The Association between Sarcopenia as a Comorbid Disease and Incidence of Institutionalisation and Mortality in Geriatric Rehabilitation Inpatients: REStORing health of acutely unwell adults (RESORT)

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Keywords

Sarcopenia · Comorbidity · Institutionalisation · Mortality

Abstract

Introduction: Sarcopenia is associated with poor health outcomes and highly prevalent in individuals with age-related diseases. This study aimed to determine whether sarcopenia as a comorbid disease is associated with the incidence of institutionalisation and mortality in geriatric rehabilitation inpatients. **Methods:** REStORing health of acutely unwell adults (RESORT) includes geriatric rehabilitation patients assessed for sarcopenia (the European Working Group on Sarcopenia in Older People [EWGSOP, 2010], EWGSOP2 [2018], and the Asian Working Group for Sarcopenia [AWGS 2019]), multimorbidity, disease severity, and specific diseases (Charlson Comorbidity Index and Cumulative Illness Rating Scale) at admission. The incidence of institutionalisation and mortality was recorded 3 months after discharge. Logistic regressions were adjusted for age and sex with “low morbidity and no sarcopenia” as the reference group. **Results:** In 549 included patients (median age was 82.2 [77.4–87.7] years,

58.3% female), sarcopenia prevalence was 37.9, 18.6, and 26.1% according to EWGSOP, EWGSOP2, and AWGS 2019, respectively. Sarcopenia as a comorbid disease with high multimorbidity, dementia, diabetes mellitus, and renal impairment had higher odds of institutionalisation incidence. Sarcopenia as a comorbid disease with high multimorbidity, high disease severity, chronic obstructive pulmonary disease, osteoporosis, and renal impairment had higher odds of mortality. **Conclusion:** Sarcopenia as a comorbid disease is associated with a higher incidence of institutionalisation and mortality in geriatric rehabilitation inpatients. This highlights the need for in-hospital sarcopenia diagnostics and interventions.

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Introduction

Sarcopenia is a disease characterised by low skeletal muscle mass (SMM), muscle strength, and physical performance [1]. The prevalence of sarcopenia is 15% in healthy older adults, 34% in geriatric outpatients [2], and

even higher amongst hospitalised patients admitted to acute (40%) [3]. Sarcopenia is associated with poor health outcomes such as falls, fractures [4], institutionalisation [5], and mortality [6].

A recent meta-analysis showed a higher prevalence of sarcopenia amongst individuals diagnosed with cardiovascular disease (CVD), dementia, diabetes mellitus (DM), and respiratory disease [7]. Multimorbidity is the coexistence of 2 or more diseases, and comorbidity is the coexistence of 1 or more diseases with respect to an index disease [8]. Geriatric rehabilitation inpatients very often suffer from multimorbidity [9], which is associated with institutionalisation and mortality [10]. However, there is a paucity of knowledge if sarcopenia as a comorbid disease worsens these health outcomes. The aim of this study was to determine if sarcopenia as a comorbid disease is associated with the incidence of institutionalisation and mortality in geriatric rehabilitation inpatients.

Materials and Methods

Study Design and Patients

REStORing health of acutely unwell adults (RESORT) is a longitudinal, observational, prospective inception cohort. Patients were recruited from geriatric rehabilitation wards (Royal Melbourne Hospital, Melbourne, Australia). The comprehensive geriatric assessment [11] was performed on all patients upon admission and discharge. The comprehensive geriatric assessment assesses a patient's functional, psychological, and medical status to establish an effective treatment plan. Follow-up phone calls were performed at 3 months post-discharge.

Wave 1 data were used for the present analysis, comprising of patients admitted from October 16, 2017 and discharged by August 31, 2018. Patients were excluded if they were palliative at admission or had no capacity to consent and no nominated proxy. Of the 995 patients admitted, 152 patients were excluded, and 150 patients refused consent. Of the remaining 693, sarcopenia diagnosis was possible in 550 patients; online suppl. Table 1 (see www.karger.com/doi/10.1159/000517461 for all online suppl. material) shows the data availability for sarcopenia diagnosis. Mortality data were available for all patients and institutionalisation for 464 patients.

Patient Characteristics

Age, sex, and the length of stay were collected from the patients' medical records. Each patient's living status was collected via a patient survey, completed at admission to geriatric rehabilitation. Cognitive impairment was assessed by physicians and defined as being present if it was endorsed on either the Charlson Comorbidity Index (CCI) [12] or Cumulative Illness Rating Scale – geriatric version (CIRS-G) [13]; dementia or mild cognitive impairment/minor neurocognitive disorder was listed in the discharge summary as a diagnosis; or in the presence of any of a standardised Mini-Mental State Examination (sMMSE) [14] score of <24 points, a Montreal Cognitive Assessment (MoCA) [15] score <26 points,

or a Rowland Universal Dementia Assessment Scale (RUDAS) [16] score <23 points. Nurses completed the malnutrition screening tool [17] with each patient and activities of daily living were assessed by occupational therapists using the Katz activities of daily living index [18], both completed at admission to geriatric rehabilitation.

