Clinical Nutrition ESPEN 45 (2021) 442–448

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Original article

Sarcopenia and malnutrition in relation to mortality in hospitalised patients in geriatric care – predictive validity of updated diagnoses

Sigvard Sobestiansky [a, b, *], Anna Cristina Åberg [c, d], Tommy Cederholm [a, e]

[a] Department of Public Health and Caring Sciences, Clinical Nutrition and Metabolism, Uppsala University, Uppsala, Sweden
[b] Department of Geriatric Medicine, Uppsala University Hospital, Uppsala, Sweden
[c] Department of Public Health and Caring Sciences, Geriatrics, Uppsala University, Uppsala, Sweden
[d] School of Education, Health and Social Studies, Dalarna University, Falun, Sweden
[e] Theme Inflammation and Ageing, Karolinska University Hospital, Stockholm, Sweden

ARTICLE INFO

Article history:
Received 19 March 2021
Accepted 3 July 2021

Keywords:
Sarcopenia
Malnutrition
EWGSOP
GLIM
Calf circumference

SUMMARY

Background and aim: The definition of sarcopenia was recently updated by the European Working Group on Sarcopenia (EWGSOP2), and consensus criteria for the diagnosis of malnutrition have been presented by the Global Leadership Initiative on Malnutrition (GLIM). The aim of this study was to investigate prevalence and mortality related to categorisation of patients according to these definitions in a geriatric hospital setting.

Method: Fifty-six consecutive geriatric inpatients (84y (SD 7.3), 68% women) underwent test of handgrip strength (HGS) and five-rise chair stand test (5CST). Muscle mass and fat free mass (FFM) were evaluated by Dual X-ray Absorptiometry (DXA). Calf circumference (CC) was recorded. Probable sarcopenia was defined, according to EWGSOP2, as low HGS (<27/16 kg for men/women) and/or 5CST >15 s; sarcopenia was confirmed when coupled with low appendicular skeletal muscle index (ASMI <7.0 and <5.5 kg/m^2 (m/w)). Malnutrition was defined according to GLIM as weight loss >5% (past 6 mo); BMI <20/22 kg/m^2 (<70/>70y); and FFM-index <17/15 kg/m^2 (m/w) combined with reduced food intake and/or disease burden/inflammatory condition. Alternatively, CC <31 cm was used as a proxy for low muscle mass for both sarcopenia and malnutrition. One- and two-year mortality was registered.

Results: All participants displayed probable sarcopenia; 46% and 20% were sarcopenic depending on whether muscle mass was estimated by DXA or CC. Malnutrition according to the GLIM criteria was prevalent in 64% or 60% (muscle mass by DXA or CC, respectively). Nine in ten with sarcopenia were also malnourished. Twenty-six participants (46%) died within two years. Sarcopenia defined by CC <31 cm, but not by DXA, was associated with increased mortality; e.g. 2-y mortality HR was 3.19 (95% CI 1.31–7.75). Similarly, malnutrition according to GLIM related to increased 1-y mortality (HR 4.83, 95% CI 1.04–22.39) when DXA was used for muscle mass estimation. All of the participants with CC <31 cm were categorised as both sarcopenic and malnourished.

Conclusion: In this small set of well-characterised geriatric inpatients all displayed probable sarcopenia. Prevalence of sarcopenia (EWGSOP2) and malnutrition (GLIM) was 20–46% and 60–64%, respectively. Both conditions related to mortality. CC <31 cm hold promises to be an acceptable alternative for DXA as a proxy for low muscle mass.

1. Introduction

Old and chronically ill adults are exposed to age- and disease-driven catabolism that often results in sarcopenia and malnutrition, conditions that are linked to reduced function and mortality [1–3]. Sarcopenia was originally defined as loss of muscle mass mainly associated with aging. However, the concept and

* Corresponding author. Department of Public Health and Caring Sciences, Clinical Nutrition and Metabolism, Uppsala University, Husargatan 3, BMC, Box 564, S-751 22, Uppsala, Sweden.
E-mail address: sigvard.sobestiansky@pubcare.uu.se (S. Sobestiansky).

https://doi.org/10.1016/j.clnesp.2021.07.002

operational definitions of sarcopenia have evolved from focusing on muscle mass reduction [4,5] to a composite definition that combines loss of muscle strength and/or reduced physical performance, and loss of muscle quantity [1,6–10]. Recently the European Working Group on Sarcopenia in Older People (EWGSOP) published a revised operational definition; i.e. low handgrip strength and/or reduced chair stand ability define "probable sarcopenia" and when there is also low muscle mass the diagnosis of sarcopenia is confirmed [11].

Malnutrition can be a causal component in the development of sarcopenia but can also be the result of similar pathological processes as sarcopenia, e.g. chronic disease-related inflammation as well as inadequate protein and energy intake. In order to unify the definition of malnutrition, a global consensus, also recently, presented diagnostic criteria for malnutrition. The so-called Global Leadership Initiative on Malnutrition (GLIM) proposed a definition [12] that combines at least one phenotypic; i.e. involuntary weight loss, reduced body mass index (BMI) or reduced muscle mass, with at least one etiologic criterion; i.e. reduced food intake or assimilation, and acute or chronic disease-related inflammation.

According to both EWGSOP2 and GLIM, Dual X-ray Absorptiometry (DXA) is one of the preferred diagnostic methods for measuring low muscle mass, though calf circumference (CC) can be used as an alternative, clinically applicable, diagnostic proxy for assessing muscle mass.

Our main hypothesis in this study was that sarcopenia and malnutrition would be associated with an increased all-cause mortality during one- and two-year follow-ups, accompanied with the sub-hypothesis that CC could serve as a proxy for muscle mass measurement in the diagnosis of sarcopenia and malnutrition. Therefore, the aim of this study was to investigate prevalence and predictive value, i.e. one- and two-year all-cause mortality, of inpatients in geriatric care diagnosed with sarcopenia and/or malnutrition by the updated formats [13]. A secondary objective was to perform the same analyses, applying calf circumference as a proxy for muscle mass measurement by DXA.

