Prevalence and Clinical Correlates of Sarcopenia, Identified According to the EWGSOP Definition and Diagnostic Algorithm, in Hospitalized Older People: The GLISTEN Study

Prevalence And Clinical Correlates of Sarcopenia in Hospitalized Older People according to the EWGSOP definition and diagnostic algorithm: The Glisten Study

Corresponding Author:

Stefano Volpato, MD,MPH

Department of Medical Science, University of Ferrara

Via Savonarola, 9

I-44100 Ferrara, ITALY

e-mail:vlt@unife.it

PHONE: +39 0532 236658

FAX +39-0532-210884

Introduction. Prevalence of sarcopenia is substantial in most geriatrics settings, but estimates varies greatly across studies because of different population characteristics, different diagnostic criteria, and different methods used to assess muscle mass, muscle strength and physical performance. We investigated the feasibility of the European Working Group on Sarcopenia in Older People (EWGSOP) algorithm assessment in hospitalized older adults and analyzed prevalence and clinical correlates of sarcopenia.

Methods. Cross sectional analysis of 655 participants enrolled in a multicenter observational study of older adults admitted to 12 acute care wards in Italy. Sarcopenia was assessed as low skeletal mass index (Kg/m2) plus either low hand-grip strength or low walking speed (EWGSOP criteria). Skeletal muscle mass was estimated using bioimpedance analysis.

Results. Of the 655 patients (age 80.7±6.6 years; women 48%) enrolled in the study, 275 (40.2%) were not able to perform the 4-meter walking test and twenty one (3%) did not perform the hand-grip test because of medical problems. The overall prevalence of sarcopenia was 34.7% (95% CI 28-37) and steeply increased with age ($p<0.001$). In multivariable analysis, patients with sarcopenia were older and were more likely to be male, to have congestive heart failure, cerebrovascular disease, and severe ADL disability. The prevalence of sarcopenia was inversely correlated with BMI.

Conclusion. Based on EWGSOP criteria, prevalence of sarcopenia is extremely high among acutely ill older adults. The EWGSOP algorithm, however, might not be suitable for routine clinical use in patients admitted to acute care wards since many patients are not able to perform the walking test.

INTRODUCTION

The aging process is often characterized by substantial change in body composition, including increase in fat mass and loss of skeletal muscle mass, resulting in loss of muscle strength and function, a condition that has been referred to as sarcopenia . Sarcopenia is therefore considered a geriatric syndrome defined as a progressive impairment of muscle function due to the loss of skeletal muscle mass, that occurs with advancing age . In older people sarcopenia is a powerful risk factor for mobility impairment, disability, loss of independence, hospitalization, and death . The clinical implications of this geriatric syndrome have been consistently reported across different settings including, community dwelling samples, nursing homes and acute care departments

According to a recent systematic review4, prevalence of sarcopenia is substantial in most geriatrics settings, but estimates varies greatly across studies because of different population characteristics, different diagnostic criteria, and different methods used to assess muscle mass, muscle strength and physical performance. When assessed according to the European Working Groups on Sarcopenia in Older People criteria , prevalence rates ranged from 1% to 29% among community-dwelling populations , and from 17.4% to 32.8% among institutionalized older people.

Previous studies have reported that sarcopenia is associated with increased risk of hospitalization and poor clinical outcomes following acute illness, including longer length of hospital stay and increased risk of death . Nevertheless, data on hospitalized patients are scant and limited to small studies. Furthermore, the feasibility of standardized assessment of the diagnostic criteria for

sarcopenia, including objective measures of physical performance, in the geriatric acute setting has not been evaluated in large samples.

We conducted therefore a multicenter observational study of older patients admitted to 12 acute care wards in Italy. The primary objective of this data analysis was to estimate the prevalence and clinical correlates of sarcopenia and to investigate the feasibility EWGSOP algorithm assessment in large sample of hospitalized older patients .

