and the people identified were not at risk of as many adverse health outcomes as those identified using the previous definition.
- Caution needs to be taken with those individuals who are not any longer sarcopenic using the new classification but still have a higher risk of adverse health outcomes.

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Abstract

Introduction- Recently, the European Working Group on Sarcopenia in Older People (EWGSOP) established a new operational definition and cut-off points for sarcopenia. The aim of this study was, therefore, to compare the prevalence of sarcopenia and its associations with different health outcome using the old (EWGSOP1) and new (EWGSOP2) definitions of sarcopenia in the UK Biobank cohort.

Methods- Sarcopenia was defined as low grip strength plus low muscle mass. Using both EWGSOP cut-off points, we created specific sarcopenia variables. Prevalence of sarcopenia derived using both EWGSOP definitions were calculated and compared as well as prospective health outcomes including all-cause mortality as well as incidence and mortality from cardiovascular disease (CVD), respiratory disease, and chronic obstructive pulmonary disease (COPD).

Results- The prevalence of sarcopenia based on the EWGSOP1 and EWGSOP2 classification were 8.14% and 0.36%, respectively. Sarcopenia defined by EWGSOP1 was associated with a higher risk of respiratory disease and COPD as well as mortality from all-cause, CVD, and respiratory diseases. However, only respiratory incidence remained associated with sarcopenia when EWGSOP2 was used (HR: 1.32 [95% CI: 1.05 to 1.66]). Moreover, although individuals classified as sarcopenic using both classifications had the highest risk of all-cause mortality and respiratory disease, those with sarcopenia based on EWGSOP1 only experienced a more extensive range of poorer health outcomes.

Conclusion- In comparison with EWGSOP1, the new classification (EWGSOP2) produced a lower estimate of sarcopenia prevalence and fewer associations with adverse health outcomes. Although these associations were higher, many become not-significant.

Keywords: sarcopenia; mortality; incidence; muscle strength; EWGSOP

Introduction

Sarcopenia is a syndrome characterised by a progressive loss of muscle quantity and quality, which results in an increased risk of falls, fractures, hospitalisation, morbidity/mortality and reduces the quality of life [1]. This leads to a worse outcome in both elderly and middle-aged adults and with a higher economic burden and health care cost (~£2.5 billion/year in the UK) [2]. Different operational definitions have been proposed to defined sarcopenia, most based on the combination of three primary physical capability markers: low muscle mass, low grip strength and slow gait speed [3-7]. In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP1) defined sarcopenia as the combination of low muscle mass and either low grip strength or slow gait speed [3]. Recently, the EWGSOP established a new operational definition and new cut-off points for sarcopenia (EWGSOP2)[8]. This new guideline suggests that low grip strength more than low muscle mass is the principal determinant of sarcopenia, thereby, the definition of sarcopenia requires both low grip strength and low muscle mass with the addition of slow gait speed being used to define severe sarcopenia.

Although experts in the field have accepted used this new sarcopenia guideline, concern has been expressed regarding its effect on the prevalence and outcomes of sarcopenia [9-13]. The aim of this study was, therefore, to compare the prevalence of sarcopenia and its associations with different health outcome using the old (EWGSOP1) and new (EWGSOP2) definitions of sarcopenia in the UK Biobank cohort.

Methods

To compare both classifications according to each EWGSOP guidelines (EGWSOP1 and EWGSOP2), sarcopenia was defined as low grip strength plus low muscle mass. Following both EWGSOP cut-off points (2010 and 2019), we create specific sarcopenia variables (Supplementary Figure 2a and 2b). More details about Uk Biobank, other procedures, sarcopenia classification and other variables are available in supplementary methods.

Statistical analyses

Associations between sarcopenia and health outcomes, by EWGSOP1 and EWGSOP2 criteria, were investigated using Cox-proportional hazard models using STATA 14 statistical software (StataCorp LP). The results are reported as hazard ratios (HR) and their 95% confidence intervals (95% CI).

Moreover, to investigate differences in the association of sarcopenia with health outcomes according to EWGSOP1 and EWGSOP2, we derived the following categories: *"Always no sarcopenia"* (individuals classified as normal in both EWGSOP1 and EWGSOP2). *"Sarcopenia-EWGSOP1"* (include individual classified as sarcopenic following the EWGSOP1). Finally, *"Sarcopenia"* (include individuals who were classified as sarcopenic in both definitions EWGSOP1 and EWGSOP2) (Supplementary Figure 2c).

More details about statistical analyses are available in supplementary methods.