Morbidity

Physicians captured the medical history and completed the CCI and the CIRS-G. The CCI is a comorbidity index including 19 diseases with a total score ranging from 0 to 37. High multimorbidity was defined as a CCI score ≥ 3 points, based on the median score of the cohort. The CIRS-G is a rating scale, where 14 organ systems are assigned an integer between 0 (no severity) and 4 (high severity) based on the most severe condition afflicting the organ system, leading to a final total score ranging from 0 to 56. The severity index was calculated as total score divided by number of affected systems and provides an estimation of severity of bodily dysfunction. High disease severity was defined as a CIRS-G severity index ≥ 1.91 (indicating moderate to severe severity), based on the mean for the cohort.

Specific diseases included were CVD (myocardial infarction, heart failure, hypertension, transient ischaemic attack, ischaemic stroke, and haemorrhagic stroke), dementia (Alzheimer's dementia, mixed dementia, Lewy body dementia, Parkinson's dementia, and vascular dementia), DM (types 1 and 2), chronic obstructive pulmonary disease (COPD), osteoporosis, and renal impairment (acute and chronic renal impairment, and renal calculi). These diseases were chosen as they are highly prevalent in the older populations [19] and are amongst the top ten leading causes of global deaths [20].

Sarcopenia Measures

Muscle mass, muscle strength, and physical performance were measured at admission to geriatric rehabilitation. Direct segmental multifrequency bioelectrical impedance analysis ([DSM-BIA], In-Body S10, Biospace Co., Ltd, Seoul, Korea) was used by trained nursing staff to assess body composition. DSM-BIA measurements were not performed on patients with cardiac pacemakers, limb amputations, or bandages or plasters which interfered with electrode placement and could not be removed. Muscle mass was expressed as SMM (kg) and appendicular lean mass (ALM, kg). DSM-BIA has been validated for whole and segmental body composition measurements against dual energy X-ray absorptiometry and is more practical than the latter in this population [21]. SMI was calculated as $\text{SMM}/\text{height}^2$ (kg/m^2) and $\text{ALM}/\text{height}^2$ was calculated as $\text{ALM}/\text{height}^2$ (kg/m^2). Height was determined by standing height or if a patient was unable to stand, knee height was used to approximate standing height, as calculated by the Longitudinal Aging Study Amsterdam (LASA) formulae [22]: $\text{height (cm)} = 74.48 - (0.15 \times \text{age}) + (2.03 \times \text{knee height [cm]})$ for males and $\text{height (cm)} = 68.74 - (0.16 \times \text{age}) + (2.07 \times \text{knee height [cm]})$ for females.

Handgrip strength (HGS) was measured by physiotherapists using a hydraulic handheld dynamometer (JAMAR, Sammons Preston, Inc. Bolingbrook, IL, USA). Patients were asked to squeeze maximally 3 times for each hand [23], alternating with each measure, in a seated position with the elbow bent at a 90° angle, adjacent to the body and unsupported. If a patient was unable to complete the test seated, they completed it in a supine position. Patients

were encouraged to maintain the correct testing posture and to exert a maximal force. The maximal value (in kg) was used for analyses.

The short physical performance battery (SPPB) [24], performed by physiotherapists, comprises 3 individual components: balance tests with eyes open, a 4-m walk test, and a timed chair stand test (CST). Each component has a maximum score of 4, leading to a maximum total SPPB score of 12. Measuring gait speed, patients were instructed to walk at their usual pace, and the test was performed twice, where the fastest time was used to calculate gait speed (m/s). For the CST, patients first performed a pretest to assess if they were able to stand without using their arms. If they were able, the 5-time timed CST was performed and measured in seconds.

Diagnostic Criteria of Sarcopenia

Three definitions of sarcopenia were applied at admission to geriatric rehabilitation.

