Accepted Manuscript

Title: Sarcopenia and Post-Hospital Outcomes in Older Adults: a Longitudinal Study

Author: Mario Ulises Pérez-Zepeda Aldo Sgaravatti Elsa Dent



Please cite this article as: Pérez-Zepeda, Mario Ulises, Sgaravatti, Aldo, Dent, Elsa, Sarcopenia and Post-Hospital Outcomes in Older Adults: a Longitudinal Study. Archives of Gerontology and Geriatrics http://dx.doi.org/10.1016/j.archger.2016.10.013

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Sarcopenia Determinants and Post-Hospital Outcomes in

Older Adults: a Longitudinal Study

Dr Mario Ulises Pérez-Zepeda^a

^a Clinical and Epidemiologic Research Department at Instituto Nacional de Geriatría,

Mexico City, México

Dr Aldo **Sgaravatti**^b

^b Geriatrics Department, Universidad de la República, Montevideo, Uruguay

Dr Elsa **Dent** ^{c,d}

* Corresponding author

NHMRC Early Career Research Fellow

^c Centre for Research in Geriatric Medicine, The University of Queensland, Brisbane,

Australia

^d School of Public Health, The University of Adelaide, Adelaide, Australia

Email: e.dent@uq.edu.au

Address: Centre for Research in Geriatric Medicine

The University of Queensland

Level 2, Building 33, Princess Alexandra Hospital

Ipswich Rd, Woolloongabba, 4102

Highlights

• In a Geriatric Evaluation and Management Unit (GEMU), sarcopenia prevalence is high (405)

- Sarcopenia was associated with dependency in both Activities of Daily Living (ADLs) and Instrumental ADLs.
- Patients with sarcopenia were twice as likely to die in the 12-months posthospitalisation
- Sarcopenia was not associated with admission to an Emergency Department (ED) in the 12-months post-hospitalisation.

Acknowledgments

The authors wish to thank GEMU staff at TQEH for their contribution to the research project. ED is currently a National Health and Medical Research Council (NHMRC) Early Career Fellow (Grant ID: 1112672). The data collected for this study was performed by ED during her PhD candidature. ED was supervised by Prof Ian Chapman and co-supervised by Prof Renuka Visvanathan during her PhD studies, and was supported by a PhD scholarship from the Centre for Research Excellence in Translating Nutritional Science into Good Health (NHMRC Grant ID: 1041687) at The University of Adelaide.

Keywords

Sarcopenia/complications Sarcopenia/mortality Aged Muscle strength Muscle mass

Running Title: Sarcopenia and Adverse Hospital Outcomes

Introduction: Sarcopenia poses a significant problem for older adults, yet very little is known about this medical condition in the hospital setting. The aims of this hospital-based study were to determine: (i) the prevalence of sarcopenia; (ii) factors associated with sarcopenia; and (iii) the association of sarcopenia with adverse clinical outcomes post-hospitalisation.

Methods: This is a longitudinal analysis of consecutive patients aged \geq 70 years admitted to a Geriatric Management and Evaluation Unit (GEMU) ward. Sarcopenia was classified using the European Working Group on Sarcopenia in Older People (EWGSOP) algorithm, which included: handgrip strength, gait speed, and muscle mass using Bioelectrical Impedance Analysis (BIA). Outcomes were assessed at 12-months post-hospital discharge, and included both mortality and admission to a hospital Emergency Department (ED). Kaplan-Meier methods were used to estimate survival, with Cox proportion hazard models then applied. All regression analyses controlled for age, sex, and co-morbidity.

Results: 172 patients (72% female) with a mean (SD) age of 85.2 (6.4) years were included. Sarcopenia was present in 69 (40.1%) of patients. Patients with sarcopenia were twice as likely to die in the 12-months post-hospitalisation (HR, 95% CI = 2.23, 1.15-4.34), but did not have an increased likelihood of ED admission.