Results

The general characteristics of the population using the old (EWGSOP1) and new (EWGSOP2) classifications are presented in Supplementary Figure 1 and Supplementary Table 1. Overall, the prevalence of sarcopenia was lower when EWGSOP2 was used in comparison to EWGSOP1 (0.36% vs 8.14%); however, the mean age was higher (63.0 versus 60.7 years). With increasing age, the relative differences between the two classifications decreased, but the absolute differences increased (<54 years: 3.98 and 0.09; 54-61 years: 9.67 and 0.41; >61 years: 14.9 and 0.93 in EWGSOP1 and EWGSOP2, respectively). In terms of sex, the prevalence of sarcopenia was higher in women than in men. Changing from the old to the new classification, reduced the prevalence of overweight, obesity, central obesity, diabetes, cardiovascular disease (CVD) and high blood pressure but increased the prevalence of falls and fractures among people defined as sarcopenic (Supplementary Table 1).

The associations between sarcopenia and health outcomes using both definitions are presented in Table 1. Individuals with sarcopenia defined by EWGSOP1 had a higher risk than individuals with no sarcopenia of all-cause (HR: 1.16 [95% CI: 1.09 to 1.25]), CVD (HR: 1.30 [95% CI: 1.10 to 1.54]), and

respiratory disease (HR: 1.19 [95% CI 1.01 to 1.41]) mortality. They also had a higher risk of incident respiratory disease (HR: 1.11 [95% CI: 1.02 to 1.16]) and COPD (HR: 1.38 [95% CI: 1.12 to 1.67]). When the new classification for defining sarcopenia was used, only respiratory disease incidence remained associated with sarcopenia (HR: 1.32 [95% CI: 1.05 to 1.66]). No associations were found for COPD incidence and mortality from all-cause, CVD and respiratory diseases.

Differences in the associations with health outcomes using the new and old classifications are presented in Figure 2. Compared to those who were classified as no sarcopenia according to both EWGSOP1 and EWGSOP2 definitions (*"always no sarcopenia*"), individuals who were classified as having *"always-sarcopenia"* had the highest increased risk of all-cause mortality (HR: 1.29 [95% CI: 1.02 to 1.64]) and respiratory disease incidence (HR: 1.35 [95% CI: 1.07 to 1.70]). Nevertheless, those who were classified as sarcopenic only according to the EWGSOP1 definition (*"sarcopenia EWGSOP1"*) had increased risk of a more significant number of health outcomes (incident respiratory disease and COPD as well as all-cause and CVD mortality).

Discussion

It is already known than sarcopenia leads to a worse health outcome. Consequently, early detection and intervention are essential to reduce frailty, falls, functional, cognitive impairments, cardiovascular disease and mortality [1, 8]. In this study, the key finding was that the new EWGSOP2 definition identifies fewer people as having sarcopenia and the people identified were not at risk of as many adverse health outcomes as those identified using the previous definition. As a result, one of the main implications of using the new definition may be not to identify people who remain at risk of adverse health outcomes, since the numbers of people with diagnose of sarcopenia decrease substantially using this new definition. However, it is also important to highlight that although the associations using the new classifications were not significant, were higher than using the EWGSOP1. Therefore, our findings suggest that further work in this area would be essential.

Except for one study [14], there has been consistent evidence that using the new EWGSOP2 definition produces a lower prevalence estimate in comparison to the EWGSOP1 definition [9-13]. However, our findings show that under the new EWGSOP2 definition, the relative prevalence of sarcopenia almost disappeared (~0.4%). One explanation for these differences could be the average age of the UK Biobank population with sarcopenia (60.7 and 63.0 years, according to EWGSOP1 and EWGSOP2, respectively), i.e., a still adult population. In this context, and although the development of sarcopenia starts during adult life [15], the prevalence of sarcopenia using the new definition could be higher in an older population.

The associations between the previous classification of sarcopenia (EWGSOP1) and adverse health outcomes have been widely studied [16-18]. However, considering that the new definition (EWGSOP2) was just published at the end of last year [19] and amended in May of this year [8], fewer studies have investigated its association with health outcomes [11, 14]. Locquet et al. reported that the new EWGSOP2 was not significantly associated with all-cause mortality in contrast to their previous results using the EWGSOP1 (HR: 2.74 [95% CI: 0.98 to 7.65] and HR: 2.93 [95% CI: 1.17 to 7.35], respectively)[11]. Dávalos-Yerovi et al. demonstrated that both classifications were associated with COPD mortality in the most adjusted model. However, once again, the EWGSOP1 association was stronger in comparison to the EWGSOP2 [14].