2. Material and methods

2.1. Study population

The study was conducted at the Department of Geriatric Medicine at Uppsala University Hospital in Uppsala, Sweden, during two study periods of altogether four and a half months between November 2009 and November 2010. A requisite for admittance to the Geriatric Medicine Department included a need of specialised geriatric rehabilitation and a clinically stable medical situation requiring hospitalisation.

Consecutively admitted patients, with a planned stay of more than a few days (and thus able to complete the study protocol), during the study periods were assessed for eligibility for participation in the study (n = 144). Exclusion criteria were severe disease with a short life expectancy (<1 month) – for example end stage cancer/heart failure/renal failure or any other medical condition in a late palliative phase, severe neuromuscular disease impeding the assessment of muscle strength/physical function, and factors affecting measurement of appendicular muscle mass for the diagnosis of sarcopenia (i.e. amputation of an extremity or severe neuromuscular disease with marked extremity muscle atrophy). Of the 144 eligible patients, 54 declined participation and 19 fulfilled the exclusion criteria. Out of 71 patients that accepted to participate, eight later declined and seven could not perform DXA due to medical reasons. Finally, 56 individuals were included in the study (Fig. 1). All subjects gave informed consent, and the Regional Ethical Review Board in Uppsala approved the study (Dnr 2009/096).

2.2. Body composition

Dual X-ray Absorptiometry (DXA) (GE Healthcare Lunar Prodigy) was used to calculate appendicular skeletal muscle mass index (ASMI, eq. ASM/height^2); i.e. the sum of skeletal muscle mass (lean mass) of both arms and legs (kg) was divided by height squared (kg/m^2) [11]. Fat free mass (FFM) was calculated as body weight minus fat mass. Fat free mass index (FFMI) was calculated as FFM divided by height squared (kg/m^2).

As a proxy for muscle mass [11], calf circumference (CC) was measured by a tape at the widest part of the calf, without compressing the subcutaneous tissue. The CC was measured with an accuracy of 0.1 cm. The participants were sitting or lying with the knee bent at 90°. Three measurements were performed for each leg, and the mean value of recordings of the non-dominant side was used.

2.3. Handgrip strength

Handgrip strength (HGS) was used to measure muscle strength. Participants (n = 54) sat in an adjustable chair with the forearm, but not the hand, supported and in a neutral position, shoulder relaxed, the elbow at 90°. Using a Jamar adjustable hand dynamometer (J.A. Preston, Michigan) [14], the participants were instructed to squeeze the dynamometer as hard as they could three times with 10 s of rest in between and the accuracy was 0.5 kg. Both hands were tested, the highest value of the strongest hand was used for the analysis. Two participants did not perform this test due to fatigue.

2.4. Chair stand test

Participants performed a five-rise chair stand test (5CST) as part of the Short Physical Performance Battery (SPPB) [15]. The 5CST test was performed with the participants seated in a chair, arms crossed over the chest. The participants were then instructed to rise as fast as they could in a safe manner and were timed from the back leaving the backrest until the final standing position after five rises. Time was measured by a stopwatch with an accuracy of 0.1 s. Twenty-two participants were able to complete the full chair stand test. Inability to perform the full test was regarded as a result above cut-off, i.e. >15 s, when used for diagnosis of probable sarcopenia and sarcopenia according to EWGSOP2.

2.5. Other measurements

All participants were assessed according to a form based on the Geriatric Minimum Data Set [16] – consisting of a full medical history, social situation, medications, smoking habits; as well as Mini Nutritional Assessment-Short Form (MNA-SF) and self-reported weight loss. Medical diagnoses were retrieved from medical records and from these the weighted Charlson Comorbidity Index (CCI) was calculated. CCI classifies comorbid medical conditions that affects mortality risk, taking into account the severity of the comorbid diagnoses in the weighted index [17]. Mortality data was collected from hospital files after two years of follow-up from the date of inclusion. Activities of daily living (ADL) was assessed according to Katz index [18] by an experienced occupational therapist.

Weight and height were measured with an accuracy of 0.5 kg and 0.5 cm, respectively. Body mass index was calculated as the ratio of the weight (kg) to the height (in metres) squared (kg/m^2).