Conclusions: Sarcopenia showed an independent association with 12-month posthospital mortality in older adults. With the new recognition of sarcopenia as a medical condition with its own unique ICD-10-CM code, awareness and diagnosis of sarcopenia in clinical settings is paramount.

Introduction

Sarcopenia, an age-related condition characterized by a decline in muscle mass and physical function (1, 2), has recently been recognised with its own International Classification of Disease (ICD-10CM) code [M62.84] (3). With this new recognition, sarcopenia awareness and management is urgently warranted. Sarcopenia is particularly problematic in the hospital setting, where it can adversely affect patient outcomes (4-8). Hospitalisation exacerbates sarcopenia which in turn, can increase an older adult's risk of functional decline, falls and mortality (9). Indeed, many chronic conditions have a worsened prognosis when a patient is sarcopenic (5, 10-14). Sarcopenia is also common in hospitals, with around 40% of older patients presenting with the condition (10, 14, 15).

To measure sarcopenia, there has been a widespread uptake of the sarcopenia algorithm from the European Working Group on Sarcopenia in Older People (EWGSOP) (2, 7, 16-21). This highly validated algorithm incorporates both handgrip strength and gait speed into its sarcopenia classification protocol (2, 22, 23). Several recent studies have applied the EWGSOP algorithm in the hospital setting, where it has been predominately used to assess both the prevalence of sarcopenia, and its association with mortality (4-8). The majority of these studies have focused on specific populations of older patients, or those patients in acute care.

For optimal care of older patients, Comprehensive Geriatric Assessment (CGA) followed by appropriate care planning is crucial. Such services can be provided in

specialised Geriatric Evaluation and Management Units (GEMU). GEMUs are designed to maximise the functional independence of older patients whose geriatric conditions benefit from comprehensive assessment and management - such conditions include falls risk, polypharmacy, cognitive decline, undernutrition, frailty, and social and functional impairment (24, 25). GEMUs are geriatrician-led, and provide multi-disciplinary care from physiotherapists, speech pathologists, pharmacists, dieticians, occupational therapists, psychologists/psychiatrists, and social workers (25). Patient outcomes are substantially improved in GEMUs, including: discharge directly back home, functional improvement, better pain management, and enhanced mental health (24, 25).

To date, very little is known about the prevalence of sarcopenia in GEMUs, and its impact on adverse clinical outcomes. Therefore, using the EWGSOP algorithm to identify sarcopenia, this study aimed to: (i) to determine the prevalence of sarcopenia; (ii) identify factors associated with sarcopenia; and (iii) examine the association of sarcopenia with 12-month GEMU discharge outcomes, including mortality, and admission to a hospital Emergency Department (ED).

Methods

Study Sample

This was a secondary, longitudinal analysis of consecutive patients aged 70 years and older recruited between October 2010 and December 2011 from the GEMU at The Queen Elizabeth Hospital (TQEH) in Adelaide, South Australia. A complete description of the study protocol is available elsewhere (26). Data were collected from either the older adult (or proxy) in the first 72 hours of GEMU admission. This study was approved by the Human Research Ethics Committee (TQEH) and all patients (or their legal proxy) signed an informed consent form (Protocol Number: 2010105). The majority of patients were transferred to the GEMU from the Acute Medical Unit (short stay <72 hours) after identification by TQEH geriatric service. All patients in the GEMU received daily physiotherapy sessions, including individual sessions and/or group physical activity classes. The study adhered to the ethical standards from the 2000 Declaration of Helsinki.