Considering that the new EWGSOP2 definition decreases the estimate prevalence of sarcopenia, it is expected that the number of events, and consequently the statistical power, were lower in the analysis using EWGSOP2 definition. Regardless of power, we did find that people categorised as sarcopenic per EWGSOP1 were of higher risk for multiple fatal and nonfatal outcomes (Table 1). This again highlights the relevance of the cut-off points used to define sarcopenia and how these could affect the association of this condition with different adverse health outcome. Therefore, caution needs to be taken with those individuals who are not any longer sarcopenic using the new classification but still have a higher risk.

Strengths and limitations

Using the UK Biobank study provided the opportunity to test our research question in a large general population cohort as well as the opportunity to work with information collected using validated and standardised methods. However, UK Biobank is not representative of the UK population in terms of lifestyle and prevalent disease [20]. Therefore, care needs to be heeded not to generalise the absolute prevalence. However, in contrast, the effect size estimates (HR) can be generalised beyond the study population. Finally, given the low prevalence of EWGSOP2 sarcopenia, the corresponding analysis is underpowered. Other limitations of this study are available in supplementary limitations.

Conclusion

Substantial changes in the estimate prevalence and association patterns were found between EWGSOP1 and EWGSOP2 definitions. Using the new operational guideline, the estimate prevalence of sarcopenia decreased considerably.

Furthermore, although the new EGWSOP2 showed a higher magnitude of association with the health outcomes, many of the associations were non-significant due to the lower numbers of individuals meeting the new classification criteria. However, more research is needed to generate a valid and realisable definition for sarcopenia. This could help us to identify high-risk individuals in an early stage and, therefore, implement prevention programs aiming to maintain or increase physical capability markers related to sarcopenia.

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Table 1. Association of mortality and incidence health outcomes using EWGSOP1 and EWGSOP2 definitions.

	No sarcopenia (normal)		Sarcopenia		
	Total n /events	**HR (95%CI)**	**Total n /events**	**HR (95% CI)**	**p-value**
All-cause mortality					
EWGSOP1	199,972 / 5,121	1.00 (Ref.)	35,221 / 1,419	1.16 (1.09; 1.25)	<0.001
EWGSOP2	358,994 / 10,081	1.00 (Ref.)	1,519 / 72	1.25 (0.99; 1.58)	0.059
CVD mortality					
EWGSOP1	195,082 / 832	1.00 (Ref.)	34,250 / 227	1.30 (1.10; 1.54)	0.002
EWGSOP2	350,405 / 1,558	1.00 (Ref.)	1,468 / 8	1.21 (0.60; 2.44)	0.588
Respiratory Mortality					
EWGSOP1	198,693 / 731	1.00 (Ref.)	34,702 / 253	1.19 (1.01; 1.41)	0.042
EWGSOP2	356,171 / 1,571	1.00 (Ref.)	1,474 / 15	1.53 (0.91; 2.56)	0.108
CVD incidence					
EWGSOP1	192,907 / 8,166	1.00 (Ref.)	33,848 / 1,556	1.05 (0.99; 1.12)	0.078
EWGSOP2	346,371 / 14,812	1.00 (Ref.)	1,446 / 67	1.11 (0.87; 1.41)	0.400
Respiratory incidence					
EWGSOP1	197,349 / 6,098	1.00 (Ref.)	34,377 / 1,419	1.11 (1.04; 1.19)	0.001
EWGSOP2	353,645 / 11,459	1.00 (Ref.)	1,457 / 76	1.32 (1.05; 1.66)	0.017
COPD incidence					
EWGSOP1	198,707 / 383	1.00 (Ref.)	34,709 / 145	1.38 (1.10; 1.74)	0.005
EWGSOP2	356,227 / 821	1.00 (Ref.)	1,476 / 10	1.76 (0.93; 3.31)	0.083

Data presented as adjusted hazard ratio (HR) and its 95% confidence interval (95%CI) by sarcopenia EWGSOP1 and EWGSOP2. Normal people were used as the reference group for the analysis. All analyses were conducted using a 2-years landmark analyses and by excluding participant with major diseases at baseline. Model was adjusted by age, sex, gross income, education attainment, smoking, sleep duration, BMI, physical activity, total discretionary sedentary time, dietary intake (including alcohol, fruit and vegetable, oily fish, red meat and processed meat intake) and illnesses (hypertension, diabetes, depression, CVD, and cancer).