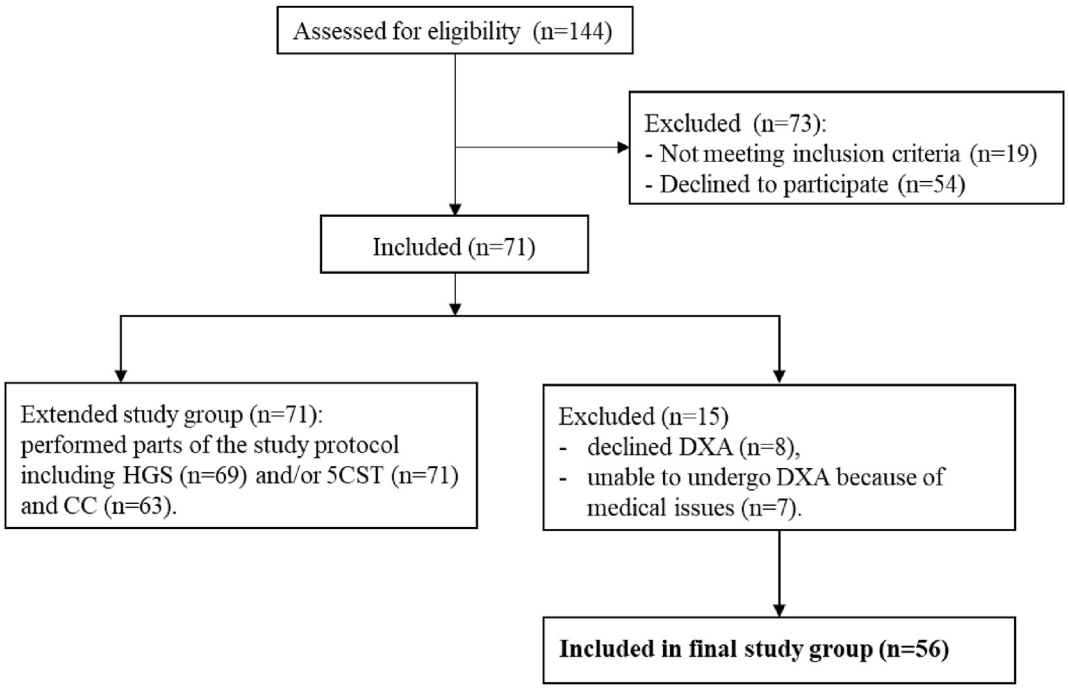

Fig. 1. Flow chart of inclusion and exclusion of study participants. HGS = handgrip strength; 5CST = five-rise chair stand test; CC = calf circumference; DXA = dual x-ray absorptiometry.

Results from blood samples drawn according to the clinical routine, close to admittance to the Geriatric Medicine Department, were retrieved from hospital records and included: c-reactive protein (CRP), haemoglobin (Hb) and creatinine (Cr). Estimated glomerular filtration rate (eGFR) was calculated according to Cockcroft-Gault formula as: coefficient*(140-age)* bodyweight/Cr (mL/min), were the coefficient was 1.04 for women and 1.23 for men.

2.6. Definition of sarcopenia

Probable sarcopenia and sarcopenia were diagnosed according to EWGSOP2; i.e. a HGS <16 kg for women and <27 kg for men, and/or 5CST >15 s indicated probable sarcopenia. When combined with low muscle mass; i.e. ASMI <5.5 kg/m^2 for women and <7.0 kg/m^2 for men (measured by DXA) the diagnosis of sarcopenia was confirmed – here denoted sarcopenia-DXA. Alternatively, sarcopenia was also confirmed by a reduced CC; i.e. <31 cm [11,19] – here denoted sarcopenia-CC.

2.7. Definition of malnutrition

Malnutrition was defined according to the GLIM consensus statement [12]; i.e. one or more of the phenotypic criteria in combination with, at least, one etiologic criterion, in patients identified as “at risk” or “malnourished” according to MNA-SF [20].

The phenotypic criteria were: weight loss >5% within the past 6 months; BMI <20 kg/m^2 if age <70 years (y), or <22 kg/m^2 if age >70 y; and FFMI <15 kg/m^2 (women) or <17 kg/m^2 (men) [12,21]. Malnutrition with FFMI measured by DXA is denoted malnutrition-DXA. As an alternative CC <31 cm was used instead of FFMI (by DXA) as a proxy for muscle mass measurement - here denoted malnutrition-CC (53 patients could be assessed for malnutrition using CC).

The etiologic criteria were reduced food intake or assimilation and/or disease burden/inflammatory condition. Reduced food intake was defined according to MNA-SF, i.e. moderate or severe loss of appetite during the past 3 months. The second etiologic criterion was defined as the presence of acute disease/injury, i.e. major infection or trauma; and/or chronic disease-related inflammation. For this study we adopted a liberal approach; i.e. a history of chronic organ disease such as heart failure, moderate/severe renal failure, inflammatory disease, chronic obstructive pulmonary disease, and cancer was enough to fulfil this criterion; a CRP above cut-off was supportive but not conclusive for this criterion.

2.8. Statistical analysis

Continuous variables are given as mean and standard deviation (SD) or median and interquartile range (IQR). Categorical variables are given as numbers and percentages. Fisher's exact test was used to analyse the association between categorical variables and two-sample unpaired t-test, or Wilcoxon rank sum-test were used for continuous variables. Pearson's correlation coefficient was calculated for the associations between various methods to measure body composition.

Mortality was chosen as the major outcome measure, with sarcopenia and malnutrition as the principal exposures. Kaplan–Meier curves display the cumulative survival according to the definitions of sarcopenia and malnutrition. Log-rank test was used to test the equality of the survival curves.

Cox regression was used to analyse hazard ratios with 95% confidence intervals for mortality by sarcopenia and malnutrition, respectively. Two models were applied for the regression analyses – a crude model with either sarcopenia or malnutrition only (model 1), and an adjusted model including age and Charlson comorbidity index (model 2) [22]. There were no violations of the proportional hazard assumption. Log-rank test was also used as a sensitivity analysis for the Cox regression (crude models). The threshold for statistical significance was set to $p < 0.05$. Statistical analyses were performed using STATA version 15.1 (StataCorp, College Station, Tx, USA).

3. Results

Baseline characteristics are described in Table 1 (and in Supplementary Tables 1 and 2). Mean age was 84.1 y (SD 7.3 y), (range 65–94 y for men and 74–96 y for women), 68% (n = 38) were women. Most of the participants (89%, n = 49) were community-dwelling; 29% (n = 16) were independent in daily activities according to Katz' ADL scale. Seventy-six percent (n = 41) had had at least one fall during the last year. Median Charlson comorbidity index score was 2 (IQR 2). The most prevalent medical diagnoses were heart failure (52%), previous or present fracture (55%) and osteoporosis (48%) (Supplementary Table 1).