Measurements

Patient hospital records were reviewed to obtain data on cognition (measured by the Mini-Mental State Examination [MMSE]) (27), co-morbidity (Charlson's Comorbidity Index [CCI]) (28), Activities of Daily Living (ADLs), and Lawton's instrumental ADLs (IADLs) (29), depression (Geriatric Depression Scale, 15-item [GDS-15]) (30), falls history, polypharmacy (\geq 6 medications), and serum levels of Creactive protein (CRP). Patient (or proxy) interview was used to collect data on socio

demographics and general health status, including appetite/weight loss risk screened using the Simplified Nutritional Appetite Questionnaire (SNAQ) (31). Standing height and seated weight were measured and Body Mass Index (BMI) (weight/height²) computed. Handgrip strength was measured using a Smedly spring-type hand held dynamometer with adjustable hand settings, and the best result of three trials with the dominant hand was used for analysis. Gait speed was measured as the time taken to walk 6m at usual speed, with or without a walking aid. Bioelectrical Impedance Analysis (BIA) was measured using a Quantum II BIA Analyser, RJL system, and Janssen prediction equations (as per the recommendation of the BIA system manufacturer) were used to convert BIA resistance and reactance values to Skeletal Muscle Mass (32). One researcher conducted all patient measurements and patient/proxy interviews.

Sarcopenia classification

Sarcopenia was classified using the EWGSOP algorithm, in which participants were classified as sarcopenic if they had low muscle mass, plus one or both of low muscle strength and low physical performance (2). Low muscle mass was defined according to EWGSOP BIA cut-off points, which in turn were based on the National Health and Nutrition Examination Survey (NHANES) recommended cut-off points: 10.76kg/m² and 6.76kg/m² for men and women respectively (2). Low muscle strength was defined as handgrip strength in the lowest quintile for BMI and sex in our study cohort. Low physical performance was defined as a gait speed in the lowest quintile for BMI and sex in the cohort. The lowest quintile for both gait speed and grip strength were used because the average age of our population was over 85 years, which is much higher than the average age used in the normative charts for the EWGSOP

Outcome measures

All study outcomes were assessed at 12-months post-hospital discharge, and included the following:

- (i) Mortality, verified using Australian Death Registry data.
- (ii) Admission (*inpatient* admission) to a hospital Emergency Department (ED).

Statistical analyses

Descriptive variables were presented as frequencies for categorical variables, as mean (standard deviation [SD]) for normally distributed continuous variables, and median (interquartile range) for non-normally distributed continuous variables. Two types of analyses were performed. Firstly, univariate analyses were performed to determine which factors were associated with sarcopenia: t-tests and chi-square tests were performed for continuous and categorical variables respectively. Secondly, Kaplan–Meier survival curves were plotted for all three study outcomes, with Cox Proportional Hazard Tests (with Hazard Ratios [HRs]) then performed to determine the association of sarcopenia with both study outcomes. Both regression models were adjusted for age, sex and CCI.

For outcomes not involving mortality, those patients who died before follow-up were excluded from analyses. Data analyses were performed using SPSS 21.0 (SPSS Inc., Chicago, Illinois), with P < 0.05 indicating clinical significance.

Results

From 427 new consecutive patients admitted to the GEMU, 172 patients were recruited. Exclusion reasons were: patient (or proxy) did not speak English (n=67), dementia/unresolved delirium within 72 hours of GEMU admission without a proxy (n=77), GEMU physician advised against patient inclusion (n = 11), missed by researcher (n=4), or the patient did not wish to be involved in the study (n=63). The most common primary GEMU admission diagnoses were: chronic conditions (71 patients, 41%), infection (52 patients, 30%), and injury/musculoskeletal condition (28 patients, 16%).

The sarcopenia categorisation for study patients using the EWGSOP algorithm is depicted in Figure 1. Sarcopenia was present in 69 (40%) patients. Table 1 displays the baseline characteristics of included patients stratified by sarcopenia status. From this table, it can be seen that patients with sarcopenia were more likely to have lower levels of function for both ADLs and IADLs upon GEMU admission, but did not differ in other baseline variables, including appetite, compared with their non-sarcopenic counterparts.