METHODS

Study Design and Data Collection

Data are from the Gruppo Lavoro Italiano Sarcopenia - Trattamento e Nutrizione (GLISTEN) project, an observational study performed in geriatric and internal medicine acute care wards of twelve Italian hospitals (see appendix). Methodology of the GLISTEN project has been described in detail elsewhere (ref). In brief, the study was designed to investigate prevalence and clinical correlates of sarcopenia in older hospitalized adults in Italy and to estimate incidence of sarcopenia during hospital stay . All patients consecutively admitted to participating wards, between February 2014 and May 2014, were screened for enrollment. Exclusion criteria were: age less than 65 years and unwillingness to take part to the study. All participants were assessed within the first 48 hours from hospital admission and followed until discharge. All participating centers obtained ethical approval from their institutions, and all participants signed a written consent.

Participants' data were collected through a standardized dedicated questionnaire including demographic characteristics, self-report functional status, cognitive, and mood assessment; medications use; admission and discharge diagnoses; and results of biochemical tests.
The questionnaire was filled within the first 48 hours from hospital admission and again within 24 hours before hos¬pital discharge before hospital discharge. Questionnaire was filled using a variety of information sources, such as direct observation, interviews with the patients, family, friends or formal service providers, and review clinical records, both medical and nursing. Furthermore objective measurers of physical performance (handgrip strength and 4-meter usual walking speed test) were also assessed at hospital admission and before hospital discharge.

Assessment of sarcopenia

Sarcopenia was defined, according to EWGSOP criteria, as presence of low muscle mass, plus low muscle strength or low physical performance5. Muscle mass was measured by BIA using a Quantum/S Bioelectrical Body Composition Analyzer (Akern Srl, Florence, Italy). Whole-body BIA measurements were taken between the right wrist and ankle with subject in a supine position. Muscle mass was calculated using the BIA equation of Janssen and colleagues : Skeletal muscle mass (kg)= [(height2/BIA resistance x 0.401) + (gender x 3.825) + (age x -0.071)] + 5.102, where height is measured in centimeters; bioelectrical impedance analyses resistance is measured in ohms; for gender, men=1 and women=0; age is measured in years. This BIA equation was previously developed and cross validated against magnetic resonance imaging measures of whole-body muscle mass. Absolute skeletal muscle mass (kg) was converted to skeletal muscle index (SMI) standardizing by meters squared (kg/m2) . Using the cutoff points indicated in the EWGSOP consensus, low muscle mass was classified as the skeletal muscle index less than 8.87 and 6.42 kg/m2 in men and women, respectively. Muscle strength was assessed by grip strength, measured

using a hand-held dynamometer (JAMAR hand dynamometer (Model BK-7498, Fred Sammons Inc., Brookfield, IL). Three trials for each hand were performed and the highest value of the strongest hand was used in the analyses . Twenty one (3%) participant had did not performed the grip strength test. BMI-adjusted values, were used as cutoff point to classify low muscle strength (see figure 1). Usual walking speed (meter/second) on a 4-m course was used as objective measures of physical performance; speed lower than 0.8 m/s identified participants with low physical performance. Two hundred and seventy five patients did not performed the walking test. Of them, 134 were not able to walk in the two weeks preceding hospital admission and were therefore classified as having low physical performance; the remaining 141 had normal self-report ADL mobility status and were considered as having normal gait speed if they have a valid grip strength assessment. For 14 patient in which both the grip strength and the gait speed evaluation were missing were excluded from the analysis leaving a sample of 655 patients .

Covariates

Sociodemographic variables (age, gender, smoking habit, education) were assessed through clinical interview at hospital admission. Functional status in basic activities of daily living (ADL) was measured according to the participants' self-reported difficulty in performing each of six activities: getting in and out of a bed, bathing, dressing, eating, continence, and using the toilet. Severe ADL disability was defined as the presence of difficulty in 3 or more activities . Cognitive functioning was assessed using the Short Portable Mental Status Questionnaire . Patients with scores ≥ 3 errors were considered to have cognitive impairment. Depressive symptoms were assessed by means of the short form of the Geriatric depression scale. Patients with scores >5 points were considered having depressive symptoms .