3.1. Prevalence of sarcopenia by method to assess muscle mass

All participants had a reduced muscle strength, i.e. probable sarcopenia. Sarcopenia-DXA was confirmed in 46% (n = 26) with a male preponderance, i.e. prevalence was 72% (n = 13) and 34% (n = 13) for men and women, respectively. For sarcopenia-CC, prevalence was reduced to 20% (n = 10 out of 49). All participants with sarcopenia-CC also displayed sarcopenia-DXA. Thus, specificity for sarcopenia-CC was 100% for sarcopenia-DXA, while sensitivity was 45%. CC showed a positive correlation with ASMI (r = 0.70, p <0.001) measured by DXA.

3.2. Prevalence of malnutrition by method to assess muscle mass

Screening for malnutrition with MNA-SF showed that the vast majority were either at risk (59%, n = 33) or regarded as malnourished (34%, n = 19). Malnutrition-DXA was diagnosed in 64% (n = 36) of the study population, while malnutrition-CC (possible to assess for n = 53) was observed in 60% (n = 32). All of the participants with malnutrition-CC also fulfilled the criteria for malnutrition-DXA. This corresponds to a specificity of 100% and sensitivity of 91% when CC replaced FFMI. Sarcopenia-DXA and malnutrition-DXA were closely related, i.e. 88% of those fulfilling the criteria for sarcopenia-DXA were also defined as having malnutrition-DXA and 64% of those with malnutrition-DXA also had sarcopenia-DXA (p <0.01). FFMI and ASMI (by DXA) showed a high positive correlation (r = 0.92, p <0.001). Low FFMI, as well as low ASMI was seen in 26 participants, of which 85% (n = 22) participants displayed both. CC and FFMI were positively correlated (r = 0.57, p <0.001).

3.3. Long-term mortality related to sarcopenia and malnutrition

During the two-year follow-up 26 participants (46%) died. The different definitions of sarcopenia and malnutrition related to mortality as follows:

For sarcopenia-DXA, i.e. when DXA was applied for the diagnosis of sarcopenia, two-year mortality with and without sarcopenia was 54% (n = 14) and 40% (n = 12), respectively. Adjusted Cox regression analyses confirmed a non-significant relation to one- and two-year all-cause mortality for sarcopenia-DXA.

In contrast, sarcopenia-CC appeared to be associated with an increased one- and two-year all-cause mortality; e.g. for 2 y-mortality HR was 3.19 (95% CI 1.31–7.75) (Table 2; Fig. 2).

For malnutrition-DXA, i.e., when DXA was applied for the diagnosis of malnutrition, one-year mortality was 33% (n = 12) compared to 10% (n = 2) for those with normal nutritional status. Corresponding figures for two-year mortality in malnourished vs. non-malnourished were 50% (n = 18) and 40% (n = 8), respectively. Adjusted Cox regression analyses indicated an increase in one-year mortality for malnutrition-DXA; HR 4.83 (95% CI 1.04–22.39). This association was not seen after two years.

For malnutrition-CC, contrasting the results for malnutrition-DXA, there was no association with one- or two-year mortality.

For the separate phenotypic criteria of the GLIM format, low BMI, and CC <31 cm showed associations with increased one- and two-year mortality, whereas weight loss and low FFMI did not (data

Table 1
Baseline characteristics – body composition, muscle strength and physical performance.

	All n = 56	Men n = 18 (32%)	Women n = 38 (68%)	No sarcopenia-DXA[a] n = 30 (54%)	Sarcopenia-DXA[a] n = 26 (46%)	No malnutrition-DXA[b] n = 20 (36%)	Malnutrition-DXA[b] n = 36 (64%)
Age, years (SD)	84.1 (7.3)	81.2 (9.7)	85.5 (5.5)*	84.4 (6.3)	83.8 (8.5)	84.3 (5.3)	84.0 (8.3)
Smoking, n (%)							
- Current	2 (3.6)	1 (5.6)	1 (2.6)	1 (3.3)	1 (3.8)	2 (10.0)	0 (0)
- Never	33 (58.9)	6 (33.3)	27 (71.1)*	20 (66.7)	13 (50.0)	13 (65.0)	20 (55.6)
MNA-SF, p, median (IQR)	9 (3.5)	7.5 (4)	9 (4)	10 (3)	7 (3)***	10.5 (3)	8 (3.5)**
0–7 points, n (%)	19 (33.9)	9 (50.0)	10 (26.3)	5 (16.7)	14 (53.8)**	4 (20.0)	15 (41.7)
8–11 points, n (%)	33 (58.9)	9 (50.0)	24 (63.2)	22 (73.3)	11 (42.3)*	12 (60.0)	21 (58.3)
12–14 points, n (%)	4 (7.1)	0 (0)	4 (10.5)	3 (10.0)	1 (3.8)	4 (20.0)	0 (0)*
CCI, median (IQR)	2 (2)	4 (3)	2 (2)**	2 (2)	2.5 (3)	2 (2.5)	2 (2)
BMI (kg/m^2), mean (SD)	23.4 (5.4)	22.6 (4.0)	23.7 (5.9)	26.2 (5.0)	20.1 (3.6)***	27.6 (4.5)	21.0 (4.3)***
ASMI (kg/m^2), mean (SD)	5.93 (0.95)	6.35 (0.99)	5.73 (0.87)*	6.47 (0.73)	5.30 (0.78)***	6.50 (0.68)	5.61 (0.93)***
<7.0/5.5 kg/m^2, n (%)	26 (46.4)	13 (72.2)	13 (34.2)*	0 (0)	26 (100)***	3 (15.0)	23 (63.9)**
FFMI (kg/m^2), mean (SD)	16.1 (2.2)	17.1 (2.3)	15.6 (2.0)*	17.2 (1.9)	14.8 (1.8)***	17.4 (1.7)	15.4 (2.1)***
<17/15 kg/m^2, n (%)	26 (46.4)	10 (55.6)	16 (42.1)	4 (13.3)	22 (84.6)***	2 (10.0)	24 (66.7)***
CC[c] (cm), mean (SD)	33.8 (4.4)	33.4 (3.2)	34.1 (4.9)	36.2 (3.5)	30.9 (3.5)***	36.3 (2.8)	32.4 (4.4)**
<31 cm, n (%)	10 (20.4)	4 (23.5)	6 (18.8)	0 (0)	10 (45.5)***	0 (0)	10 (32.3)**
HGS[d] (kg), mean (SD)	12.8 (6.4)	17.7 (7.2)	10.4 (4.3)***	12.5 (6.0)	13.1 (7.0)	13.3 (5.6)	12.5 (6.9)
<27/16 kg, n (%)	48 (88.9)	17 (94.4)	31 (86.1)	24 (82.8)	24 (96.0)	15 (75.0)	33 (97.1)*
5CST[e] >15 s, n (%)	49 (87.5)	13 (72.2)	36 (94.7)*	27 (90.0)	22 (84.6)	18 (90.0)	31 (86.1)

