

RESEARCH PAPER

Sarcopenia is associated with 3-month and 1-year mortality in geriatric rehabilitation inpatients: RESORT

JANE XU¹, ESMEE M. REIJNIERSE^{1,2}, JACOB PACIFICO¹, CHING S. WAN^{1,3}, ANDREA B. MAIER^{1,4,5}

¹Department of Medicine and Aged Care, @AgeMelbourne, The Royal Melbourne Hospital, The University of Melbourne, Parkville, VIC, Australia

²Department of Rehabilitation Medicine, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam Movement Sciences, Amsterdam, The Netherlands

³Nursing Research Institute, St Vincent's Health Network Sydney, St Vincent's Hospital Melbourne & Australian Catholic University, Melbourne, VIC, Australia

⁴Department of Human Movement Sciences, @AgeAmsterdam, Vrije Universiteit Amsterdam, Amsterdam Movement Sciences, Amsterdam, The Netherlands

⁵Healthy Longevity Program, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; Centre for Healthy Longevity, @AgeSingapore, National University Health System, Singapore

Address correspondence to: Andrea B. Maier, @Age, Department of Human Movement Sciences, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam Movement Sciences, Van der Boechorststraat 7, 1081 BT, Amsterdam, the Netherlands. Tel: +31 20 5982000. Email: a.b.maier@vu.nl

Abstract

Background: Sarcopenia is highly prevalent in geriatric rehabilitation patients and can worsen prognosis. This study aimed to investigate the association of sarcopenia and components of sarcopenia with 3-month and 1-year post-discharge mortality in geriatric rehabilitation inpatients.

Methods: REStORing health of acutely unwell adults (RESORT) is an observational, prospective longitudinal cohort of geriatric rehabilitation inpatients. Sex-stratified Cox proportional-hazards analyses were used to associate sarcopenia (and its components) at admission, by the European Working Group on Sarcopenia in Older People (EWGSOP, EWGSOP2) and the Asian Working Group for Sarcopenia 2019 (AWGS 2019), with 3-month and 1-year post-discharge all-cause mortality.

Results: Patients ($n = 1,406$) had a median interquartile ranges [IQR] age of 83.0 [77.4–88.2] years (58% females). Sarcopenia was significantly associated with 3-month and 1-year mortality in females (EWGSOP, EWGSOP2 and AWGS 2019) and males (EWGSOP2, AWGS 2019). In females, low muscle mass (EWGSOP, EWGSOP2 and AWGS 2019) was significantly associated with 3-month and 1-year mortality; low muscle strength (EWGSOP, EWGSOP2 and AWGS 2019) was significantly associated with 1-year mortality. For males, low muscle mass (EWGSOP2, AWGS 2019) was significantly associated with 3-month and 1-year mortality; low muscle strength (EWGSOP2, AWGS 2019) was significantly associated with 3-month mortality. The association between physical performance with mortality was not analysed due to less than five events (death) in patients with normal physical performance.

Conclusions: Sarcopenia, low muscle mass and low muscle strength at admission are associated with a significantly higher risk of mortality post-discharge from geriatric rehabilitation, highlighting the need to measure muscle mass and strength in clinical practice.

Keywords: sarcopenia, muscles, muscle strength, mortality, geriatric rehabilitation, older people

Key Points

- Muscle measures should be investigated in geriatric rehabilitation patients.
- Sarcopenia is associated with mortality.
- Muscle mass is associated with mortality.

- Muscle strength is associated with mortality.

Introduction

Geriatric rehabilitation aims to restore functional capacity through individualised treatment plans [1]. Geriatric rehabilitation inpatients have experienced an acute illness requiring hospitalisation and often suffer from multiple diseases [2]. Sarcopenia is a prevalent comorbid disease [3] in 56% of patients at admission to geriatric rehabilitation [4], can worsen prognosis of many chronic conditions [5, 6] and is associated with multiple adverse health outcomes such as functional decline [7], falls, fractures [8], frailty [9], hospitalisation [7] and mortality in community-dwelling, outpatients, inpatients and nursing home residents [10].

The association between sarcopenia and mortality in geriatric rehabilitation inpatients has been reported in two small cohorts; one study ($n = 99$) showing no difference between patients with and without sarcopenia and 3-month mortality [11] and one study ($n = 172$) showing an association between sarcopenia and a two times higher 1-year mortality risk [12]. Since geriatric rehabilitation gives a window of opportunity for tailored interventions to increase muscle mass, muscle strength and/or physical performance because of the multi-disciplinary approach [1], the investigation of the association of sarcopenia and individual sarcopenia components (low muscle mass, muscle strength and/or physical performance) with mortality post-discharge may be beneficial for the development of treatment plans during geriatric rehabilitation and for the purpose of post-discharge care planning [1].

This study aimed to investigate the association of sarcopenia and its components (low muscle mass, muscle strength, physical performance) with 3-month and 1-year post-discharge mortality in geriatric rehabilitation inpatients.

Methods

Study design

REStORing health of acutely unwell adults (RESORT) is an observational, prospective longitudinal cohort at the Royal Melbourne Hospital in Melbourne, Victoria, Australia. All patients admitted to geriatric rehabilitation wards between 16 October 2017 and 18 March 2020 were eligible for inclusion. Written informed consent was provided by included patients or a nominated proxy. Patients were excluded if they were unable to consent and had no nominated proxy to consent on their behalf, or if patients were receiving palliative care at admission. Of the 2,246 patients who were considered eligible for participation, 356 refused consent, leaving 1,890

potential patients. Sarcopenia diagnosis was completed in 1,452 patients at admission. Forty-six patients died during hospitalisation leaving 1,406 patients for analyses. The study was approved by the Melbourne Health Human Research Ethics Committee (no. HREC/17/MH/103) and followed national and international ethical guidelines according to the Helsinki Declaration.