Diagnoses of specific medical conditions were gathered from the patient, attending physicians and by a careful review of medical charts; comorbidity was assessed using the Charlson Comorbidity

Index by adding scores assigned to specific discharge diagnoses . Assessors recorded all drugs currently taken by the participants at admission: brand name, formulation, and daily dose were registered. All the drugs were coded according to the Anatomical Therapeutic and Chemical codes and the number of drugs used was then calculated.

Statistical Analysis

For descriptive purpose, baseline characteristics of the study population were compared according to presence or absence of sarcopenia, using a CHI square test for categorical variables and the ANOVA or the non parametric Wilcoxon Mann Whitney test continuous variables. Cox Proportional Hazard models with robust variance were used to assess the association between potential clinical and functional characteristics and sarcopenia prevalence . Candidate variables to be included in the Cox model were selected on the basis of biological and clinical plausibility as risk factor for sarcopenia. To identify factors independently associated with prevalent sarcopenia, we first estimated crude Prevalnce Rate Ratio (PRR) and 95% C.I. and then controlling for age and gender. A multivariable Cox model was computed including all the variables that were associated with the outcome at a level of 0.5, after adjustment for age and gender. Finally, in order to remove unnecessary variables a more parsimonious model was selected using a stepwise backward selection technique (p for removal 0.1). All analyses were performed using Stata 13.0 for Windows (StataCorp, College Station, TX).

RESULTS

In this sample of 655 hospitalized older patients individuals mean SMI was 8.16±2.10 kg/m2 (6.58±1.37 kg/m2 and 9.00±1.93 for participants with and without sarcopenia, respectively). SMI was higher in men ($p < 0.0001$), inversely related to age ($r=-0.2424$; $p < 0.0001$) and directly correlated with grip strength ($r=0.3528$; $p<0.0001$) and walking speed ($r=0.1743$; $p=0.0005$). Using the algorithm proposed by the EWGSOP (figure 1), 227 patients (34.7%) were identified as affected by sarcopenia. Among them, 101 (44.5%) were sarcopenic because of low gait speed (n=43, 18.9%) or poor grip strength (n=58, 25.6%), whereas 126 (55.5%) had the concomitant presence of reduced muscle strength, and slow gait speed.

Prevalence of sarcopenia increased steeply with age (Figure 2): from 11.1% and 30.2% respectively in women and men aged 65-74 years, to 46.7% and 50.7% in women and men older than 85 years, respectively. General characteristics of participants aged 65 years or older according to the presence of sarcopenia are presented in Table 1. Mean age of study participants was 81.0 (standard deviation 6.8) years, and 51.9% were women . Compared with participants without sarcopenia those diagnosed with sarcopenia were significantly older, had lower BMI, and higher number of errors at the SPMSQ. Patients with sarcopenia were more likely to report unintentional weight loss; furthermore they had greater prevalence of severe ADL disability, congestive heart failure, stroke, and dementia and lower prevalence of type 2 diabetes.

After multivariable adjustment, we found an increased and independent likelihood of being sarcopenic with increasing age (PR 1.03; 95% CI 1.01-1.04), severe ADL disability (PR:1.32; 95% CI 1.06-1.63), history of congestive heart failure (PR: 1.32 95% CI 1.06-1.66) and stroke (PR:1.42; 95%

CI 1.09-1.84). Conversely, a decreased probability of being sarcopenic was detected for women (PR: 0.79; 95%; CI 0.65-0.97) and with increasing BMI (PR: 0.92; 95% CI 0.90-0.95).

DISCUSSION

Among older Italian patients admitted to the hospital, sarcopenia, defined according to the EWGSOP operational criteria, is very common and its prevalence raises steeply with increasing age in both gender. After adjustment for age and gender, several socio-demographic characteristics and clinical conditions were significantly associated with sarcopenia prevalence, but after adjustment for potential confounders, increasing age, diagnosis of CHF, history of stroke and severe ADL disability were directly associated with sarcopenia, whereas higher BMI and being woman were inversely associated with the presence of sarcopenia. More than 40% of patients enrolled in the study were not able to perform the 4-meter usual walking speed test, as required by the EWGSOP diagnostic algorithm.