*p <0.05; **p <0.01; ***p <0.001.
DXA = dual x-ray absorptiometry; CC = calf circumference; SD = standard deviation; MNA-SF = Mini Nutritional Assessment-short form; IQR = inter-quartile range; CCI=Charlson comorbidity index; BMI = body mass index; ASMI = appendicular skeletal muscle mass index; FFMI = fat free mass index; HGS = handgrip strength; 5CST = five-rise chair stand test.
[a] For sarcopenia-DXA (EWGSOP2), muscle mass was measured by DXA, i.e. ASMI [11].
[b] For malnutrition-DXA (GLIM), muscle mass was measured by DXA, i.e. FFMI [12].
[c] CC: n = 49.
[d] HGS: n = 54.
[e] 5CST: a result >15 s or inability to complete the full test (n = 22 out of 56).

Table 2
Hazard ratios (95% CI) for 1- and 2-year all-cause mortality according to sarcopenia and malnutrition diagnosis.

	1-year mortality					2-year mortality				
	Model 1 HR (95% CI)	p-value	Log-rank p-value	Model 2 HR (95% CI)	p-value	Model 1 HR (95% CI)	p-value	Log-rank p-value	Model 2 HR (95% CI)	p-value
Sarcopenia-DXA[a]	2.22 (0.74–6.63)	0.153	0.142	2.13 (0.71–6.37)	0.177	1.56 (0.72–3.38)	0.259	0.254	1.53 (0.71–3.32)	0.281
Sarcopenia-CC[c]	4.40 (1.41–13.70)	0.010	0.005	4.06 (1.29–12.82)	0.017	3.26 (1.36–7.80)	0.008	0.005	3.19 (1.31–7.75)	0.011
Malnutrition-DXA[b]	3.78 (0.85–16.91)	0.082	0.061	4.83 (1.04–22.39)	0.044	1.53 (0.66–3.52)	0.318	0.314	1.78 (0.75–4.21)	0.189
Malnutrition-CC[d]	2.75 (0.77–9.85)	0.121	0.106	3.04 (0.83–11.12)	0.092	1.23 (0.56–2.71)	0.606	0.605	1.29 (0.58–2.87)	0.539

EWGSOP2 = European Working Group on Sarcopenia in Older People, 2019 update [11]; GLIM = Global Leadership Initiative on Malnutrition [12]; CC = calf circumference; Model 1: crude model; Model 2: adjusted for age and Charlson comorbidity index. Log-rank = log-rank test.
[a] For sarcopenia-DXA (EWGSOP2), muscle mass was measured by DXA, i.e. ASMI [11].
[b] For malnutrition-DXA (GLIM), muscle mass was measured by DXA, i.e. FFMI [12].
[c] For sarcopenia-CC (total n = 49), calf circumference was used as a proxy for muscle mass [11].
[d] For malnutrition-CC (total n = 53), calf circumference was used as a proxy for muscle mass [12].