Patient characteristics

Patients were assessed within 48 hours after admission by physicians, nurses, physiotherapists, occupational therapists and dietitians following a standardised Comprehensive Geriatric Assessment. Age, sex and length of stay at geriatric rehabilitation were extracted from medical records. Living situation and ethnicity were collected through a questionnaire complete by the patient, carer, a researcher assisting the patient or data were extracted from medical records. Standing height in metres was measured when patients were able to stand (footwear removed); when unable to stand, knee height was measured. Knee height was measured using a sliding calliper with knee positioned at 90° and then the Chumlea equation was used to calculate standing height from knee height [13]. Weight in kilogrammes was measured on a calibrated standing weighing scale, weighing chair or hoist (footwear and heavy clothing removed). Body mass index was calculated by dividing weight by height squared and presented as kg/m². Activities of Daily Living was assessed using the Katz index with scores ranging from 0 to 6 points [14], Independent Activities of Daily Living was assessed using the Lawton and Brody scale with scores ranging from 0 to 8 [15], with a higher score indicating greater independence for both tests. Frailty was assessed using Clinical Frailty Scale with scores ranging from 0 to 9, a higher score meaning greater severity of frailty [16]. Morbidity was assessed using the Charlson Comorbidity Index (CCI) with scores ranging from 0 to 37 [17], with a higher score indicative of higher morbidity. Disease severity was assessed using the Cumulative Illness Rating Scale with scores ranging from 0 to 56 [18]. Cognitive impairment was defined by either a dementia diagnosis documented in medical records, or an abnormal score through cognitive screening tools: a score of <24 on the standardised Mini-Mental State Examination [19], a score of <26 on the Montreal Cognitive Assessment [20]; a score of <23 on the Rowland Universal Dementia Assessment [21]. Delirium was defined as a delirium reported in medical records or the risk of delirium by the short Confused Assessment Method [22]. The Malnutrition Screening Tool was used to determine nutritional status; a score of ≥ 2 indicated risk of malnutrition [23].

Sarcopenia components

Direct segmental bio-electrical impedance analysis (DSM-BIA, InBody S10, Biospace Co., Ltd., Seoul, South Korea) was used to measure skeletal muscle mass (SMM) and appendicular lean mass (ALM), both expressed in kilogrammes. Skeletal muscle mass index (SMI) was defined as SMM divided by height squared and expressed in kg/m^2 . BIA was not performed in case of a pacemaker or other electronic medical device ($n = 25$); amputation ($n = 2$); cast/dressing ($n = 7$); contact precautions ($n = 4$); medical contraindication ($n = 9$); refusing ($n = 3$); technical issues ($n = 2$). Reasons were unknown/missing reason in 59 patients.

Handgrip strength (HGS) was measured using a Jamar Hydraulic Handheld Dynamometer (JAMAR, Sammons Preston, Inc., 119 Bollingbrook, IL, USA) in a sitting position with the elbow bent at 90° to the body, exerting maximum force, three times alternating for both hands. The maximum value of the three trials, expressed in kilogrammes, was used for the analysis [24].

The Short Physical Performance Battery (SPPB) includes balance tests, 4-metre walk test and chair stand test, with a total score ranging from 0 to 12 points, where a higher score indicates better physical function [25]. Gait speed (m/s) was measured as the time taken to walk 4 m at a usual pace with or without a walking aid, measured twice and the fastest time was used for analysis. The chair stand test was timed from the beginning of the first rise until seated again after the fifth rise in seconds (s) [26]. Patients were instructed to stand up as fast as possible.

If a patient was unable to complete the muscle strength and/or physical performance tests due to medical reasons such as fatigue and pain, their assessments were classified as abnormal.

Sarcopenia diagnosis

Patients were assessed for sarcopenia by the following sarcopenia definitions: European Working Group on Sarcopenia in Older People (EWGSOP), the current operational definition in Australia [27], European Working Group on Sarcopenia in Older People 2018 (EWGSOP2) [28] and Asian Working Group for Sarcopenia 2019 (AWGS 2019) [29].

The EWGSOP definition includes the following criteria: (i) low muscle mass ($\text{SMI} \leq 10.75 \text{ kg}/\text{m}^2$ in males and $\text{SMI} \leq 6.75 \text{ kg}/\text{m}^2$ in females [30]) and; (ii) low muscle strength (HGS of $< 30 \text{ kg}$ in males and $< 20 \text{ kg}$ in females [31]) and/or (iii) low physical performance (gait speed of $\leq 0.8 \text{ m}/\text{s}$ or SPPB score of ≤ 8 points).

The EWGSOP2 definition includes (i) low muscle strength (HGS of $< 27 \text{ kg}$ for males and $< 16 \text{ kg}$ for females or a chair stand time $> 15 \text{ s}$) and (ii) low muscle mass ($\text{ALM}/\text{height}^2 < 7.0 \text{ kg}/\text{m}^2$ for males and $\text{ALM}/\text{height}^2 < 5.5 \text{ kg}/\text{m}^2$ for females), indicating confirmed sarcopenia. Low physical performance (gait speed of $\leq 0.8 \text{ m}/\text{s}$ or a SPPB score of ≤ 8 points) was used to define severe sarcopenia.

The AWGS 2019 definition includes (i) low muscle mass ($\text{ALM}/\text{height}^2 < 7.0 \text{ kg}/\text{m}^2$ in males and $\text{ALM}/\text{height}^2 < 5.7 \text{ kg}/\text{m}^2$ in females) and (ii) low muscle strength (HGS of $< 28 \text{ kg}$ for males and $< 18 \text{ kg}$ for females) and/or (iii) low physical performance (gait speed $< 1.0 \text{ m}/\text{s}$ or SPPB score ≤ 9 or chair stand $\geq 12 \text{ s}$).

Mortality

All-cause mortality was assessed at 3-month and 1-year post-discharge from geriatric rehabilitation through the Registry of Births, Deaths and Marriages Victoria and through medical records.

Statistical analyses

Patient characteristics were reported using descriptive statistics. Categorical variables were presented as a frequencies (n) with percentages (%). Continuous variables that were normally distributed were displayed as means \pm standard deviations. Continuous variables that were skewed were presented as medians and interquartile ranges [IQR].

