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The incidence of sarcopenia among hospitalized older patients: results from the Glisten study

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Abstract

Background New evidence is emerging on the importance of lean body mass during periods of illness and recovery. The preservation of lean body mass during such periods of intense stress impacts both patient and treatment outcomes. However, data concerning the incidence of sarcopenia among older people during hospitalization are scarce. The objective of this study was to evaluate the development of sarcopenia in a sample of hospitalized older subjects.

Methods We used data of 394 participants from the multicentre Italian Study conducted by the Gruppo Lavoro Italiano Sarcopenia—Trattamento e Nutrizione (GLISTEN) in 12 Acute Care Wards (Internal Medicine and Geriatrics) of University Hospitals across Italy. This study was designed to determine the prevalence of sarcopenia at hospital admission and the change in muscle mass and strength during hospitalization. Sarcopenia was defined as low skeletal mass index (kg/m^2) along with either low handgrip strength or slow walking speed [European Working Groups on Sarcopenia in Older People (EWGSOP) criteria]. Estimation of skeletal muscle mass was performed by bioelectrical impedance analysis (BIA).

Results The mean age of the 394 enrolled patients (including 211 females who accounted for 53% of the sample) was 79.6 ± 6.4 years. Among those without sarcopenia at hospital admission, 14.7% of the study sample met the EWGSOP sarcopenia diagnostic criteria at discharge. The incidence of sarcopenia during hospitalization was significantly associated with the number of days spent in bed but was not correlated with the total length of hospital stay. In particular, patients who developed sarcopenia spent an average of 5.1 days in bed compared with 3.2 days for those with no sarcopenia at discharge (P = 0.02). Patients with sarcopenia showed a significantly lower body mass index compared with non-sarcopenic peers (25.0 ± 3.8 kg/m^2 vs. 27.6 ± 4.9 kg/m^2, respectively; $P < 0.001$). Similarly, the skeletal mass index at admission was significantly lower among patients who developed sarcopenia during hospital stay.

Conclusions Incident sarcopenia during hospital stay is relatively common and is associated with nutritional status and the number of days of bed rest.

Keywords Acute care; Incidence; Muscle; Bed rest; Malnutrition

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Introduction

Sarcopenia is one of the most important risk factors for mobility impairment, falls, disability, loss of independence, hospitalization, and death among older people.[1] The concept of sarcopenia is encountered increasingly often in research and clinical practice, not only in geriatric medicine but also in other specialties.[1] New evidence is emerging on the importance of lean body mass during periods of illness and recovery.[2] Sarcopenia is considered a geriatric syndrome described as the impairment of muscle function due to the loss of skeletal muscle mass, which occurs during the aging process.[3,4]

The clinical implications of sarcopenia have been consistently described across different settings, including community dwelling samples, nursing homes, and acute care units.[5,6] According to a recent systematic review, the prevalence of sarcopenia is significantly high in most of the geriatrics settings, but estimations impressively vary across studies because of different population characteristics, diagnostic criteria, and methods used to assess muscle mass and physical performance. When assessed according to the European Working Groups on Sarcopenia in Older People (EWGSOP) criteria,[7] prevalence rates range from 1 to 29% among community-dwelling populations and from 17.4 to 32.8% among institutionalized persons.[8] More recently, Bianchi and colleagues[9] demonstrated that among older Italian patients admitted to hospital, sarcopenia, defined according to the EWGSOP criteria,[7] was very common, and its prevalence raised steeply with increasing age in both genders.

Data concerning the incidence of sarcopenia among older people during hospital stay are scarce. In older patients, besides the negative effect of the acute event, hospitalization itself might represent an additional stressor in terms of reduced caloric intake, extremely low physical activity, or prolonged bed rest. For example, experimental studies suggest that in healthy older people, prolonged bed rest is associated with significant decrease in muscle protein synthesis, lower extremity lean mass, and strength.[10,11] The aim of this study was to evaluate the onset of sarcopenia in a sample of hospitalized older patients. We conducted a multicentre observational study of older patients admitted to 12 acute care wards in Italy. The primary objective of this study was to estimate the incidence and the clinical correlates of sarcopenia in a large sample of hospitalized older patients without sarcopenia at the time of hospital admission.