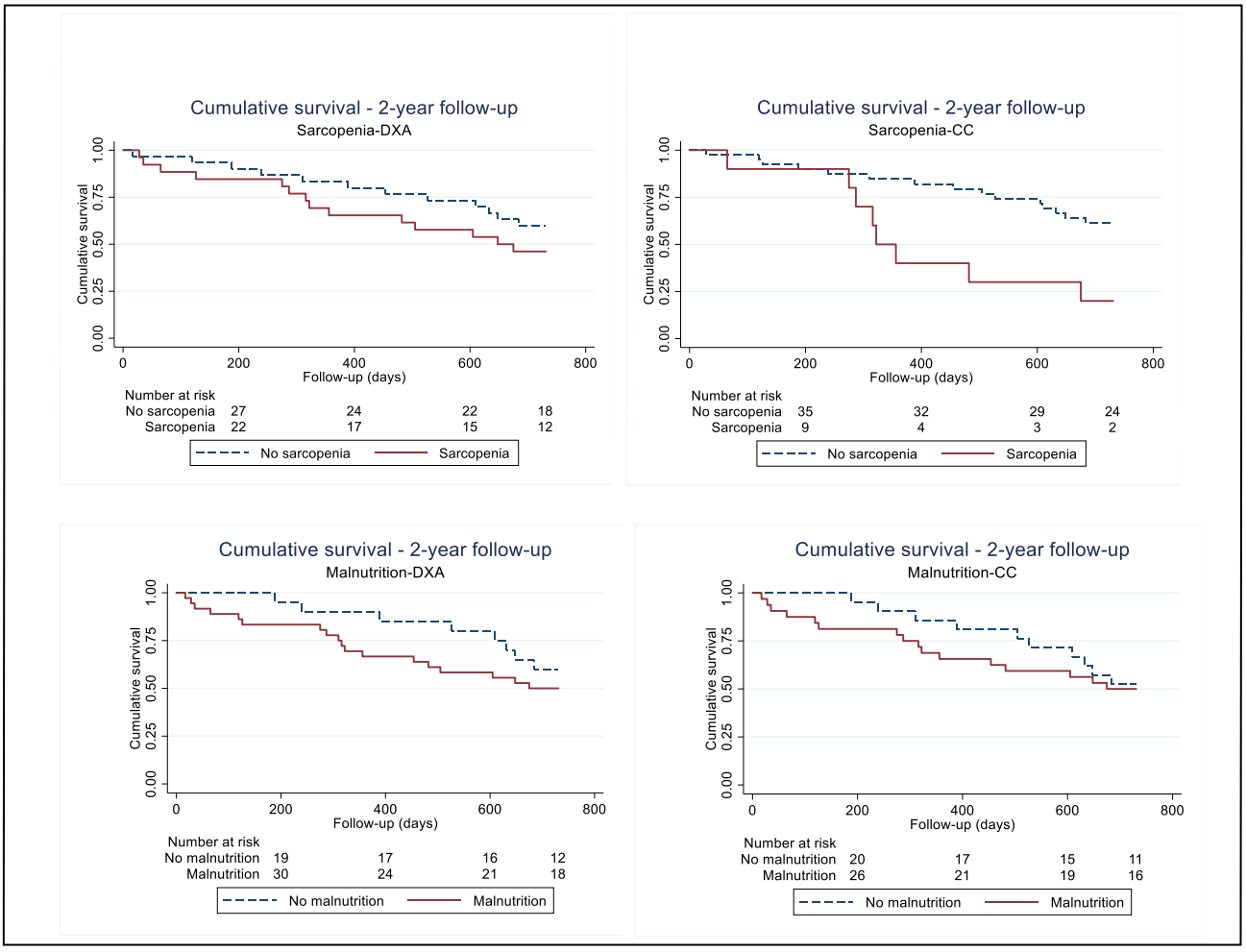

Fig. 2. Kaplan–Meier curves of cumulative 2-y survival according to sarcopenia (EWGSOP2) and malnutrition (GLIM) status using different methods of estimating muscle mass. Sarcopenia-DXA - muscle mass measured by DXA (ASMI; EWGSOP2); Sarcopenia-CC - muscle mass measured by CC (EWGSOP2); Malnutrition-DXA - muscle mass measured by DXA (FFMI; GLIM); Malnutrition-CC - muscle mass measured by CC (GLIM); EWGSOP2 = European Working Group on Sarcopenia in Older People, 2019 update [11]; GLIM = Global Leadership Initiative on Malnutrition [12]; DXA = dual x-ray absorptiometry; ASMI = appendicular skeletal muscle mass index; CC = calf circumference; FFMI = fat free mass index.

not shown). For malnutrition-DXA using ASMI instead of FFMI the one-year mortality association was weaker and non-significant (HR 2.22, 95% CI 0.61–8.09). This exchange caused the malnutrition diagnosis to differ for three participants. Finally, we also analyzed the mortality predictive value of the combined diagnosis of sarcopenia-DXA and malnutrition-DXA using the same Cox regression models as above. This combined diagnosis was related to an increased two-year mortality in the fully adjusted model (HR 2.25, 95% CI 1.02–4.94; all data not shown).

Fifteen individuals participated in parts of the study but did not perform DXA, 7 out of these 15 individuals had their CC measured. All 15 individuals fulfilled the definition for probable sarcopenia. There were no statistically significant differences in demographics, reduced muscle strength or mortality between those who did not

perform DXA and those who did, neither were the outcome measures for those that had CC measured (sarcopenia-CC, n = 63).

4. Discussion

In this small study of well-characterized older, hospitalised men and women, the prevalence of sarcopenia as well as malnutrition was high. All the participants exhibited low muscle strength (eq. probable sarcopenia), whereas 46% displayed confirmed sarcopenia (by DXA). This prevalence of sarcopenia is in fair agreement with some, but not all, studies in corresponding hospital settings using the original EWGSOP definition. These studies report prevalence figures from 10% (4.9% in women) to 42% (75.9% in men) [23–27].

The finding of two thirds being malnourished according to the GLIM criteria may indicate that the GLIM criteria are less conservative than other tools to diagnose malnutrition. For example, in a meta-analysis using the full MNA as tool for diagnosing malnutrition, 22% and 29.4% were classified as malnourished within hospital and rehabilitation/sub-acute care, respectively [28]. Interestingly, in our study, almost 9 out of 10 of the participants with sarcopenia-DXA also suffered from malnutrition-DXA. This reflects the close association between, and emphasizes the importance of assessing, the two conditions concomitantly in geriatric inpatients.

To quantify muscle mass, EWGSOP2 and GLIM [11,12] recommends DXA. Even though DXA was accessible in the clinical setting of this study, still 15 individuals (21%) could not perform the test for various reasons. Bioelectrical impedance analysis (BIA) is also a recommended technique but may provide different results compared to DXA when classifying sarcopenia in geriatric inpatients [29]. The EWGSOP2 suggest CC <31 cm as a diagnostic proxy for muscle mass if other muscle mass measurements are not available [11]. Mean CC was low in this study (Table 1), i.e. for men it was equal to the 10th percentile (33.3 cm) and for women the 25th percentile (34.0 cm) of CC when compared to a Swedish population study of 3053 individuals aged 60–99 years [30]. In our study, the prevalence of reduced muscle mass measured by DXA was high, i.e. 72% and 34% for men/women, respectively. The CC positively correlated with ASMI.

Replacing low muscle mass by DXA (sarcopenia-DXA) with CC <31 cm (sarcopenia-CC), resulted in high specificity (100%) for CC, although sensitivity was lower, i.e. 45%. The corresponding figures for malnutrition-CC showed a similar specificity (100%) and a sensitivity of 91% for malnutrition-DXA. For sarcopenia, this result is in line with a previous study that found CC <31 cm to have high specificity (91.4%), but lower sensitivity (44.3%) for defining sarcopenia, when defined by low DXA only [19].