The estimated prevalence of sarcopenia from this multicenter study is in line, although somehow higher, with the findings of previous reports that investigated conducted in similar samples of older hospitalized patients using the same diagnostic criteria11. Conversely, our estimated prevalence was lower if compared to studies that enrolled patients admitted to specific clinical settings including in-hospital rehabilitation ward in which sarcopenia prevalence was estimated as high as 60% , or significantly higher if compared to studies that used anthropometric measures to assess the skeletal muscle index10. Furthermore, our study demonstrated that sarcopenia is more common in geriatric inpatient as compared to community-dwelling population4 , indirectly confirming that sarcopenia is a risk factor for hospitalization3 and, at the same time, supporting the potential effectiveness of screening sarcopenia in the acute care setting.

In agreement with previous studies11,14, we found a statistically significant association between BMI value and prevalence of sarcopenia, with patients with higher BMI levels having a lower likelihood of being sarcopenic. BMI is considered a rough marker of nutritional status and a measure of overall adiposity. Malnutrition is a powerful risk factor for sarcopenia4, and might well explain the increased prevalence of sarcopenia in patients with lower BMI levels. On the other hand, although sarcopenia often coexists with elevated BMI, a condition referred to as sarcopenic obesity , it has been demonstrated that compared to normal weight individuals, obese people have increased cross-sectional area of type I skeletal muscle fibers, increased muscle lipid content, and greater thigh muscle volume . Of interest, overweight people have also greater absolute lower extremity strength but a lower ratio of muscle strength to muscle volume suggesting a lower muscle quality in people with increased fat mass .

We found a greater prevalence of severe ADL disability is patients with sarcopenia compared to the non sarcopenic counterpart and the association remained statistically significant after adjustment for age, comorbidities and other potential confounding factors. These results are not surprising and in line with previous cross-sectional and longitudinal studies who demonstrated an independent relationship of sarcopenia with the risk of functional impairment and disability12, . From this point of view our findings reinforce the important clinical implications of sarcopenia in older people and support the usefulness of sarcopenia screening in older disabled patients; indeed in our sample among the 183 patients with severe disability, almost one out of two (47%) were sarcopenic.

Congestive heart failure was more prevalent among patients with sarcopenia compared to those with normal skeletal muscle mass and function, with an adjusted relative prevalence excess of 30%. Sarcopenia affects approximately 20 % of ambulatory patients with heart failure , but its prevalence is likely greater among hospitalized decompensated patients; indeed in our sample the prevalence of sarcopenia among patients with a diagnosis of congestive heart was as high as 45%. Heart failure is currently considered a systemic and multiorgan syndrome sustained by activated feedback signals from peripheral reflex circuits, systemic dysregulation of several hormonal pathways, and a global metabolic imbalance characterized by decreased oxidative capacity, impaired substrate use and energy transfer, and an overall catabolic/anabolic imbalance that not only affect the myocardium but also peripheral tissues including skeletal muscle .

Sarcopenia was also more common in patients with history of stroke. Only a few studies formally investigated this association with conflicting results with some studies reporting a significant association only in men and others failing to show a significant association . Within four hours after cerebral damage is observed an initial reduction of motoneurons in the musculature of the paretic limb. Loss of muscle innervation leads to muscular weakness, inactivity, and immobilization and results in muscle atrophy. Within the first week after stroke muscle weakness occurs also in the non-paretic limb and patients who are not able to relearn walking within 2 months after stroke revealed similar lean mass reduction in paretic and non-paretic leg . A combination of mechanisms, including malnutrition, immobilization, disuse, inflammation, metabolic, and neurovegetative imbalance after stroke frequently contribute to muscle wasting and may progress to the stroke-related sarcopenia .