Methods

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 12 Italian hospitals (Monza, Turin, Ferrara, Verona, Parma, Florence, Ancona, Rome, Napoli I, Napoli II, Cagliari, Messina). Methodology of the GLISTEN project has been described in detail elsewhere.[9] In brief, the study was designed to investigate the prevalence and clinical correlates of sarcopenia in older hospitalized patients in Italy and to estimate the incidence of sarcopenia during hospital stay. All participating centres obtained ethical approval from their institutions, and all participants signed a written consent.

Study design, data collection, and sample

All patients aged 65 years or more (n = 655) consecutively admitted to participating wards from February 2014 to May 2014 entered the study protocol. The only exclusion criterion was the unwillingness to take part to the study. For the present study, we included only patients without sarcopenia at baseline assessment (n = 428). Six patients died during the hospital stay, and 28 were not included for missing values in the variables of interest. The final sample was therefore comprised of 394 participants (*Figure* 1).

All patients were assessed within the first 2 days of hospital admission and followed until discharge (within 24 h of hospital discharge). Participants underwent comprehensive geriatric assessment (CGA), including demographic characteristics, functional status, cognitive and mood assessment, medications use, admission and discharge diagnoses, and biochemical tests. A variety of information sources, such as direct observation, interviews with the patient, family, friends or formal service providers, and review of clinical records, both medical and nursing, were used. Finally, objective measurers of physical performance (handgrip strength and 4 m usual walking speed test) were assessed at hospital admission and before discharge.

Assessment of sarcopenia

Sarcopenia was defined, according to EWGSOP criteria, as the presence of low muscle mass plus low muscle strength or low physical performance.[7]

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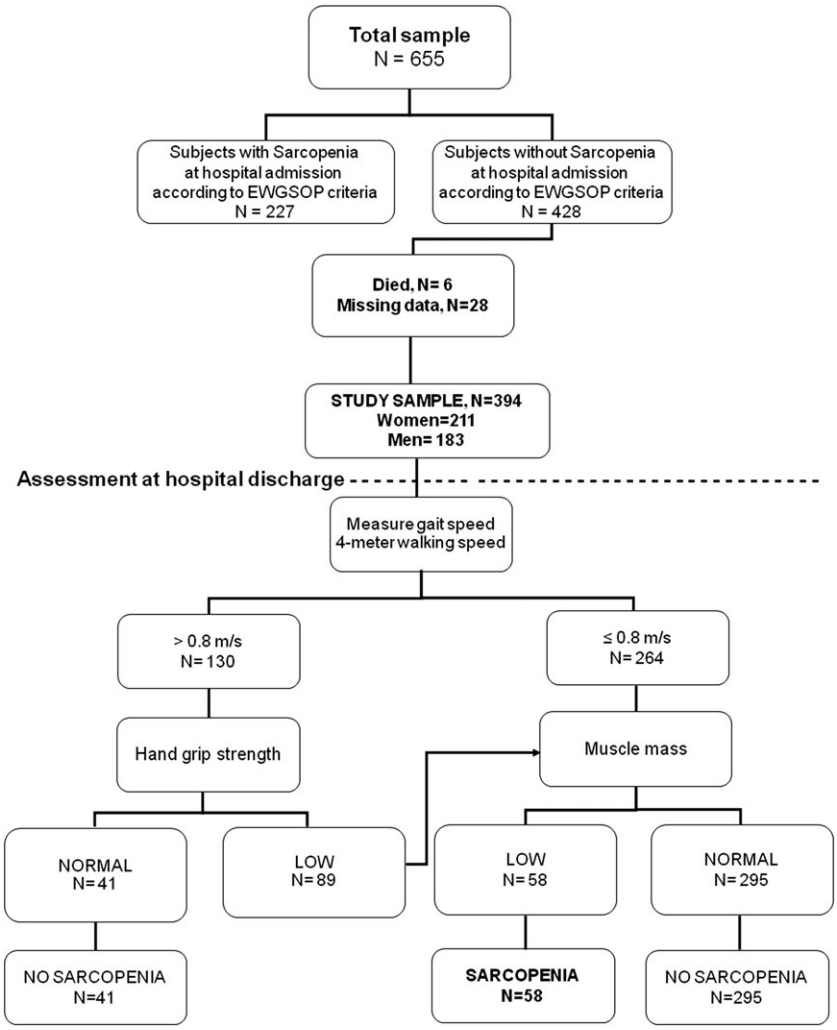
Figure 1 Application of the EWGSOP algorithm for sarcopenia case finding in the GLISTEN sample.