Mortal outcome in the two years follow-up was observed in close to half of the participants. First, we discuss the association between mortality and sarcopenia. It was obvious that sarcopenia-DXA was not strongly associated with an increased mortality in this study population. The small number of participants could explain this result. Another possible explanation could be that the discriminatory power of the cut-offs used in the EWGSOP2 sarcopenia definition is low for a population of geriatric inpatients since all fulfilled the definition of "probable sarcopenia" in our study. In contrast to the results for sarcopenia-DXA, mortality appeared to be increased for the smaller number of participants with sarcopenia-CC. The recommended cut-off of CC <31 cm has been shown to associate with poorer physical strength, disability, and higher frailty score [19,31]. Our results, indicating an increased mortality using CC <31 cm as measure of low muscle mass, is in line with several other reports from, for example, Mexico (mean age 78.5y) [32], Brazilian community-dwelling adults >60 years of age [33], and Dutch older individuals (per SD lower CC) [34]. A possible explanation for the result that sarcopenia-CC, but not sarcopenia-DXA, showed an association with mortality might be that CC <31 cm defines study participants that have reached a critical threshold of low muscle mass, low enough to affect mortality. Another interpretation might be that low CC is associated with a higher morbidity, though adjusting for comorbid states did not alter the mortality association indicated by our results.

The result of our study indicates that CC <31 cm might be a comprehensive measure for the identification of sarcopenia and malnutrition. Measurement of calf circumference is easily applied in resource scarce settings. The chosen cut-off for defining sarcopenia/malnutrition, or to assess risk of adverse outcome, is likely population specific [35–37].

Next, we report that malnutrition-DXA seemed to relate to increased one-year mortality in this study population. This is also in line with previous reports [38,39]. However, the result should be interpreted cautiously with regard to the wide 95% confidence interval in the fully adjusted model (Table 2). After two years there was no difference implying that malnutrition-DXA, in geriatric inpatients, is primarily a risk factor for short-term all-cause mortality. When low FFMI was replaced by CC <31 cm as the phenotypic criteria of low muscle mass in the composite definition of malnutrition there was no association with mortality. However, for CC <31 cm alone there was an association with mortality, the same applied for low BMI alone. Thus, the result might indicate that weight loss and low FFMI have a lower mortality predicting value in the composite definition of malnutrition in geriatric inpatients. The results need to be interpreted cautiously due to the small number of patients.

There are strengths and limitations of this study that need to be addressed. The major limitation is the small number of participants, and the fact that close to half of those eligible for inclusion declined to participate further hampering the generalizability of the results. Another limitation might be the number of possible confounders in the Cox regression analyses that were kept low due to the somewhat low number of outcome events. Even so, the addition of gender as a confounder in the Cox regressions, using the various definitions of sarcopenia and malnutrition, did not alter the results in any decisive way. One strength is that the study participants are well characterised with DXA, anthropometry and measures of muscle strength and physical performance. Our study also includes the most recent definitions of sarcopenia and malnutrition and we have reliable data on medical diagnoses.

In conclusion, in this small set of well-characterized geriatric inpatients, applying the updated diagnostic criteria of EWGSOP2 and GLIM resulted in a prevalence of sarcopenia of up to 46%, while malnutrition was diagnosed in 60–64%, when CC or DXA were used for muscle mass assessment. Our results indicate that malnutrition-DXA was a risk factor for increased one-year mortality even in this small study population. Likewise, sarcopenia-CC was associated with one- and two-year mortality. We also think our results imply that calf circumference hold promises to be an acceptable proxy for muscle mass when more sophisticated techniques are not available.

Statement of authorship

All authors: study concept and study design, data interpretation. S. Sobestiansky: data acquisition, writing the manuscript, data analyses. All authors contributed to a critical revision of the manuscript and approved its final version.

Funding sources

This work was supported by the Swedish Research Council (2012-34045-93814-28, 2015-02338); the Thuréus Foundation for

Geriatric Research; the Uppsala Geriatric Foundation, and the Uppsala County Council. These funding sources had no role in the design, conduct of research or decision of publication.

Declaration of competing interest

S. Sobestiansky, A.C. Åberg, T. Cederholm: no conflicts of interest.

Acknowledgements

The authors would like to thank all the participants of the study and the personnel at the Geriatric Medicine Department, ward 30A, Uppsala University Hospital. We would also like to thank associate professor Lars Berglund, Department of Public Health and Caring Sciences, Geriatrics, Uppsala University, for statistical advice.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2021.07.002.