In interpreting these findings, some limitations should be considered. The cross-sectional and observational design of the study did not allow us to clarify any temporal or cause-effect relationships between sarcopenia and its associated factors. The use of BIA for muscle mass

assessment presents some drawbacks mainly due to the hydratation problems usually observed in older persons that may result in an underestimation of the body fat and an overestimation of fat-free mass. On the other hand, BIA is inexpensive, easy to use, readily reproducible and appropriate for both ambulatory and bedridden patients, considered as a portable alternative to dual energy X-ray absorptiometry (DXA) , and its standardized use may favour a widespread assessment of body composition in everyday clinical practice. Finally, more than 40% of the patients enrolled were not able to perform the 4-meter walking test because inability to walk or coexisting medical conditions that contraindicated the test administration at hospital admission. Previous work conducted on community-dwelling older people suggested that a sarcopenia definition based only on the presence of low muscle mass and low grip strength predicts the risk of incident disability and mortality as well as the original EWGSOP phenotype suggesting that low walking speed might not be an essential criterion for the diagnosis of sarcopenia3. Our results support the idea that in the acute care setting, in order to facilitate the diagnosis of sarcopenia it might be useful, in persons with low muscle mass, focusing on the assessment of handgrip strength only. Finally, we were not able to formally differentiate cases of sarcopenia from cases of cachexia, a condition highly prevalent in the acute care words . Although after the exclusion of cases with very low BMI (<20 Kg/m2), the prevalence of sarcopenia was not substantially modified (31.9 %), we cannot rule out the possibility that we have overestimated the true prevalence of sarcopenia.

In summary, in this sample of Italian hospitalized geriatrics patients, the EWGSOP criteria identify sarcopenia as a very common conditions strongly related to the age and the clinical status of the patients, including functional and nutritional status and selected chronic conditions. Whether a prompt diagnosis and adequate nutritional and pharmacological interventions would modify the prognosis of these patients remains to be determinated.

Acknowledgements.

Legend to Figures

Figure 1: Application of the EWGSOP algorithm for the case finding of sarcopenia to the GLISTEN sample

Figure 2: Crude prevalence of sarcopenia in men (black) and women (gray) according to age group

GLISTEN Study Group Investigators

1. Department of Medical Sciences, University of Ferrara, Italy: Gloria Brombo, Elisabetta Savino.

2. Dipartimento di Scienze mediche traslazionali, Università di Napoli "Federico II"

3. Dipartimento di Scienze della Salute, Università degli Studi Milano Bicocca e Clinica Geriatrica Ospedale San Gerardo, Monza

4. Dipartimento di Scienze Mediche, SCDU Geriatria e Malattie Metaboliche dell'Osso, Città della Salute e della Scienza, Torino: Mario Bo. Hanno collaborato Lorenzo Marchese, Luca Agosta

5. Azienda Sanitaria Locale di Cagliari, U.O. di Geriatria:

6. Geriatria e Accettazione Geriatrica d'urgenza, INRCA, Ancona

7. Dipartimento di Medicina Clinica e Sperimentale, Università di Messina

8. Dipartimento di Area Critica Medico-Chirurgica, Unità di Gerontologia e Geriatria. Università di Firenze

9. Dipartimento di Medicina Clinica e Sperimentale, Sezione di Geriatria, Università di Parma

10. Dipartimento di Scienze Mediche, Chirurgiche, Neurologiche, Metaboliche e dell'Invecchiamento, Seconda Università di Napoli

11. Dipartimento di Medicina Interna, Sezione di Geriatria, Università di Verona

12. Dipartimento di Geriatria, Neuroscienze e Ortopedia, Università Cattolica del Sacro Cuore, Roma

Table 1. Selected general characteristics and comorbidities of study participants according to the presence of Sarcopenia