Muscle mass was measured by bioelectrical impedance analysis (BIA). Bioelectrical impedance analysis resistance (Ohms, Ω) was obtained using a Quantum/S Bioelectrical Body Composition Analyser (Akern Srl, Florence, Italy) with an operating frequency of 50 kHz at 800 mA. Whole-body BIA measurements were taken between the right wrist and ankle with the patient in a supine position.[12] Muscle mass was estimated using the equation developed by Janssen and colleagues[13,14]:

$$\text{skeletal muscle mass (kg)} = [(\text{height}^2/\text{BIA resistance} \times 0.401) + (\text{gender} \times 3.825) + (\text{age} \times -0.071)] + 5.102,$$

where height is measured in cm; BIA resistance is measured in Ω; for gender, men = 1 and women = 0; and age is measured in years. This BIA equation was developed and cross-validated against magnetic resonance imaging measures of whole-body muscle mass.

The skeletal muscle index [SMI (kg/m^2)] was obtained dividing absolute muscle mass by squared height.[14] Using the cutoffs indicated in the EWGSOP consensus paper,[7] low muscle mass was classified as SMI less than 8.87 and 6.42 kg/m^2 in men and women, respectively. These cutoffs were similar to those obtained among 2276 elderly women and 2223 elderly men from the Third National Health and Nutrition Examination Survey (NHANES III).[15,16]

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. BMI-adjusted values were used to identify low muscle strength. Cut-points were similar to those obtained among 469 men and 561

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women (age range from 20 to 102 years) from the InCHIANTI study population.[17]

Walking speed was evaluated measuring participants' usual gait speed (in meters per second) over a 4 m course. A cutoff point of 0.8 m/s or less identified participants with low physical performance.[7]

Covariates

Socio-demographic 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 three or more activities.[18] Cognitive functioning was assessed using the Short Portable Mental Status Questionnaire.[19] Patients with scores ≥ 3 were considered to be cognitively impaired. Depression was assessed by means of the 15-item Geriatric Depression Scale, where the cutoff of > 5 points suggests significant depressive symptoms.[20]

During hospital stay, days of bed rest were considered those spent in the bed for 24 h. The days of fasting were considered according to the non-consumption of at least two main meals.

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 dosage were registered. All drugs were coded according to the Anatomical Therapeutic and Chemical codes. The number of drugs taken was also calculated.

Statistical analysis

For the present study, we selected all patients without sarcopenia at baseline (hospital admission). After excluding six patients who died during hospital stay and 28 for missing values, the final sample was composed of 394 participants. Patients with incident sarcopenia during hospital stay were identified using the algorithm developed by the EWGSOP[7] for sarcopenia case-finding and screening in practice (*Figure* 1). Data were analysed to obtain descriptive statistics. Continuous variables are presented as mean ± standard deviation. Differences in socio-demographic, functional, and clinical characteristics between patients with or without incident sarcopenia were analysed in different ways. Quantitative parameters with normal distribution were tested by one-way analysis of variance, after a pretest for homogeneity of variances. If distribution was not normal, the non-parametric Kruskal–Wallis rank test was used. Categorical variables were analysed by the χ^2 test. A P value lowers than 0.05 was chosen for statistical significance.

The relationship between incident sarcopenia and clinical and functional variables was estimated by deriving odds ratios (ORs) from multiple logistic regression models. Sarcopenia was included as the dependent variable in such models. Based on previous researches, we considered age, gender, length of hospital stay, functional ability (ADL score), cognitive performance, comorbidity, and BMI as factors potentially associated with incident sarcopenia and included them as independent variables in the models. We provide estimates of association while adjusting for potential confounders by deriving crude and adjusted ORs and the corresponding 95% confidence intervals (CIs) from these models. All analyses were performed using SPSS software (version 11.0, SPSS Inc., Chicago, IL).

Results

The mean age of the 655 enrolled patients in the GLISTEN study (including 340 females who accounted for 51.9% of the sample) was 81.0 ± 6.8 years (82.3 ± 6.6 and 79.6 ± 6.0, in women and men, respectively). Sarcopenia at hospital admission was diagnosed in 227 (34.7%) patients (*Figure* 1).