Kaplan–Meier survival curves stratified by sex, grouped by sarcopenia definition, visualised the cumulative survival probability over the 1-year follow-up period. As the prevalence of sarcopenia is found to be higher in males [32], sex was tested as an effect modifier through interaction terms, revealing a positive result, therewith all analysis were sex stratified [33]. Univariable Cox proportional hazard analyses were performed to analyse the association between sarcopenia and mortality at 3-month and 1-year post-discharge. The multivariable Cox proportional hazard analyses were adjusted for age and CCI score. Sex was tested as a potential effect modifier using an interaction term. The association between components of sarcopenia (muscle mass, muscle strength, physical performance) and 3-month and 1-year mortality was analysed if there were ≥ 5 events (death) in each of the normal and low groups [34]. Results were presented as hazard ratios (HR) and 95% confidence intervals (CI). P -values < 0.05 were considered statistically significant. Statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS Advanced Statistics 25.0, Armonk, NY: IBM Corp.).

Results

Table 1 shows the characteristics of 1,406 included patients. The median [IQR] age was 83.0 years [77.4–88.2] and 58.0% were female. The median [IQR] length of stay in geriatric rehabilitation was 19.7 [13.0–30.0] days. The prevalence of sarcopenia for females and males ranged from 7.0% to 24.4% and 25.0% to 81.4% depending on the sarcopenia definitions used. Of patients classified as having sarcopenia by the EWGSOP2, 96.9% were considered as having severe sarcopenia. The prevalence of low muscle mass ranged from 7.0% to 24.4% for females and from 30.3% to 82.9% for males and the prevalence of low muscle strength

Table 1. Patient characteristics at admission to geriatric rehabilitation and mortality 3-month and 1-year post-discharge

	<i>n</i>	Total <i>n</i> = 1,406	<i>n</i>	Females <i>n</i> = 816	<i>n</i>	Males <i>n</i> = 590
Demographics						
Age, years	1,406	83.0 [77.4–88.2]	816	83.0 [77.9–88.3]	590	82.8 [76.1–88.1]
Living alone, <i>n</i> (%)	1,404	623 (44.4)	814	391 (48.0)	590	232 (39.3)
Length of stay, days	1,406	19.7 [13.0–30.0]	816	19.7 [10.1–30.7]	590	19.5 [12.9–29.9]
Ethnicity						
European/Caucasian, <i>n</i> (%)	1,363	1,194 (87.6)	797	694 (87.1)	566	500 (88.3)
Asian, <i>n</i> (%)	1,363	70 (5.10)	797	42 (5.30)	566	28 (4.90)
Physical characteristics						
BMI, kg/m ²	1,399	26.3 [22.8–30.6]	810	27.0 [22.9–31.4]	589	25.6 [22.7–29.7]
CFS, score	1,289	6 [5–7]	750	6 [5–7]	539	6 [5–7]
ADL, score	1,392	2 [1–3]	806	2 [1–3]	586	2 [1–3]
IADL, score	1,392	1 [0–2]	806	1 [0–2]	586	1 [0–2]
Morbidity and nutritional status						
CCI, score	1,406	2 [1–4]	816	2 [1–3]	590	3 [1–4]
CIRS, score	1,405	12 [8–15]	816	12 [8–15]	589	12 [9–16]
Malnutrition risk, <i>n</i> (%)	1,317	678 (51.5)	756	251 (33.2)	561	427 (76.1)
Cognitive condition						
Cognitively impaired, <i>n</i> (%)	1,204	750 (62.3)	705	419 (59.4)	499	331 (66.3)
Delirium, <i>n</i> (%)	1,406	319 (22.7)	816	174 (21.3)	590	145 (24.6)
Sarcopenia						
EWGSOP, <i>n</i> (%)	1,296	503 (38.8)	742	52 (7.00)	554	451 (81.4)
EWGSOP2 ^a , <i>n</i> (%)	1,399	266 (19.0)	812	112 (13.8)	587	154 (26.2)
EWGSOP2 ^b , <i>n</i> (%)	1,390	249 (17.9)	806	103 (12.8)	584	146 (25.0)
AWGS 2019, <i>n</i> (%)	1,287	346 (26.9)	737	180 (24.4)	550	166 (30.2)
Sarcopenia components						
EWGSOP						
Low muscle mass, <i>n</i> (%)	1,295	511 (39.5)	741	52 (7.00)	554	459 (82.9)
Low muscle strength, <i>n</i> (%)	1,355	1121 (82.7)	782	650 (83.1)	573	471 (82.2)
Low physical performance, <i>n</i> (%)	1,390	1326 (95.4)	808	784 (97.0)	582	542 (93.1)
EWGSOP2						
Low muscle mass, <i>n</i> (%)	1,288	304 (23.6)	737	137 (18.6)	551	167 (30.3)
Low muscle strength, <i>n</i> (%)	1,405	934 (66.5)	815	510 (62.6)	590	424 (71.9)
Low physical performance, <i>n</i> (%)	1,390	1326 (95.4)	808	784 (97.0)	582	542 (93.1)
AWGS 2019						
Low muscle mass, <i>n</i> (%)	1,288	347 (26.9)	737	180 (24.4)	551	167 (30.3)
Low muscle strength, <i>n</i> (%)	1,355	972 (71.7)	782	557 (71.2)	573	415 (72.4)
Low physical performance, <i>n</i> (%)	1,396	1374 (98.4)	808	798 (98.8)	588	576 (98.0)
Mortality						
3-month, <i>n</i> (%)	1,406	91 (6.47)	816	43 (5.30)	590	48 (8.10)
1-year, <i>n</i> (%)	1,406	225 (16.0)	816	96 (11.8)	590	129 (21.9)

All data presented as median [IQR] unless otherwise stated. ADL, Activities of Daily Living; AWGS 2019, Asian Working Group for Sarcopenia 2020; BMI, body mass index; CFS, Clinical Frailty Scale; CIRS, Cumulative Illness Rating Scale; IADL, Independent Activities of Daily Living. ^aNon-severe (confirmed) sarcopenia.