	n. obs	Sarcopenia No (n= 428)	Sarcopenia Yes (n=227)	p-value
Age, mean ± sd	655	79.9 ± 6.5	83.2 ± 7.0	<0.001
Female, n (%)	655	228 (53.3)	112 (49.3)	0.338
Education (years), median [IQR]	598	5 [5; 8]	5 [5; 8]	0.189
Ever Smoking, n (%)	640	197 (47.0)	99 (44.8)	0.806
Weight loss, n (%)	648	174 (41.0)	116 (51.8)	0.009
BMI, mean ± sd	655	27.3 ± 4.9	24.3 ± 4.7	<0.001
Emergency Admission, n (%)	652	289 (67.7)	182 (80.9)	<0.001
Previous falls, n (%)	634	112 (26.9)	63 (29.0)	0.587
Disability in ADL, n (%) (score >2)	655	97 (22.7)	86 (37.9)	<0.001
ADL score, median [IQR]	655	1 [0; 2]	1 [0; 5]	<0.001
GDS, median [IQR]	532	4 [2; 8]	5 [3; 8]	0.170
SPMSQ, median [IQR]	616	2 [1; 3]	2 [1; 5]	0.001
Number of drugs, mean ± sd	655	6.0 ± 3.0	6.0 ± 2.7	0.920
Charlson Comorbidity Index, median [IQR]	655	3 [2;5]	3 [2;4]	0.705
Hypertension, n (%)	655	318 (74.3)	173 (76.2)	0.591
CHD, n (%)	654	117 (27.3)	62 (27.4)	0.979
Atrial Fibrillation, n (%)	654	111 (26.0)	61 (26.9)	0.808
CHF, n (%)	655	63 (14.7)	53 (23.4)	0.006
Diabetes, n (%)	655	137 (32.0)	52 (22.9)	0.014
Artrosis, n (%)	655	100 (23.4)	53 (23.4)	0.996
COPD, n (%)	655	110 (25.7)	57 (25.1)	0.869
Stroke, n (%)	655	44 (10.3)	38 (16.7)	0.017
Dementia, n (%)	655	44 (10.3)	49 (21.6)	<0.001
Chronic Kidney dis. (%)	655	94 (22.0)	51 (22.5)	0.882
Cancer, n (%)	655	57 (13.3)	36 (15.9)	0.375
Length of hospital stay (days), median [IQR]	655	8 [5; 13]	9 [6; 12]	0.712

Table 2. Unadjusted and multivariable adjusted Prevalence Race Ratio of sarcopenia according to selected characteristics

Cox model (equal time)	**Unadjusted** PR (95% CI)	**Age-gender adjusted** PR (95% CI)	**Full adjusted** PR (95% CI)	**Parsimonious Model*** PR (95% CI)
Age (years)	1.05 (1.03; 1.06)	1.05 (1.03; 1.07)	1.03 (1.01; 1.04)	1.03 (1.01; 1.04)
Female Gender	0.90 (0.73; 1.11)	0.80 (0.65; 0.98)	0.81 (0.66; 0.99)	0.79 (0.65; 0.97)
Weight loss	1.33 (1.08; 1.64)	1.28 (1.04; 1.57)	1.05 (0.85; 1.30)	
BMI (Kg/m^2)	0.92 (0.89; 0.94)	0.93 (0.90; 0.95)	0.93 (0.90; 0.96)	0.92 (0.90; 0.95)
Emergency Admission	1.60 (1.21; 2.12)	1.31 (0.98; 1.75)	1.17 (0.88; 1.54)	
Disability in ADL	1.57 (1.28; 1.93)	1.33 (1.07; 1.65)	1.28 (1.01; 1.64)	1.32 (1.06; 1.63)
SPMSQ	1.07 (1.03; 1.10)	1.03 (1.00; 1.07)	0.98 (0.94; 1.03)	
CHF	1.42 (1.12; 1.79)	1.27 (1.01; 1.60)	1.31 (1.04; 1.64)	1.32 (1.06; 1.66)
Diabetes,	0.73 (0.57; 0.95)	0.84 (0.65; 1.09)	0.94 (0.73; 1.22)	
Stroke	1.40 (1.08; 1.82)	1.32 (1.01; 1.73)	1.46 (1.12; 1.89)	1.42 (1.09; 1.84)
Dementia	1.66 (1.32; 2.09)	1.42 (1.13; 1.78)	1.26 (0.93; 1.70)	

PR: Prevalence Ratio

*****Backward stepwise logistic regression model (p value for removal >0.1). For variables removed from the initial model OR and 95% CI are not displayed in table. Variable included in the initial model are all the same variables included in the full model

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