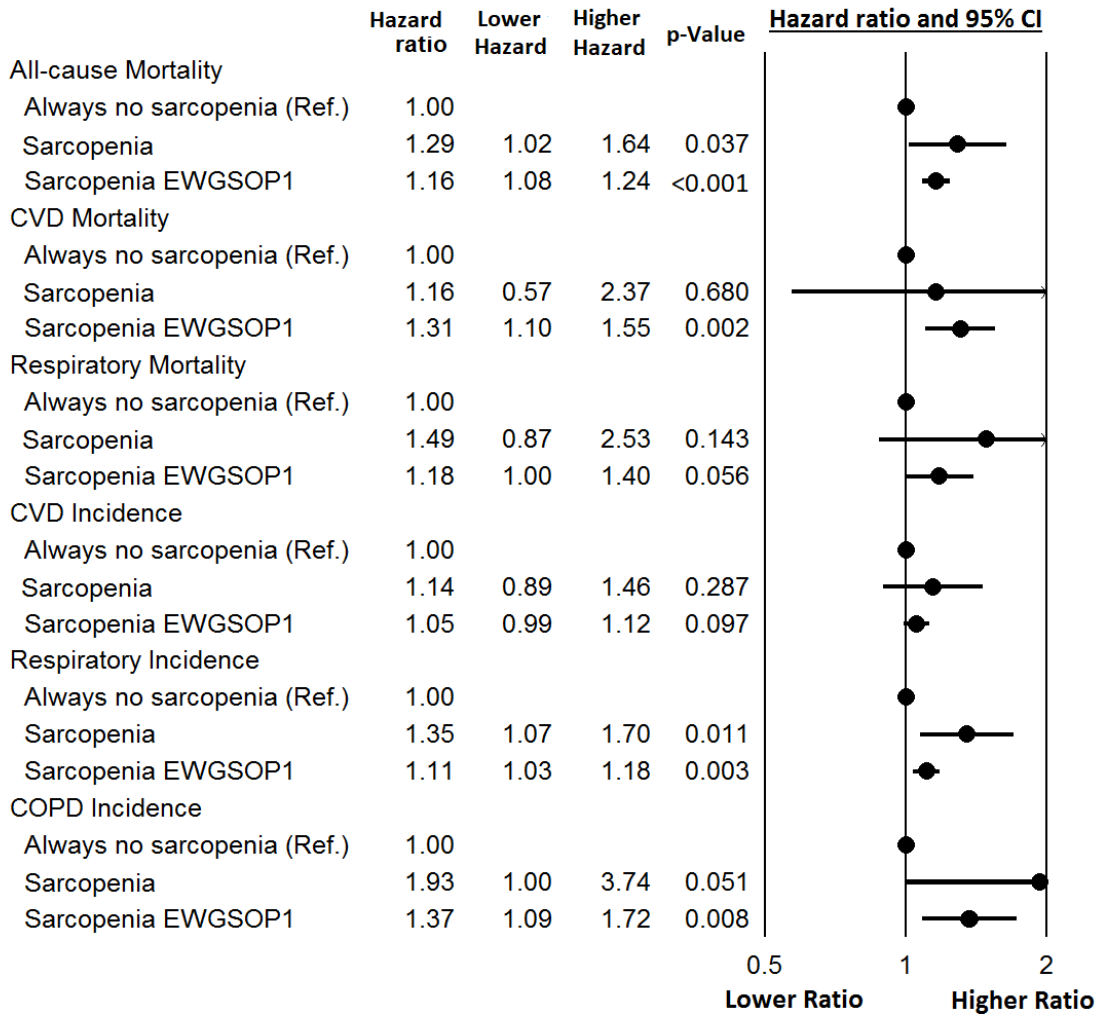

Figure 1. Association of mortality and incidence health outcomes with sarcopenia classifications from EWGSOP1 and EGSOP2.

Data presented as adjusted hazard ratio (HR) and its 95% confidence interval (95%CI) by sarcopenia categories. Sarcopenia classifications: always no sarcopenia: individuals classified as normal in both EWGSOP1 and EWGSOP2; Sarcopenia-EWGSOP1: include individual classified as sarcopenic following the EWGSOP1; Sarcopenia: include individuals who were classified as sarcopenic in both definitions EWGSOP1 and EWGSOP2. Always no sarcopenia people were used as the reference group for the analysis. All analyses were conducted using a 2-years landmark analyses and by excluding participant with major diseases at baseline. Model was adjusted by age, sex, gross income, education attainment, smoking, sleep duration, BMI, physical activity, total discretionary sedentary time, dietary intake (including alcohol, fruit and vegetable, oily fish, red meat and processed meat intake) and illnesses (hypertension, diabetes, depression, CVD, and cancer).