1. The European Working Group on Sarcopenia in Older People 2010 (EWGSOP) [1] defines sarcopenia as low muscle mass and low muscle strength or low physical performance to define sarcopenia. Cut-off values used were SMI $\leq 10.75 \text{ kg/m}^2$ and $\leq 6.75 \text{ kg/m}^2$, HGS $< 30 \text{ kg}$ and $< 20 \text{ kg}$ (for males and females, respectively), and gait speed $\leq 0.8 \text{ m/s}$. If gait speed was not expressed as meter per second (but expressed as an SPPB sub-score out of 4), total SPPB was used with a cut-off of ≤ 8 points.
2. The EWGSOP 2018 (EWGSOP2) [25] defines sarcopenia as low muscle mass and low muscle strength. Cut-off values used were ALM/height² $< 7.0 \text{ kg/m}^2$ and $< 5.5 \text{ kg/m}^2$ and HGS $< 27 \text{ kg}$ and $< 16 \text{ kg}$ (for males and females, respectively). If HGS was unavailable, the CST was used with a cut-off of $> 15 \text{ s}$.
3. The Asian Working Group for Sarcopenia 2019 (AWGS 2019) [26] defines sarcopenia as low muscle mass and at least 1 of low muscle strength or low physical performance. Cut-off values used were ALM/height² $\leq 7.0 \text{ kg/m}^2$ and $\leq 5.7 \text{ kg/m}^2$, HGS $< 28 \text{ kg}$ and $< 18 \text{ kg}$ (for males and females, respectively), and gait speed $< 1.0 \text{ m/s}$. If gait speed was not expressed as m/s (but expressed as an SPPB sub-score out of 4), either CST or a total SPPB score was used with cut-off values of $\geq 12 \text{ s}$ and ≤ 9 , respectively.

If patients had 2 or more of the sarcopenia measures missing to complete the EWGSOP and AWGS 2019 diagnoses, sarcopenia could not be diagnosed. If either muscle strength or physical performance was missing, sarcopenia diagnosis was possible if the available component was abnormal. If patients had missing muscle strength to complete the EWGSOP2 diagnoses, sarcopenia could not be diagnosed. If muscle mass was missing to complete all 3 definitions' diagnoses and the available components were normal, patients could be classified as not having sarcopenia.

Institutionalisation and Mortality

The incidence of institutionalisation was defined as a new admission to a residential aged care facility within 3 months of discharge from geriatric rehabilitation. These data were collected by researchers from a 3-month follow-up phone call with either the patient or carer. Three-month mortality information was received from the Australian births, deaths, and marriages registry on 24 July, 2020, as well as patient medical records.

Table 1. Patient characteristics at admission to geriatric rehabilitation

	N	Total (N = 549)
Age, years, median [IQR]	549	82.2 (77.4–87.7)
Female	549	320 (58.3)
Institutionalised at admission	549	19 (3.5)
LOS, days, median [IQR]	549	19 (13–29)
Cognitive impairment	549	344 (62.7)
MST (points), median [IQR]	543	1 (0–2)
ADL (points), median [IQR]	533	2 (1–3)
Morbidity		
CCI score (points), median [IQR]	549	2 (1–4)
High multimorbidity	549	253 (46.1)
CIRS-G total score (points), mean $\pm$ SD	549	11.6 $\pm$ 4.62
CIRS-G severity index, mean $\pm$ SD	549	1.91 $\pm$ 0.43
High disease severity	549	280 (51.0)
CVD	549	464 (84.5)
COPD	549	97 (17.7)
Dementia	549	140 (25.5)
DM	549	198 (36.1)
Osteoporosis	549	169 (30.8)
Renal impairment	549	200 (36.4)
Sarcopenia prevalence		
EWGSOP	507	192 (37.9)
EWGSOP2	544	101 (18.6)
AWGS 2019	501	131 (26.1)
Follow-up measures		
Incidence of institutionalisation	463	120 (25.9)
Mortality	549	53 (9.7)

Data presented as *n* (%) unless otherwise stated. IQR, interquartile range; LOS, length of stay; MST, malnutrition screening tool; ADL, activities of daily living; CCI, Charlson Comorbidity Index; CIRS-G, Cumulative Illness Rating Scale – geriatric version; SD, standard deviation; EWGSOP, European Working Group on Sarcopenia in Older People; AWGS, Asian Working Group for Sarcopenia; CVD, cardiovascular disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus.

Statistical Analyses

Normally distributed data were presented as mean $\pm$ standard deviation, and nonnormally distributed data were presented as median (interquartile range). The cohort was grouped into 4 categories per analysis: low morbidity and no sarcopenia, low morbidity and sarcopenia, high morbidity and no sarcopenia, and high morbidity and sarcopenia, where the former most group was the reference group. Logistic regression models were used to analyse the association of sarcopenia as a comorbid disease with the incidence of institutionalisation and mortality, adjusted for age and sex. Interaction effects of the 4 groups with age and sex were tested to determine if stratification for these variables was required. If any group had insufficient numbers (*n* < 5), analyses were not reported. Backward stepwise binomial logistic regression was also used.

Fig. 1. Association between multimorbidity and sarcopenia and the incidence of institutionalisation (**a**) and mortality within 3 months post-discharge from geriatric rehabilitation (**b**), adjusted for age and sex with low multimorbidity/no sarcopenia as the reference group. EWGSOP, European Working Group on Sarcopenia in Older People; AWGS, Asian Working Group for Sarcopenia; CI, confidence interval.

to analyse the association between sarcopenia, high multimorbidity, and high disease severity and the incidence of institutionalisation and mortality. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported, and p values <0.05 were considered significant. All statistical analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS Advanced Statistics 27.0, Armonk, NY, USA: IBM Corp.).