References

[1] Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: report of the European working group on sarcopenia in older People. Age Ageing 2010;39:412–23.
[2] Biolo G, Cederholm T, Muscaritoli M. Muscle contractile and metabolic dysfunction is a common feature of sarcopenia of aging and chronic diseases: from sarcopenic obesity to cachexia. Clin Nutr 2014;33:737–48.
[3] Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, et al. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr 2019;38:10–47.
[4] Rosenberg IH. Summary comments. Am J Clin Nutr 1989;50:1231–3.
[5] Baumgartner R, Koehler K, Gallagher D, Romero L, Heymsfield S, Ross R, et al. Epidemiology of sarcopenia among the elderly in New Mexico. Am J Epidemiol 1998;147:755–63.
[6] Muscaritoli M, Anker SD, Argiles J, Aversa Z, Bauer JM, Biolo G, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups (SIG) "cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics". Clin Nutr 2010;29:154–9.
[7] Morley JE, Abbatecola AM, Argiles JM, Baracos V, Bauer J, Bhasin S, et al. Sarcopenia with limited mobility: an international consensus. J Am Med Dir Assoc 2011;12:403–9.
[8] Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. J Am Med Dir Assoc 2011;12:249–56.
[9] Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian working group for sarcopenia. J Am Med Dir Assoc 2014;15:95–101.
[10] Studenski SA, Peters KW, Alley DE, Cawthon PM, McLean RR, Harris TB, et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J Gerontol A Biol Sci Med Sci 2014;69:547–58.
[11] Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48:16–31.
[12] Cederholm T, Jensen GL, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition - a consensus report from the global clinical nutrition community. Clin Nutr 2019;38:1–9.
[13] de van der Schueren MAE, Keller H, Cederholm T, Barazzoni R, Compher C, Correia M, et al. Global Leadership Initiative on Malnutrition (GLIM): guidance on validation of the operational criteria for the diagnosis of protein-energy malnutrition in adults. Clin Nutr 2020;39:2872–80.
[14] Roberts HC, Denison HJ, Martin HJ, Patel HP, Syddall H, Cooper C, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing 2011;40:423–9.
[15] Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85–94.
[16] Abellan Van Kan G, Sinclair A, Andrieu S, Olde Rikkert M, Gambassi G, Vellas B, et al. The geriatric Minimum data set for clinical trials (GMDS). J Nutr Health Aging 2008;12:197–200.
[17] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis 1987;40:373–83.
[18] Brorsson B, Åsberg KH. Katz index of independence in ADL. Reliability and validity in short-term care. Scand J Rehabil Med 1984;16:125–32.
[19] Rolland Y, Lauwers-Cances V, Cournot M, Nourhashemi F, Reynish W, Riviere D, et al. Sarcopenia, calf circumference, and physical function of elderly women: a cross-sectional study. J Am Geriatr Soc 2003;51:1120–4.
[20] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003;22:415–21.
[21] Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 2017;36:49–64.
[22] Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. Am J Epidemiol 2007;165:710–8.
[23] Bianchi L, Abete P, Bellelli G, Bo M, Cherubini A, Corica F, 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;72:1575–81.
[24] Gingrich A, Volkert D, Kiesswetter E, Thomanek M, Bach S, Sieber CC, et al. Prevalence and overlap of sarcopenia, frailty, cachexia and malnutrition in older medical inpatients. BMC Geriatr 2019;19:120.
[25] Reijnierse EM, Buljan A, Tuttle CSL, van Ancum J, Verlaan S, Meskers CGM, et al. Prevalence of sarcopenia in inpatients 70 years and older using different diagnostic criteria. Nurs Open 2019;6:377–83.
[26] Smoliner C, Sieber CC, Wirth R. Prevalence of sarcopenia in geriatric hospitalized patients. J Am Med Dir Assoc 2014;15:267–72.
[27] Gariballa S, Alessa A. Sarcopenia: prevalence and prognostic significance in hospitalized patients. Clin Nutr 2013;32:772–6.
[28] Cereda E, Pedrolli C, Klersy C, Bonardi C, Quarleri L, Cappello S, et al. Nutritional status in older persons according to healthcare setting: a systematic review and meta-analysis of prevalence data using MNA®. Clin Nutr 2016;35:1282–90.
[29] Reiss J, Iglseder B, Kreutzer M, Weilbuchner I, Treschnitzer W, Kässmann H, et al. Case finding for sarcopenia in geriatric inpatients: performance of bioimpedance analysis in comparison to dual X-ray absorptiometry. BMC Geriatr 2016;16:52.
[30] Gavriilidou NN, Pihlsgård M, Elmståhl S. Anthropometric reference data for elderly Swedes and its disease-related pattern. Eur J Clin Nutr 2015;69:1066–75.
[31] Landi F, Onder G, Russo A, Liperoti R, Tosato M, Martone AM, et al. Calf circumference, frailty and physical performance among older adults living in the community. Clin Nutr 2014;33:539–44.
[32] Arango-Lopera VE, Arroyo P, Gutierrez-Robledo LM, Perez-Zepeda MU, Cesari M. Mortality as an adverse outcome of sarcopenia. J Nutr Health Aging 2013;17:259–62.
[33] de Almeida Roediger M, de Fatima Nunes Marucci M, Quintiliano Scarpelli Dourado DA, de Oliveira C, Licio Ferreira Santos J, de Oliveira Duarte YA. Body composition changes and 10-year mortality risk in older Brazilian adults: analysis of prospective data from the SABE study. J Nutr Health Aging 2019;23:51–9.
[34] Wijnhoven HA, van Bokhorst-de van der Schueren MA, Heymans MW, de Vet HC, Kruizenga HM, Twisk JW, et al. Low mid-upper arm circumference, calf circumference, and body mass index and mortality in older persons. J Gerontol A Biol Sci Med Sci 2010;65:1107–14.
[35] Chen LK, Lee WJ, Peng LN, Liu LK, Arai H, Akishita M. Recent advances in sarcopenia research in Asia: 2016 update from the Asian working group for sarcopenia. J Am Med Dir Assoc 2016;17:767. e1-7.
[36] Kawakami R, Murakami H, Sanada K, Tanaka N, Sawada SS, Tabata I, et al. Calf circumference as a surrogate marker of muscle mass for diagnosing sarcopenia in Japanese men and women. Geriatr Gerontol Int 2015;15:969–76.
[37] Maeda K, Koga T, Nasu T, Takaki M, Akagi J. Predictive accuracy of calf circumference measurements to detect decreased skeletal muscle mass and European society for clinical nutrition and metabolism-defined malnutrition in hospitalized older patients. Ann Nutr Metab 2017;71:10–5.
[38] Felder S, Lechtenboehmer C, Bally M, Fehr R, Deiss M, Faessler L, et al. Association of nutritional risk and adverse medical outcomes across different medical inpatient populations. Nutrition 2015;31:1385–93.
[39] Schuetz P, Fehr R, Baechli V, Geiser M, Deiss M, Gomes F, et al. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. Lancet 2019;393:2312–21.