Regarding study outcomes 12-months post-hospitalisation, 36 (21%) patients died, 121 (74%) were admitted into an ED, and 66 (59%) were admitted to an ED as a

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result of a fall. The Kaplan-Meier survival curves for all outcomes are plotted in Figure 2. The results of the Cox Regression models (controlling for co-variates) comparing the Kaplan-Meier curves for both study outcomes are shown in Table 2. Patients with sarcopenia were statistically more likely to die in the 12 months post-hospitalisation, with HR 2.23 (95% CI = 1.15-4.34). However, there was no statistically significant association between sarcopenia and ED admission. Of note, there was a high rate of 12-month ED admission (>90%) for both sarcopenic and non-sarcopenic patients (see Figure 2).

Discussion

The present study is the first, to our knowledge, to investigate sarcopenia determinants, prevalence and outcomes in a GEMU. Sarcopenia prevalence was high (40%), and showed a strong relationship with dependency in both ADLs and IADLs. There was no association between sarcopenia and appetite, CRP levels, depression, falls history, cognition, CCI, or polypharmacy. Patients classified as sarcopenic were twice as likely to die in the 12-months post-hospitalisation, but did not have an increased likelihood of 12-month ED admission.

The high prevalence of sarcopenia found in the present study was similar to that found by Sánchez-Rodríguez and colleagues in their study of older patients in sub-acute care, which also used the EWGSOP algorithm to classify sarcopenia (20). Similarly, the close association of sarcopenia and mortality in our study concurs with many studies, both in the acute-care setting (4, 33) and in the community (22, 34), although not all studies have reported an association (20). It could likely be that the association of sarcopenia with mortality is transient, with nutritional, physical and pharmaceutical interventions likely to ameliorate the association (18, 35).

This study's finding that sarcopenia was not associated with 12-month ED admission differs from the findings of a recent study by Gariballa & Alessa (5), who suggested that sarcopenic patients in acute care are more likely to be admitted to an ED in the 6-months post-hospitalisation. This difference in findings could likely reflect our longer follow-up period, the older average of our patients (85 years vs 79 years), the different recovery trajectories of sarcopenic patients in acute care compared with those in sub-acute care, or because their modified version of the EWGSOP algorithm did not use gait speed. Alternatively, it could be because of the high rate of ED admissions in both sarcopenic and non-sarcopenic patients – indicating that GEMU patients were a vulnerable population, regardless of sarcopenia status.

The lack of association between appetite and sarcopenia in the present study was unexpected. Low appetite is generally considered to be a risk factor for sarcopenia, at least in community dwelling older adults (37). A possible explanation for this lack of association is that hospitalisation itself was affecting the appetite of all patients, not just those classified as sarcopenic.

Managing sarcopenia could further prevent disability caused directly through sarcopenia, or by slowing its progression to frailty (38-40). Additionally, if sarcopenia is detected early, it can potentially be managed proactively with nutritional, physical activity, and/or pharmacological interventions (18, 35). Importantly, the recognition of sarcopenia as a medical condition by the ICD will progress both the clinical management and research surrounding this condition. For instance, targeted nutritional interventions may be developed, and the condition will be reported on patient medical records.

The present study had many strengths, including its lack of inter-tester bias, the recruitment of consecutive patients and the comprehensive dataset. The study however did have its limitations, including the small sample size, and the use of BIA to measure muscle mass, the latter of which can be affected by many factors in older patients, including oedema and polypharmacy. Nonetheless, the use of BIA in older patients is a rapid, easy and inexpensive means to measure skeletal muscle mass, and been used in previous large-scale studies in both hospitals and in the community (4, 7, 21, 41). Importantly, the use of the tailored cut-off points (lowest quintile) for handgrip strength and gait speed in our current study would have likely under-estimated the actual prevalence of sarcopenia. Our study was also observational by design, so no assumptions of causation can be made. Also of note, the majority of patients in the present study were in hospital for three days prior to GEMU admission, and accordingly, they may have experienced muscle mass/functional decline prior to GEMU admission.