Results

Table 1 shows the median age was 82.2 (77.4–87.7) years, 58.3% of patients were female, and the median length of stay in geriatric rehabilitation was 19 (13–29) days. The prevalence of high multimorbidity was 46.1 and

51.0% for high disease severity. The prevalence of specific diseases was 84.5% CVD, 17.7% COPD, 25.5% dementia, 36.1% DM, 30.8% osteoporosis, and 36.4% renal impairment. The prevalence of sarcopenia was 37.9%, 18.6%, and 26.1% according to EWGSOP, EWGSOP2, and AWGS 2019, respectively. Online suppl. Table 2 shows the sarcopenia measures for geriatric rehabilitation inpatients at admission. The median SMI and ALM/height² scores, respectively, were 8.83 (7.92–9.75) kg/m² and 7.10 (6.19–8.13) kg/m². The median HGS was 17 (12–22) kg, and the median scores for gait speed, CST, and total SPPB, respectively, were 0.42 (0.29–0.57) m/s, 21.4 (16.9–29.6) s, and 1 (0–4) points. For all measures, except CST, males had higher medians than females. Within 3

Fig. 2. Association between disease severity and sarcopenia and the incidence of institutionalisation (**a**) and mortality within 3 months post-discharge from geriatric rehabilitation (**b**), adjusted for age and sex with low disease severity/no sarcopenia as the reference group. EWGSOP, European Working Group on Sarcopenia in Older People; AWGS, Asian Working Group for Sarcopenia; CI, confidence interval.

months of discharge, the incidence of institutionalisation was 25.9%, and 9.7% died either in hospital or within 3 months of discharge (Table 1). Online suppl. Tables 3 and 4 show the incidence of institutionalisation and mortality, respectively, dependent on morbidity and sarcopenia definition.

Multimorbidity

Patients with high multimorbidity and sarcopenia (EWGSOP2: OR = 2.80, 95% CI = 1.26–6.23) and patients with low multimorbidity and sarcopenia (EWGSOP2: OR = 2.69, 95% CI = 1.37–5.28; AWGS 2019: OR = 2.08, 95% CI = 1.10–3.95) had higher odds of institutionalisation than patients with low multimorbidity and no sarco-

penia. No association was found for patients with high multimorbidity and no sarcopenia on institutionalisation (shown in Fig. 1a; online suppl. Table 5).

Patients with high multimorbidity and sarcopenia (EWGSOP: OR = 6.61, 95% CI = 1.93–22.7; EWGSOP2: OR = 5.75, 95% CI = 2.25–14.7; AWGS 2019: OR = 4.02, 95% CI = 1.68–9.61), patients with high multimorbidity and no sarcopenia (EWGSOP: OR = 3.44, 95% CI = 1.38–8.58; EWGSOP2: OR = 2.10, 95% CI = 1.01–4.38), and patients with low multimorbidity and sarcopenia (EWGSOP: OR = 6.04, 95% CI = 1.86–19.6; EWGSOP2: OR = 3.19, 95% CI = 1.26–8.11) had higher odds of mortality than patients with low multimorbidity and no sarcopenia (shown in Fig. 1b; online suppl. Table 5).

Fig. 3. Association between CVD (a), COPD (b), dementia (c), DM (d), osteoporosis (e), and (f) renal impairment and sarcopenia with the incidence of institutionalisation 3 months post-discharge from geriatric rehabilitation, adjusted for age and sex with no disease/no sarcopenia as the reference group. CVD, cardiovascular

disease; EWGSOP, European Working Group on Sarcopenia in Older People; AWGS, Asian Working Group for Sarcopenia; NA, not applicable; CI, confidence interval; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus.

Disease Severity

Patients with low disease severity and sarcopenia (EWGSOP2: OR = 3.22, 95% CI = 1.57–6.60; AWGS 2019: OR = 2.71, 95% CI = 1.38–5.32) had higher odds of institutionalisation than patients with low disease severity and no sarcopenia. No association was found for patients with

high disease severity and sarcopenia and patients with high disease severity and no sarcopenia on institutionalisation (shown in Fig. 2a; online suppl. Table 6).

Patients with high disease severity and sarcopenia (EWGSOP: OR = 6.56, 95% CI = 1.94–22.2; EWGSOP2: OR = 4.33, 95% CI = 1.47–12.8; AWGS 2019: OR = 3.35,

Fig. 4. Association between CVD (**a**), COPD (**b**), dementia (**c**), DM (**d**), osteoporosis (**e**), and renal impairment (**f**) with mortality 3 months post-discharge from geriatric rehabilitation, adjusted for age and sex with no disease/no sarcopenia as the reference group. CVD, cardiovascular disease; EWGSOP, European Working Group on Sarcopenia in Older People; AWGS, Asian Working Group for Sarcopenia; NA, not applicable; CI, confidence interval; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus.