^bSevere sarcopenia.

was between 62.6% and 83.1% for females and 71.9% and 82.2% for males dependent on sarcopenia definitions. The prevalence of low physical performance ranged from 97.0% to 98.8% for females and from 93.1% to 98.0% for males. At 3-month post-discharge, 5.3% of females and 8.1% of males were deceased. At 1-year post-discharge, 11.8% of females and 21.9% of males were deceased. The prevalence of sarcopenia and sarcopenia components, stratified by deceased and alive at 3-month and 1-year post-discharge can be found in Appendix Table 1 (a, b, c). The association between low physical performance by the EWGSOP, EWGSOP2 and AWGS 2019 with 3-month and 1-year mortality was not analysed due to the occurrence of <five events (death) in the normal physical performance groups (Appendix Table 1 (c)).

Sex was found to be an effect modifier and therefore all analyses were stratified by sex. Figure 1 shows the survival curves of groups with and without sarcopenia stratified by sex. Tables 2 and 3 show the results of the cox-regression analysis of sarcopenia, and sarcopenia components with mortality, stratified by sex. In females, sarcopenia diagnosed by the EWGSOP (HR: 4.81, 95% CI: 2.27–10.2, HR: 3.74, 95% CI: 2.13–6.56), EWGSOP2 (HR: 2.95, 95% CI: 1.56–5.60, HR: 2.93, 95% CI: 1.89–4.54) and AWGS 2019 (HR: 2.13, 95% CI: 1.12–4.02, HR: 1.93, 95% CI: 1.25–2.99) was significantly associated with 3-month and 1-year mortality, respectively after adjusting for age and CCI score.

In males, sarcopenia diagnosed by the EWGSOP2 (HR: 3.72, 95% CI: 2.06–6.72, HR: 1.92, 95% CI: 1.34–2.77) and AWGS 2019 (HR: 1.26, 95% CI: 1.14–1.38, HR:

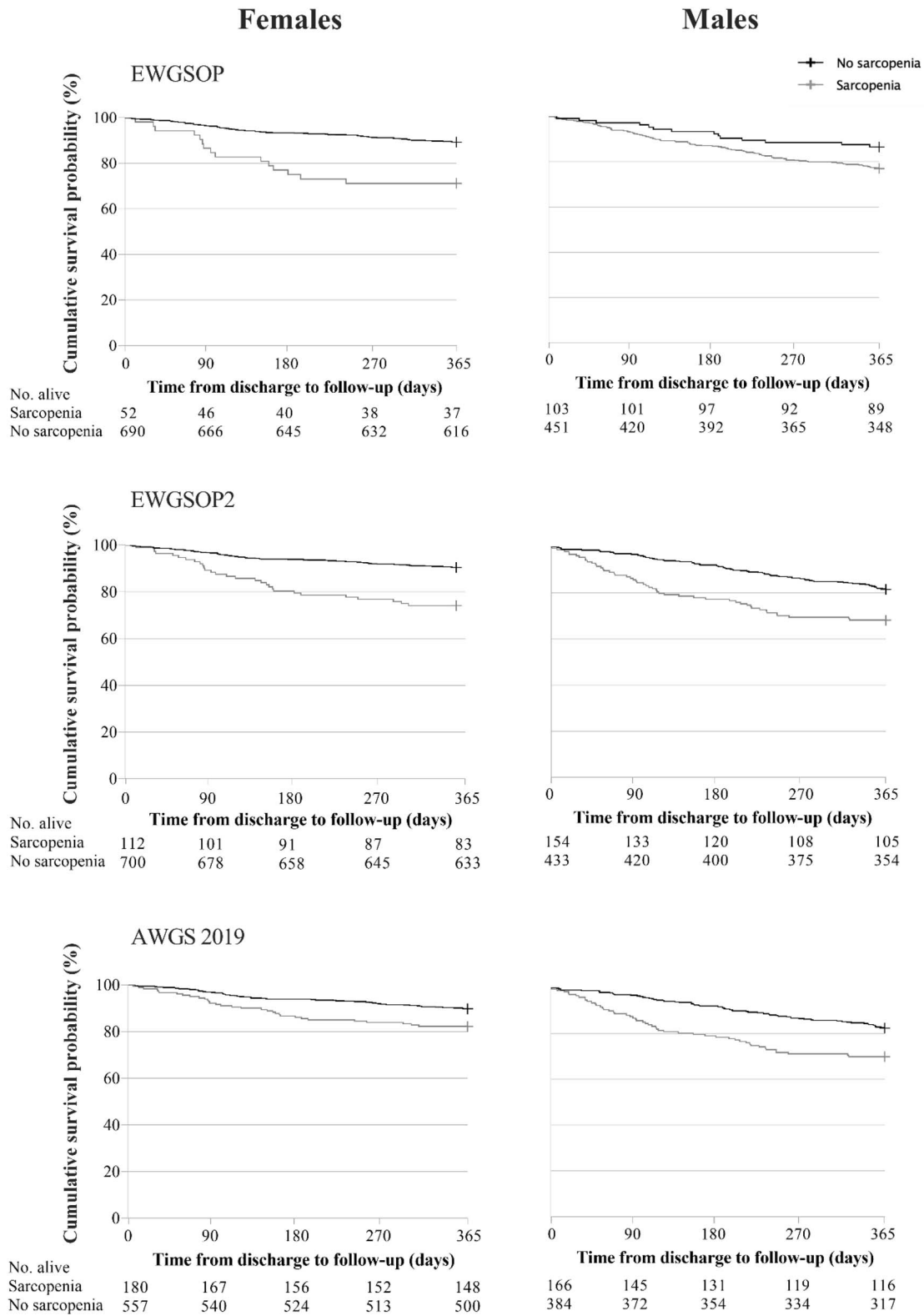


Figure 1. Kaplan–Meier survival curves for the association between sarcopenia and 1-year mortality in geriatric rehabilitation inpatients.