This study highlights the high prevalence of sarcopenia in GEMU patients, and its strong association with mortality post-hospitalisation. The recent recognition of sarcopenia as a medical condition with its own unique ICD-10-CM code, is a much needed first step to identifying, managing and treating this condition. Future research with larger sample sizes should be performed to determine the association of sarcopenia with diverse adverse clinical outcomes. More comprehensive methods for muscle mass assessment, such as dual-energy X-ray absorptiometry, and computed tomography, should be used for this purpose. Randomized controlled trials in both the acute and subacute care settings are also needed to determine the optimal treatment/management of

sarcopenia patients, particularly with regards to pharmacological, nutritional, and physical activity interventions (18, 35). The predictive ability of change in sarcopenia status across hospitalisation should also be considered for additional research.

Conflict of interest

The authors declare no conflict of interest.

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Tables and Figures

Variable	Total <i>n</i> (%)	Sarcopenic (n=69)	Not Sarcopenic (n=103)	Р
Age [†]	85.2 (6.4)	85.5 (6.8)	85.0 (6.2)	0.592
Married	59 (34.3)	26 (37.7)	33 (32.0)	0.445
Lives alone	105 (61.1)	37 (53.6)	68 (66.1)	0.102
Completed higher education	15 (8.7)	6 (8.7)	9 (8.7)	0.992
Charlson's Co-morbidity Index \ddagger	3 (0-12)	2.5 (0-8)	3 (0-12)	0.481
ADL [‡]	3 (0-7)	1 (0-7)	4 (0-7)	< 0.001
IADL [‡]	3 (0-8)	2 (0-8)	3 (0-8)	< 0.001
Current smoker	9 (5.2)	2 (2.9)	7 (6.8)	0.261
Currently drinks alcohol	19 (11.1)	9 (13.0)	10 (9.7)	0.494
MMSE < 24	38 (22.1)	19 (27.5)	19 (18. 5)	0.159
GDS score [†]	5.68 (4.6)	6.39 (5.0)	5.21 (4.4)	0.103
$SNAQ \ score^{\dagger}$	13.14 (3.2)	12.76 (3.6)	13.39 (2.9)	0.206
Fall in the 12 months before hospital	54 (31.4)	18 (26.1)	36 (35.0)	0.220
Polypharmacy (≥ 6 medications)	147 (85.5)	59 (85.51)	88 (85.44)	0.990
C-reactive protein mg/L^{\dagger}	3.39 (4.0)	3.69 (4.12)	3.18 (3.96)	0.416

Table 1. Baseline Characteristics of GEMU Patients Stratified by Sarcopenia Status (n=172)

[†] Mean (SD) [‡] Median (interquartile range)

ADL= Activities of Daily Living, IADL= Instrumental Activities of Daily Living, MMSE= Mini Mental Status Examination, GDS = Geriatric Depression Scale, SNAQ = Simplified Nutrition Appetite Questionnaire



Figure 1. EWGSOP Sarcopenia Algorithm

Categorization of sarcopenia is as follows: older adults with abnormal gait speed and abnormal muscle mass (n=34) plus older adults with normal gait speed but abnormal handgrip strength and abnormal muscle mass (n=35)



Figure 2. Kaplan-Meier Curves for GEMU patients (n=172): a) Mortality, and b) 12-Month admission to a hospital via the Emergency Department Visit. Analysis time = days, and all patients were followed up for 365 days. The steepest decline curve for all outcomes was for sarcopenic patients.

Outcomes	Adjusted HR, (95% CI) [‡]	Р
12-Month mortality	2.23 (1.15 - 4.34)	0.018
12-Month ED admission	0.92 (0.62 - 1.37)	0.703
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Table 2. Results of Cox Regression Models showing the Association of Sarcopenia with Study Outcomes $(n=172)^{\dagger}$

[†]Adjusted for age, sex and Charlson's Comorbidity Index [‡]Adjusted Hazard Ratios Correspond to Sarcopenia Status

ED = Emergency Department