95% CI = 1.23–9.12), patients with high disease severity and no sarcopenia (EWGSOP: OR = 3.06, 95% CI = 1.22–7.70; EWGSOP2: OR = 3.66, 95% CI = 1.61–8.33; AWGS 2019: OR = 3.41, 95% CI = 1.47–7.91), and patients with low disease severity and sarcopenia (EWGSOP: OR = 5.61, 95% CI = 1.70–18.5; EWGSOP2: OR = 7.89, 95% CI = 3.01–20.7; AWGS 2019: OR = 5.56, 95% CI = 2.07–13.9) had higher odds of mortality than patients with low disease severity and no sarcopenia (shown in Fig. 2b; online suppl. Table 6).

Specific Diseases

Patients with dementia and sarcopenia (EWGSOP: OR = 4.53, 95% CI = 1.79–11.5; EWGSOP2: OR = 5.90, 95% CI = 2.69–13.0; AWGS 2019: OR = 4.24, 95% CI = 2.07–8.66), patients with DM and sarcopenia (EWGSOP2: OR = 2.42, 95% CI = 1.02–5.70), and patients with renal impairment and sarcopenia (EWGSOP2: OR = 2.54, 95% CI = 1.13–5.72) had higher odds of institutionalisation than patients without these diseases and without sarcopenia. Patients with dementia and without sarcopenia

Table 2. Results of the backward stepwise logistic regression between sarcopenia, high multimorbidity, and high disease severity on the incidence of institutionalisation and mortality

	Incidence of institutionalisation				Mortality			
	<i>n</i>	OR	95% CI	<i>p</i> value	<i>n</i>	OR	95% CI	<i>p</i> value
EWGSOP	425				507			
Sarcopenia		1.91	1.23–2.96	0.004		2.02	1.13–3.62	0.017
High multimorbidity		NS	NS	NS		1.80	1.00–3.24	0.050
High disease severity		NS	NS	NS		NS	NS	NS
EWGSOP2	459				544			
Sarcopenia		2.87	1.74–4.75	<0.001		3.01	1.62–5.59	0.001
High multimorbidity		NS	NS	NS		1.90	1.05–3.44	0.035
High disease severity		NS	NS	NS		0.59	0.32–1.06	0.079
AWGS 2019	420				501			
Sarcopenia		1.93	1.21–3.09	0.006		2.19	1.20–3.99	0.010
High multimorbidity		NS	NS	NS		1.90	1.05–3.43	0.033
High disease severity		NS	NS	NS		NS	NS	NS

OR, odds ratio; CI, confidence interval; EWGSOP, European Working Group on Sarcopenia in Older People; NS, not selected; AWGS, Asian Working Group for Sarcopenia; CI, confidence interval.

nia (EWGSOP: OR = 2.71, 95% CI = 1.42–5.15; EWGSOP2: OR = 2.85, 95% CI = 1.68–4.84; AWGS 2019: OR = 3.18, 95% CI = 1.78–5.67) had higher odds of institutionalisation than patients without dementia and without sarcopenia. Patients without COPD and with sarcopenia (EWGSOP2: OR = 2.63, 95% CI = 1.51–4.57; AWGS 2019: OR = 1.75, 95% CI = 1.05–2.94), patients without dementia and with sarcopenia (EWGSOP2: OR = 2.38, 95% CI = 1.21–4.67), patients without DM and with sarcopenia (EWGSOP2: OR = 2.44, 95% CI = 1.31–4.57), patients without osteoporosis and with sarcopenia (EWGSOP2: OR = 2.71, 95% CI = 1.46–5.04; AWGS 2019: OR = 1.93, 95% CI = 1.08–3.42), and patients without renal impairment and with sarcopenia (EWGSOP2: OR = 2.20, 95% CI = 1.15–4.20) had higher odds of institutionalisation than patients without these diseases and without sarcopenia (shown in Fig. 3; online suppl. Table 7).

Patients with COPD and sarcopenia (EWGSOP: OR = 4.10, 95% CI = 1.41–12.0; EWGSOP2: OR = 6.66, 95% CI = 2.41–18.4; AWGS 2019: OR = 4.68, 95% CI = 1.85–11.9), patients with osteoporosis and sarcopenia (EWGSOP: OR = 4.16, 95% CI = 1.48–11.7; EWGSOP2: OR = 3.21, 95% CI = 1.28–8.05; AWGS 2019: OR = 2.41, 95% CI = 1.00–5.80), and patients with renal impairment and sarcopenia (EWGSOP2: OR = 3.16, 95% CI = 1.24–8.04) had higher odds of mortality than patients without these diseases and without sarcopenia. Patients without dementia and with sarcopenia (EWGSOP: OR = 2.99, 95% CI = 1.12–8.00; EWGSOP2: OR = 4.23, 95% CI = 2.07–8.65; AWGS 2019: OR = 2.73, 95% CI = 1.35–5.52), pa-