Table 2. Association of sarcopenia with 3-month and 1-year mortality in geriatric rehabilitation inpatients

		<i>N</i>	Crude		Adjusted ^d	
			HR (95% CI)	<i>P</i> -value	HR (95% CI)	<i>P</i> -value
3-month mortality						
EWGSOP ^a	F	742	4.08 (1.94, 8.56)	<0.001	4.81 (2.27, 10.2)	<0.001
	M	554	2.33 (0.84, 6.52)	0.106	1.49 (0.51, 4.32)	0.465
EWGSOP2 ^b	F	812	3.13 (1.66, 5.93)	<0.001	2.95 (1.56, 5.60)	0.001
	M	587	4.08 (2.29, 7.28)	<0.001	3.72 (2.06, 6.72)	<0.001
AWGS 2019 ^c	F	737	2.12 (1.13, 3.99)	0.020	2.13 (1.12, 4.02)	0.020
	M	550	3.92 (2.14, 7.19)	<0.001	1.26 (1.14, 1.38)	<0.001
1-year mortality						
EWGSOP ^a	F	742	3.08 (1.77, 5.36)	<0.001	3.74 (2.13, 6.56)	<0.001
	M	554	1.77 (1.01, 3.10)	0.045	1.19 (0.66, 2.13)	0.565
EWGSOP2 ^b	F	812	2.99 (1.93, 4.63)	<0.001	2.93 (1.89, 4.54)	<0.001
	M	587	2.01 (1.41, 2.88)	<0.001	1.92 (1.34, 2.77)	<0.001
AWGS 2019 ^c	F	737	1.84 (1.19, 2.83)	0.006	1.93 (1.25, 2.99)	0.003
	M	550	1.96 (1.36, 2.83)	<0.001	1.86 (1.28, 2.70)	0.001

Bold values indicate statistical significance $P < 0.05$. F, females; M, males. Patients able to be diagnosed by the definition as having sarcopenia or not having sarcopenia: ^a1,296. ^b1,399. ^c1,287. ^dAdjusted for age and CCI score.

Table 3. Association of sarcopenia components (muscle mass, muscle strength) and 3-month and 1-year mortality in geriatric rehabilitation inpatients

		N	Crude		Adjusted ^a	
			HR (95% CI)	P-value	HR (95% CI)	P-value
3-month mortality						
EWGSOP						
Muscle mass	F	741	4.19 (2.06, 8.52)	<0.001	4.91 (2.39, 10.1)	<0.001
	M	554	1.78 (0.70, 4.50)	0.223	1.14 (0.43, 3.00)	0.795
Muscle strength	F	782	2.02 (0.73, 5.61)	0.175	1.72 (0.61, 4.84)	0.305
	M	573	3.61 (1.13, 11.6)	0.031	2.71 (0.84, 8.74)	0.095
EWGSOP2						
Muscle mass	F	737	2.71 (1.46, 5.06)	0.002	2.70 (1.44, 5.03)	0.002
	M	551	3.53 (1.94, 6.33)	<0.001	3.18 (1.75, 5.79)	<0.001
Muscle strength	F	815	1.68 (0.89, 3.18)	0.110	1.58 (0.83, 3.00)	0.167
	M	590	3.05 (1.32, 7.06)	0.009	2.56 (1.10, 5.94)	0.039
AWGS 2019						
Muscle mass	F	737	2.11 (1.14, 3.91)	0.017	2.16 (1.16, 4.02)	0.015
	M	551	3.53 (1.97, 6.33)	<0.001	3.18 (1.75, 5.79)	<0.001
Muscle strength	F	782	2.10 (0.95, 4.66)	0.067	1.81 (0.81, 4.07)	0.151
	M	573	2.83 (1.22, 6.57)	0.016	2.36 (1.01, 5.48)	0.047
1-year mortality						
EWGSOP						
Muscle mass	F	741	3.21 (1.90, 5.43)	<0.001	3.91 (2.29, 6.66)	<0.001
	M	554	1.55 (0.90, 2.66)	0.112	1.05 (0.59, 1.84)	0.875
Muscle strength	F	782	2.74 (1.28, 5.87)	0.010	2.40 (1.11, 5.19)	0.027
	M	573	2.00 (1.13, 3.52)	0.017	1.57 (0.88, 2.78)	0.124
EWGSOP2						
Muscle mass	F	737	2.51 (1.64, 3.83)	<0.001	2.58 (1.69, 3.95)	<0.001
	M	551	1.90 (1.32, 2.72)	<0.001	1.78 (1.23, 2.57)	0.002
Muscle strength	F	815	1.71 (1.12, 2.61)	0.013	1.60 (1.04, 2.45)	0.033
	M	590	1.49 (0.99, 2.24)	0.053	1.27 (0.84, 1.91)	0.249
AWGS 2019						
Muscle mass	F	737	1.81 (1.19, 2.76)	0.006	1.92 (1.25, 2.93)	0.003
	M	551	1.90 (1.32, 2.72)	<0.001	1.77 (1.23, 2.57)	0.002
Muscle strength	F	782	1.96 (1.18, 3.29)	0.010	1.73 (1.02, 2.89)	0.044
	M	573	1.53 (1.01, 2.33)	0.048	1.30 (0.85, 1.99)	0.22

Bold values indicate statistical significance $P < 0.05$. F, females; M, males. ^aAdjusted for age and CCI score.

1.86, 95% CI: 1.28–2.70) was significantly associated with 3-month and 1-year mortality, respectively after adjusting for age and CCI score, but was not associated when using EWGSOP criteria.

Subgroup analysis in females showed that low muscle mass defined by the EWGSOP, EWGSOP2 and AWGS 2019 was significantly associated with 3-month and 1-year mortality after adjusting for age and CCI score. Low muscle strength by the three definitions was significantly associated with 1-year mortality after adjusting for age and CCI score but not associated with 3-month mortality.

Subgroup analysis in males showed that low muscle mass by the EWGSOP2 and AWGS 2019 was significantly associated with 3-month and 1-year mortality after adjusting for age and CCI but not for the EWGSOP definition. Low muscle strength by the EWGSOP2 and AWGS 2019 was significantly associated with 3-month mortality but not associated with 1-year mortality. Low muscle strength by the EWGSOP was not associated with mortality in males.