tients without DM and with sarcopenia (EWGSOP: OR = 3.13, 95% CI = 1.16–8.44; EWGSOP2: OR = 2.43, 95% CI = 1.17–5.07), patients without osteoporosis and with sarcopenia (EWGSOP2: OR = 2.20, 95% CI = 1.01–4.81), and patients without renal impairment and with sarcopenia (EWGSOP: OR = 3.09, 95% CI = 1.10–8.70; EWGSOP2: OR = 2.37, 95% CI = 1.06–5.28) had higher odds of mortality than patients without these diseases and no sarcopenia. No association was found for patients with specific disease and without sarcopenia on mortality (shown in Fig. 4; online suppl. Table 8).

Sarcopenia, High Multimorbidity, and High Disease Severity

Backward stepwise logistic regressions showed that sarcopenia, irrespective of definition, had increased odds incidence of institutionalisation (EWGSOP: OR = 1.91, 95% CI = 1.23–2.96; EWGSOP2: OR = 2.87, 95% CI = 1.74–4.75; AWGS 2019: OR = 1.93, 95% CI = 1.21–3.09). High multimorbidity and high disease severity were not selected to be included in the models (Table 2).

Backward stepwise logistic regressions showed that sarcopenia, defined by EWGSOP (OR = 2.02, 95% CI = 1.13–3.62), and high multimorbidity (OR = 1.80, 95% CI = 1.00–3.24) had increased odds of mortality, but high disease severity was not selected to be included. EWGSOP2 sarcopenia (OR = 2.97, 95% CI = 1.60–5.51) and high multimorbidity (OR = 2.02, 95% CI = 1.12–3.65) had increased odds of mortality and high disease severity was selected but did not have a significant association. AWGS

2019 sarcopenia (OR = 2.19, 95% CI = 1.20–3.99) and high multimorbidity (OR = 1.90, 95% CI = 1.05–3.43) had increased odds of mortality, and high disease severity was not selected (Table 2).

Discussion

Patients with high multimorbidity and sarcopenia and patients with low disease severity and sarcopenia had higher odds of incidence of institutionalisation and mortality. Patients with sarcopenia as a comorbid disease of CVD, dementia, and DM had higher odds of incidence of institutionalisation, and patients with sarcopenia as a comorbid disease of COPD, osteoporosis, and renal impairment had higher odds of mortality.

Multimorbidity

Patients with sarcopenia, independent of multimorbidity, had higher odds of incidence of institutionalisation and all patients had higher odds of mortality. Multimorbidity [10] has been associated with both institutionalisation and mortality, and sarcopenia has also been associated with institutionalisation [5]. Furthermore, both lead to negative health outcomes such as functional decline [6, 27] and frailty, which in turn contribute to institutionalisation and mortality [28]. Sarcopenia is also associated with other outcomes such as falls and fractures [4] which also contribute to the above outcomes. This may explain why patients with high multimorbidity and sarcopenia had a higher association with the incidence of institutionalisation and mortality in this study.

Disease Severity

Patients with low disease severity and sarcopenia had higher odds of incidence of institutionalisation and all patients (high disease severity with sarcopenia, high disease severity without sarcopenia, and low disease severity with sarcopenia) had higher odds of mortality. This is in contrast with the study's hypothesis as high disease severity [29], in hospitalised older adults, is associated with institutionalisation and mortality and the 2 together were expected to have an association with both outcomes. Interestingly, high disease severity with sarcopenia was only associated with mortality. This may be because a high disease severity would lead to a patient's death before they are institutionalised, as evidenced by the group with the highest mortality rates being the patients with high disease severity and sarcopenia (EWG-SOP2 and AWGS2).

Specific Diseases

Sarcopenia and these age-related diseases share risk factors, namely, sedentary behaviour, inflammation, and malnutrition [7, 30, 31], and therefore, a combination of sarcopenia with another disease might worsen health outcomes. This may explain why no disease without sarcopenia (except for dementia without sarcopenia) was significantly associated with either outcome.

Sarcopenia, as well as renal impairment [32], is associated with frailty, which is in turn associated with institutionalisation and mortality. It also, alongside dementia [33], is associated with loss of function, which is in turn associated with institutionalisation. Sarcopenia, as well as COPD [34] and osteoporosis [35], is associated with falls, which is in turn associated with mortality. This may explain how sarcopenia as a comorbid disease of these diseases has higher odds of poor health outcomes.