Discussion

Females with sarcopenia diagnosed by the EWGSOP, EWGSOP2 and AWGS 2019 and males with sarcopenia diagnosed by the EWGSOP2 and AWGS 2019 had a significantly higher risk of mortality 3-month and 1-year post-discharge from geriatric rehabilitation. Low muscle mass and strength were associated with mortality in both females and males.

To the best of our knowledge, our study is the first to evaluate the association of sarcopenia with mortality using recently established definitions of sarcopenia (EWGSOP2, AWGS 2019) in geriatric rehabilitation inpatients. Only two small studies have previously examined the association of sarcopenia with mortality in geriatric rehabilitation inpatients, both reporting sex-unstratified results and using the EWGSOP definition. Of the two studies, one showed a negative result [11] and one reported a two times higher risk of 1-year mortality in patients with sarcopenia [12]. However, in the latter study, patients with delirium and dementia were excluded and adopted cut-off values for muscle strength and gait speed were applied [12]. Our finding that sarcopenia by the EWGSOP2 is significantly associated with mortality is in agreement with a recent meta-analysis showing the positive association independent of population [10]. Two studies have evaluated the sex-specific association of sarcopenia by the EWGSOP and mortality, both conducted in community-dwelling individuals. One revealed a significant association for both females and males [35], the other found an association in males only [36]. A modified EWGSOP algorithm was used in the latter study [34].

Male sex is a risk factor for mortality across all ages and tend to have higher morbidity burden than females [37]. Individuals with more comorbidities and more severe diseases are likely to have poorer base-line health and independently associated with an increased risk of mortality [38–40].

Irrespective of the definition used for the diagnosis, sarcopenia was associated with a significantly higher risk of 3-month and 1-year mortality in females. Only males diagnosed by the EWGSOP2 and AWGS 2019 were associated with a significantly higher risk of 3-month and 1-year mortality. The absence of association observed between the EWGSOP and mortality may be a result of the higher prevalence of males with sarcopenia observed when using the EWGSOP, due to the cut-off points being applied [41]. The adoption of higher cutoffs, translating to a higher prevalence of sarcopenia, leads to the inclusion of a less severe phenotype of the disease. When a sarcopenia definition that uses muscle mass [27] rather than muscle strength [28, 29] as the core component of the diagnostic algorithm is used, a higher HR was observed in females, which is in accordance with our finding that low muscle mass is consistently associated with mortality.

The finding that the association was independent of the follow-up time is also in agreement with a previous study conducted in hospitalised individuals evaluating the association of sarcopenia by the EWGSOP with short- (in hospital) and long-term (1-year) mortality [42]. Sarcopenia is characterised by low muscle mass and strength, which can contribute to impaired balance [43] leading to falls [44]. Falls can be fatal alone [45] or lead to major consequences such as hospitalisation [46]. As hospitalisation can contribute to a decline in muscle mass [47], it could perpetuate the cycle of muscle mass loss and ultimately, mortality. As the time from discharge increases and the body recovers from the acute illness and the hospital stay, the risk of falls and inturn mortality may lower, explaining the weaker association with 1-year mortality. However, there is currently no evidence that interventions to combat sarcopenia are leading to improved survival, which would underline the causal relationship of sarcopenia and mortality.

Muscle mass was consistently associated with both 3-month and 1-year mortality in females and males. Many studies have shown that low muscle mass is associated with adverse outcomes such as surgical complications [48], discharge to a rehabilitation or nursing facility [49] and mortality [50, 51]. Although unlike other determinants for mortality, such as cognitive impairment [52], muscle mass is sensitive to changes through dietary and exercise interventions [53, 54], making it a targetable modifiable determinant for mortality. Likewise, muscle strength also increases by exercise and nutritional interventions [55, 56], which makes it a modifiable risk factor for mortality. As the purpose of geriatric rehabilitation is to facilitate the functional recovery of individuals through individualised treatment plans [57], and studies have shown that mortality risk is lower in those with normal muscle mass [58] and strength [59], the risks of adverse health outcomes associated with sarcopenia could potentially be reduced. Although the association of low physical performance and mortality could not be analysed in this study, previous meta-analyses have reported that low physical performance (SPPB < 10) [60] and a slower gait speed [60] are associated with higher risk of mortality.

Further research is required to confirm these findings in the geriatric rehabilitation population where opportunities for interventions are present.

Sarcopenia is significantly associated with mortality irrespective of the definition used for the diagnosis, this underlines the importance of identifying individuals who are at risk of sarcopenia through screening and sequential diagnosis at admission to geriatric rehabilitation, followed by interventions. As knowledge about sarcopenia among healthcare professionals [61, 62] and older adults [63] is still poor, there is a high need for educational programs to enable changing clinical practice.

Strengths and limitations

This is the largest study evaluating the association between sarcopenia and mortality within geriatric rehabilitation inpatients and the first to evaluate the individual components of sarcopenia, which are important to guide the development of an internationally recognised sarcopenia definition and to design interventions to combat sarcopenia [60]. The BIA is known to be influenced by hydration status and may have also under-/overestimated fat-free mass and therewith sarcopenia prevalence [64].

Conclusion

In geriatric rehabilitation inpatients, sarcopenia, low muscle mass and strength at admission are significantly associated with higher risk of mortality post-discharge mortality in both females and males. Future research should investigate whether maintenance or increase in muscle mass and strength during hospitalisation leads to better health outcomes.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

Acknowledgements: The authors would like to thank all clinicians and health care professionals at the Royal Park Campus of the Royal Melbourne Hospital for their clinical work and all members of @AgeMelbourne for data collection and data cleaning.

Declaration of Conflicts of Interest: None.

Declaration of Sources of Funding: This research was funded by an unrestricted grant of the University of Melbourne received by Professor Andrea B. Maier and the Medical Research Future Fund (MRFF) provided by the Melbourne Academic Centre for Health (MACH).

References

1. Organisation WH. World Report on Disability 2011. Geneva, Switzerland: World Health Organization. Available from: https://www.who.int/disabilities/world_report/2011/report.pdf (10 October 2020, date last accessed).
2. Achterberg, Cameron ID, Bauer JM, Schols JM. Geriatric rehabilitation-state of the art and future priorities. *J Am Med Dir Assoc* 2019; 20: 396–8.
3. Pacifico J, Geerlings MAJ, Reijnierse EM, Phassoulotis C, Lim WK, Maier AB. Prevalence of sarcopenia as a comorbid disease: a systematic review and meta-analysis. *Exp Gerontol* 2020; 131: 110801.
4. Churilov I, Churilov L, MacIsaac R, Ekinici EI. Systematic review and meta-analysis of prevalence of sarcopenia in post acute inpatient rehabilitation. *Osteoporos Int* 2017; 28: S278–9.
5. Valero V, Amini N, Spolverato G *et al.* Sarcopenia adversely impacts postoperative complications following resection or transplantation in patients with primary liver tumors. *J Gastrointest Surg* 2015; 19: 272–81.
6. Joglekar S, Asghar A, Mott SL *et al.* Sarcopenia is an independent predictor of complications following pancreatic resection for adenocarcinoma. *J Surg Oncol* 2015; 111: 771–5.
7. Beaudart C, Zaaria M, Pasleau F, Reginster JY, Bruyère O. Health outcomes of sarcopenia: a systematic review and meta-analysis. *PLoS One* 2017; 12: e0169548–8.
8. Yeung SSY, Reijnierse EM, Pham VK *et al.* Sarcopenia and its association with falls and fractures in older adults: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle* 2019; 10: 485–500.
9. Greco EA, Pietschmann P, Migliaccio S. Osteoporosis and sarcopenia increase frailty syndrome in the elderly. *Front Endocrinol* 2019; 10: 255–5.
10. Xu J, Wan CS, Ktoris K *et al.* Sarcopenia is associated with mortality in adults: a systematic review and meta-analysis. *Gerontology*. In press. doi: 10.1159/000517099.
11. Sánchez-Rodríguez D, Marco E, Miralles R *et al.* Sarcopenia, physical rehabilitation and functional outcomes of patients in a subacute geriatric care unit. *Arch Gerontol Geriatr* 2014; 59: 39–43.
12. Pérez-Zepeda MU, Sgaravatti A, Dent E. Sarcopenia and post-hospital outcomes in older adults: a longitudinal study. *Arch Gerontol Geriatr* 2017; 69: 105–9.
13. Chumlea WC, Guo SS, Steinbaugh ML. Prediction of stature from knee height for black and white adults and children with application to mobility-impaired or handicapped persons. *J Am Diet Assoc* 1994; 94: 1385–891 quiz 89–90.
14. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *Gerontologist* 1970; 10: 20–30.
15. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969; 9: 179–86.
16. Rockwood K, Song X, MacKnight C *et al.* A global clinical measure of fitness and frailty in elderly people. *Can Med Assoc J* 2005; 173: 489–95.
17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40: 373–83.
18. Miller MD, Paradis CF, Houck PR *et al.* Rating chronic medical illness burden in geropsychiatric practice and research: application of the Cumulative Illness Rating Scale. *Psychiatry Res* 1992; 41: 237–48.
19. Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; 12: 189–98.