Sarcopenia Diagnostics and Interventions

Clinicians often do not consider sarcopenia diagnostics and they report the main reason for this as not having the tools for diagnosis and not feeling responsible for sarcopenia diagnosis. Interestingly, older adults are willing to partake sarcopenia interventions, at least in the community setting, despite not knowing what sarcopenia is. The additive effect of sarcopenia as a comorbid disease on institutionalisation and mortality highlights the need of treating sarcopenia during hospitalisation and post-hospitalisation with the attempt to improve patients' outcomes.

Sarcopenia interventions include resistance exercise training and/or nutritional intervention [36]. There is a lack of knowledge in sarcopenia interventions in the geriatric rehabilitation setting, but current knowledge on the efficacy of in-hospital exercise interventions indicates that HGS and physical performance can either be maintained or improved during hospitalisation [37]. In contrast, there is more ambiguity with regards to in-hospital nutritional interventions, where a recent meta-analysis showed conflicting impacts on muscle mass, muscle strength, physical performance and sarcopenia prevalence [38]. The geriatric rehabilitation setting provides the ideal opportunity to initiate interventions as this setting often provides exercise and nutritional interventions that may be continued in the home environment. Therefore, research into the efficacy of sarcopenia interventions in geriatric rehabilitation is required.

Strengths and Limitations

The strengths of this study can be attributed to the strengths of RESORT, which is a representative sample of

all geriatric rehabilitation patients as it has very limited exclusion criteria, allowing for inclusion of most patients. Furthermore, all tests were performed by trained clinicians, ensuring the higher quality and accuracy of collected data. There is no globally accepted definition of sarcopenia [39]; therefore, 3 definitions of sarcopenia were included in this analysis. Finally, this study is the first with a large cohort to provide a prevalence of sarcopenia according to AWGS 2019. A limitation of this study is that DSM-BIA may be affected by hydration status, which affects the fat/muscle mass ratio [40].

Conclusion

Sarcopenia as a comorbid disease is associated with the incidence of institutionalisation and mortality 3 months post-discharge from geriatric rehabilitation. This highlights the need for research evaluating in-hospital diagnostics and interventions continued in the community setting.

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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(4):412–23.
- 2 Reijnierse EM, Trappenburg MC, Leter MJ, Blauw GJ, Sipilä S, Sillanpää E, et al. The impact of different diagnostic criteria on the prevalence of sarcopenia in healthy elderly participants and geriatric outpatients. *Gerontology*. 2015;61(6):491–6.
- 3 Reijnierse EM, Buljan A, Tuttle CSL, van An-cum J, Verlaan S, Meskers CGM, et al. Prevalence of sarcopenia in inpatients 70 years and older using different diagnostic criteria. *Nurs Open*. 2019;6(2):377–83.
- 4 Yeung SSY, Reijnierse EM, Pham VK, Trappenburg MC, Lim WK, Meskers CGM, 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(3):485–500.
- 5 Hirani V, Blyth F, Naganathan V, Le Couteur DG, Seibel MJ, Waite LM, et al. Sarcopenia is associated with incident disability, institutionalization, and mortality in community-dwelling older men: the concord health and ageing in men project. *J Am Med Dir Assoc*. 2015;16(7):607–13.
- 6 Beaudart C, Zaaria M, Pasleau F, Reginster JY, Bruyère O. Health outcomes of sarcopenia: a systematic review and meta-analysis. *PLoS One*. 2017;12(1):e0169548.
- 7 Pacifico J, Geerlings MAJ, Reijnierse EM, Phassoulis C, Lim WK, Maier AB. Prevalence of sarcopenia as a comorbid disease: a systematic review and meta-analysis. *Exp Gerontol*. 2020;131:110801.
- 8 van den Akker M, Buntinx F, Knottnerus JA. Comorbidity or multimorbidity. *Eur J Gen Pract*. 1996;2(2):65–70.
- 9 Bernard S, Inderjeeth C, Raymond W. Higher charlson comorbidity index scores do not influence functional independence measure score gains in older rehabilitation patients. *Australas J Ageing*. 2016;35(4):236–41.
- 10 Soh CH, Ul Hassan SW, Sacre J, Maier AB. Morbidity measures predicting mortality in inpatients: a systematic review. *J Am Med Dir Assoc*. 2020;21(4):462–8.e7.
- 11 Ellis G, Gardner M, Tsiachristas A, Langhorne P, Burke O, Harwood RH, et al. Comprehensive geriatric assessment for older adults admitted to hospital. *Cochrane Database Syst Rev*. 2017;9(9):Cd006211.
- 12 Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol*. 1994;47(11):1245–51.
- 13 Miller MD, Paradis CF, Houck PR, Mazumdar S, Stack JA, Rifai AH, et al. Rating chronic medical illness burden in geropsychiatric practice and research: application of the cumulative illness rating scale. *Psychiatry Res*. 1992;41(3):237–48.
- 14 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(3):189–98.
- 15 Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53(4):695–9.
- 16 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(1):13–31.

Statement of Ethics

Ethics approval was obtained from Melbourne Health Human Research Ethics Committee (HREC/17/MH/103), and the study was performed in accordance with the Helsinki Declaration. Patients were included if they gave written informed consent, or if a nominated proxy gave written informed consent in case the patient had no capacity to consent for themselves.

Conflict of Interest Statement

Jacob Pacifico, Esmee M. Reijnierse, Wen Kwang Lim, and Andrea B. Maier declare that they have no conflicts of interest.

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Author Contributions

Jacob Pacifico: study design, data analysis, and manuscript writing. Esmee M. Reijnierse, Wen Kwang Lim, and Andrea B. Maier: supervision, manuscript review, and manuscript editing.

- 17 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(6):458–64.
- 18 Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. the index of adl: a standardized measure of biological and psychosocial function. *JAMA*. 1963;185:914–9.
- 19 Armas LA, Recker RR. Pathophysiology of osteoporosis: new mechanistic insights. *Endocrinol Metab Clin North Am*. 2012;41(3):475–86.
- 20 Organisation WH. The top 10 causes of death 2018. Available from: <https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death>. Accessed 2019 Apr 16.
- 21 Ling CH, de Craen AJ, Slagboom PE, Gunn DA, Stokkel MP, Westendorp RG, et al. Accuracy of direct segmental multi-frequency bioimpedance analysis in the assessment of total body and segmental body composition in middle-aged adult population. *Clin Nutr*. 2011;30(5):610–5.
- 22 Chumlea WC, Roche AF, Steinbaugh ML. Estimating stature from knee height for persons 60 to 90 years of age. *J Am Geriatr Soc*. 1985;33(2):116–20.
- 23 Reijnierse EM, de Jong N, Trappenburg MC, Blauw GJ, Butler-Browne G, Gapeyeva H, et al. Assessment of maximal handgrip strength: how many attempts are needed? *J Cachexia Sarcopenia Muscle*. 2017;8(3):466–74.
- 24 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(2):M85–94.
- 25 Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(1):601–31.
- 26 Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc*. 2020;21(3):300–7.e2.
- 27 Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. *Ageing Res Rev*. 2011;10(4):430–9.
- 28 Divo MJ, Martinez CH, Mannino DM. Ageing and the epidemiology of multimorbidity. *Eur Respir J*. 2014;44(4):1055–68.
- 29 Osborn KP, Nothelle S, Slaven JE, Montz K, Hui S, Torque AM. Cumulative illness rating scale (CIRS) can be used to predict hospital outcomes in older adults. *J Geriatr Med Gerontol*. 2017.
- 30 Kirk B, Al Saedi A, Duque G. Osteosarcopenia: a case of geroscience. *Ageing Med*. 2019;2(3):147–56.
- 31 Souza VA, Oliveira D, Mansur HN, Fernandes NM, Bastos MG. Sarcopenia in chronic kidney disease. *J Bras Nefrol*. 2015;37(1):98–105.
- 32 Kittiskulnam P, Sheshadri A, Johansen KL. Consequences of CKD on functioning. *Semin Nephrol*. 2016;36(4):305–18.
- 33 Toot S, Swinson T, Devine M, Challis D, Orrell M. Causes of nursing home placement for older people with dementia: a systematic review and meta-analysis. *Int Psychogeriatr*. 2017;29(2):195–208.
- 34 Crisan AF, Oancea C, Timar B, Fira-Mladinescu O, Tudorache V. Falls, an underestimated risk in COPD. *Eur Res J*. 2015;46(Suppl 59):PA3070.
- 35 Kirk B, Zanker J, Duque G. Osteosarcopenia: epidemiology, diagnosis, and treatment-facts and numbers. *J Cachexia Sarcopenia Muscle*. 2020.
- 36 Beaudart C, Dawson A, Shaw SC, Harvey NC, Kanis JA, Binkley N, et al. Nutrition and physical activity in the prevention and treatment of sarcopenia: systematic review. *Osteoporos Int*. 2017;28(6):1817–33.
- 37 Valenzuela PL, Morales JS, Castillo-García A, Mayordomo-Cava J, García-Hermoso A, Izquierdo M, et al. Effects of exercise interventions on the functional status of acutely hospitalised older adults: a systematic review and meta-analysis. *Ageing Res Rev*. 2020;61:101076.
- 38 Rus GE, Porter J, Brunton A, Crocker M, Kotsimbos Z, Percic J, 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(1):90–102.
- 39 Suetta C, Maier AB. Is muscle failure a better term than sarcopenia? *J Cachexia Sarcopenia Muscle*. 2019;10(5):1146–7.
- 40 Sergi G, De Rui M, Stubbs B, Veronese N, Manzato E. Measurement of lean body mass using bioelectrical impedance analysis: a consideration of the pros and cons. *Ageing Clin Exp Res*. 2017;29(4):591–7.