20. Nasreddine ZS, Phillips NA, Bäckström VÁ© *et al.* The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005; 53: 695–9.
21. Storey JE, Rowland JT, Basic D, Conforti DA, Dickson HG. The Rowland Universal Dementia Assessment Scale (RUDAS): a multicultural cognitive assessment scale. *Int Psychogeriatr* 2004; 16: 13–31.
22. Inouye SK, van Dyck CH, Alessi CA, Balkin S, Siegel AP, Horwitz RI. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Ann Intern Med* 1990; 113: 941–8.
23. Ferguson M, Capra S, Bauer J, Banks M. Development of a valid and reliable malnutrition screening tool for adult acute hospital patients. *Nutrition* 1999; 15: 458–64.
24. Reijnierse EM, de Jong N, Trappenburg MC *et al.* Assessment of maximal handgrip strength: how many attempts are needed? *J Cachexia Sarcopenia Muscle* 2017; 8: 466–74.
25. Guralnik JM, Simonsick EM, Ferrucci L *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.
26. Cesari M, Kritchevsky SB, Newman AB *et al.* Added value of physical performance measures in predicting adverse health-related events: results from the health, aging and body composition study. *J Am Geriatr Soc* 2009; 57: 251–9.
27. 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: 412–23.
28. Cruz-Jentoft AJ, Bahat G, Bauer J *et al.* Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2018; 48: 16–31.
29. Chen LK, Woo J, Assantachai P *et al.* Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc* 2020; 21: 300–07.e2.
30. Janssen I, Baumgartner RN, Ross R, Rosenberg IH, Roubenoff R. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. *Am J Epidemiol* 2004; 159: 413–21.
31. Lauretani F, Russo CR, Bandinelli S *et al.* Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol* (1985) 2003; 95: 1851–60.
32. Janssen I. The epidemiology of sarcopenia. *Clin Geriatr Med* 2011; 27: 355–63.
33. Miettinen O. Confounding and effect-modification. *Am J Epidemiol* 1974; 100: 350–3.
34. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and cox regression. *Am J Epidemiol* 2007; 165: 710–8.
35. Woo J, Leung J, Morley JE. Defining sarcopenia in terms of incident adverse outcomes. *J Am Med Dir Assoc* 2015; 16: 247–52.
36. Kim JH, Lim S, Choi SH *et al.* Sarcopenia: an independent predictor of mortality in community-dwelling older Korean men. *J Gerontol A Biol Sci Med Sci* 2014; 69: 1244–52.
37. Almagro P, López García F, Cabrera FJ *et al.* Comorbidity and gender-related differences in patients hospitalized for COPD. The ECCO study. *Respir Med* 2010; 104: 253–9.
38. Kuwabara K, Imanaka Y, Matsuda S *et al.* The association of the number of comorbidities and complications with length of stay, hospital mortality and LOS high outlier, based on administrative data. *Environ Health Prev Med* 2008; 13: 130–7.
39. Sanyaolu A, Okorie C, Marinkovic A *et al.* Comorbidity and its Impact on Patients with COVID-19. *SN Compr Clin Med* 2020; 2: 1–8.
40. Lee YK, Hong N, Park SH *et al.* The relationship of comorbidities to mortality and cause of death in patients with differentiated thyroid carcinoma. *Sci Rep* 2019; 9: 11435.
41. Van Ancum JM, Alcazar J, Meskers CGM *et al.* Impact of using the updated EWGSOP2 definition in diagnosing sarcopenia: a clinical perspective. *Arch Gerontol Geriatr* 2020; 90: 104125.
42. 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: 1154–61.
43. Bijlsma AY, Pasma JH, Lambers D *et al.* Muscle strength rather than muscle mass is associated with standing balance in elderly outpatients. *J Am Med Dir Assoc* 2013; 14: 493–8.
44. Muir SW, Berg K, Chesworth B, Klar N, Speechley M. Quantifying the magnitude of risk for balance impairment on falls in community-dwelling older adults: a systematic review and meta-analysis. *J Clin Epidemiol* 2010; 63: 389–406.
45. Spaniolas K, Cheng JD, Gestring ML *et al.* Ground level falls are associated with significant mortality in elderly patients. *J Trauma* 2010; 69: 821–5.
46. AIHW. Falls Most Common Cause of Hospitalised Injury—With Numbers Rising. Williamstown, Victoria, Australia: Australian Government, 2018 Available from: <https://www.aihw.gov.au/news-media/media-releases/2018/may/falls-most-common-cause-of-hospitalised-injury-wit>.
47. van Ancum JM, Scheerman K, Jonkman NH *et al.* Change in muscle strength and muscle mass in older hospitalized patients: a systematic review and meta-analysis. *Exp Gerontol* 2017; 92: 34–41.
48. Harada K, Ida S, Baba Y *et al.* Prognostic and clinical impact of sarcopenia in esophageal squamous cell carcinoma. *Dis Esophagus* 2016; 29: 627–33.
49. Bokshan SL, Han AL, DePasse JM *et al.* Effect of sarcopenia on postoperative morbidity and mortality after thoracolumbar spine surgery. *Orthopedics* 2016; 39: e1159–64.
50. Wang H, Hai S, Liu Y, Liu Y, Dong B. Skeletal muscle mass as a mortality predictor among nonagenarians and centenarians: a prospective cohort study. *Sci Rep* 2019; 9: 2420.
51. Ginzburg Y, Shmilovitz I, Monastyrsky N, Endevelt R, Shahr DR. Barriers for nutritional care in the transition from hospital to the community among older patients. *Clin Nutr ESPEN* 2018; 25: 56–62.
52. Wang M-C, Li T-C, Li C-I *et al.* Cognitive function and its transitions in predicting all-cause mortality among urban community-dwelling older adults. *BMC Psychiatry* 2020; 20: 203–3.
53. McGlory C, van Vliet S, Stokes T, Mittendorfer B, Phillips SM. The impact of exercise and nutrition in the regulation of skeletal muscle mass. *J Physiol* 2018; 597: 1251–8.
54. Martin-Cantero A, Reijnierse EM, Gill BMT, Maier AB. Factors influencing the efficacy of nutritional interventions

- on muscle mass in older adults: a systematic review and meta-analysis. *Nutr Rev* 2020; 79: 315–30.
55. Liberman K, Forti LN, Beyer I, Bautmans I. The effects of exercise on muscle strength, body composition, physical functioning and the inflammatory profile of older adults: a systematic review. *Curr Opin Clin Nutr Metab Care* 2017; 20: 30–53.
56. Rus GE, Porter J, Brunton A *et al.* Nutrition interventions implemented in hospital to lower risk of sarcopenia in older adults: A systematic review of randomised controlled trials. *Nutr Diet* 2020; 77: 90–102.
57. Organization WH. World Report on Disability 2011. Geneva, Switzerland: World Health Organization, 2011.
58. Xiao J, Caan BJ, Cespedes Feliciano EM *et al.* Association of low muscle mass and low muscle radiodensity with morbidity and mortality for colon cancer surgery. *JAMA Surg* 2020; 155: 942–9.
59. García-Hermoso A, Cavero-Redondo I, Ramírez-Vélez R *et al.* Muscular strength as a predictor of all-cause mortality in an apparently healthy population: a systematic review and meta-analysis of data from approximately 2 million men and women. *Arch Phys Med Rehabil* 2018; 99: 2100–13.e5.
60. Pavasini R, Guralnik J, Brown JC *et al.* Short physical performance battery and all-cause mortality: systematic review and meta-analysis. *BMC Med* 2016; 14: 215.
61. Reijnierse EM, de van der Schueren MAE, Trappenburg MC, Doves M, Meskers CGM, Maier AB. Lack of knowledge and availability of diagnostic equipment could hinder the diagnosis of sarcopenia and its management. *PLoS One* 2017; 12: e0185837.
62. Yeung SSY, Reijnierse EM, Trappenburg MC *et al.* Current knowledge and practice of Australian and New Zealand health-care professionals in sarcopenia diagnosis and treatment: time to move forward! *Australas J Ageing* 2020; 39: e185–93.
63. van Ancum JM, Meskers CGM, Reijnierse EM *et al.* Lack of knowledge contrasts the willingness to counteract sarcopenia among community-dwelling adults. *J Aging Health* 2020; 32: 787–94.
64. Leahy S, O'Neill C, Sohun R, Jakeman P. A comparison of dual energy X-ray absorptiometry and bioelectrical impedance analysis to measure total and segmental body composition in healthy young adults. *Eur J Appl Physiol* 2012; 112: 589–95.

Received 14 January 2021; editorial decision 3 May 2021