Among patients without sarcopenia at hospital admission (n = 394), 58 participants (14.7%) met the EWGSOP sarcopenia diagnostic criteria at hospital discharge (*Figure* 1). More than 50% of those who developed sarcopenia during hospital stay showed over 10% muscle mass loss compared with baseline values.

Patients who developed sarcopenia (Table 1) were significantly older than those who did not (82.0 ± 7.2 vs. 79.2 ± 6.2 years, respectively; $P < 0.01$). Participants with incident sarcopenia during hospital stay showed significantly lower baseline BMI compared with patients who did not develop sarcopenia (25.0 ± 3.8 kg/m^2 vs. 27.6 ± 4.9 kg/m^2, respectively; $P < 0.001$). Similarly, SMI at hospital admission was significantly lower among patients who developed sarcopenia during hospital stay (8.4 ± 1.5 kg/m^2 vs. 9.0 ± 1.8 kg/m^2, respectively; P = 0.01). Participants with greater impairments in daily activities (by means ADL score) and cognitive performance (according to the SPMSQ score) showed higher incidence of sarcopenia at discharge. Finally, the incidence of sarcopenia during hospitalization was significantly associated with the number of days spent in bed, while it was only marginally correlated with the total length of hospital stay. In particular, patients with incident sarcopenia spent an average of 5.4 ± 6.7 days in bed (more than 28% of the length of hospital stay) compared with 3.2 ± 5.3 days (18% of the length of hospital stay) among participants without sarcopenia at discharge (P = 0.02).

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Table 1 Selected general characteristics and comorbidities of study participants according to the incidence of sarcopenia

Characteristics	Total sample (n = 394)	Incidence of sarcopenia		
		No (n = 336)	Yes (n = 58)	P-value
Age, mean ± SD	79.6 ± 6.4	79.2 ± 6.2	82.0 ± 7.2	0.002
Female, n (%)	211 (53.6)	182 (54.2)	29 (50.0)	0.32
BMI, mean ± SD	27.2 ± 4.9	27.6 ± 4.9	25.0 ± 3.8	<0.001
Emergency admission, n (%)	256 (65.1)	211 (63.0)	45 (77.6)	0.02
ADL score, mean ± SD	1.3 ± 1.8	1.2 ± 1.7	2.1 ± 2.3	0.001
Severe ADL disability, n (%)	87 (22.1)	65 (19.3)	22 (37.9)	0.02
GDS, mean ± SD	4.9 ± 3.6	4.9 ± 3.6	4.5 ± 3.5	0.45
SPMSQ, mean ± SD	2.3 ± 2.9	2.1 ± 2.0	3.3 ± 2.9	<0.001
Number of drugs, mean ± SD	6.0 ± 3.0	6.0 ± 3.0	6.0 ± 2.7	0.920
Charlson Comorbidity Index, mean ± SD	3.1 ± 2.3	3.1 ± 2.3	3.0 ± 2.1	0.63
Hypertension, n (%)	294 (74.6)	256 (76.2)	38 (65.5)	0.06
CHD, n (%)	104 (26.4)	86 (25.6)	18 (31.0)	0.23
CHF, n (%)	56 (14.2)	46 (13.7)	10 (17.2)	0.29
Diabetes, n (%)	126 (32.0)	114 (33.9)	12 (20.7)	0.03
COPD, n (%)	99 (25.1)	82 (24.4)	17 (29.3)	0.26
Stroke, n (%)	41 (10.4)	35 (10.4)	6 (10.3)	0.61
Cancer, n (%)	51 (12.9)	41 (12.2)	10 (17.2)	0.19
Serum albumin, mean ± SD	3.6 ± 0.7	3.6 ± 0.7	3.5 ± 0.6	0.29
Haemoglobin, mean ± SD	11.9 ± 2.2	11.9 ± 2.2	11.9 ± 2.1	0.79
Length of hospital stay (days), mean ± SD	10.2 ± 8.1	9.9 ± 7.6	12.1 ± 10.3	0.05
Length of bed rest (days), mean ± SD	3.5 ± 5.6	3.2 ± 5.3	5.1 ± 6.7	0.02
Days of fasting, mean ± SD	0.3 ± 0.9	0.3 ± 0.8	0.5 ± 1.5	0.09
SMI at admission (kg/m^2), mean ± SD	8.9 ± 1.8	9.0 ± 1.8	8.4 ± 1.5	0.01

CHD, coronary heart disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; SMI, skeletal muscle index.

Table 2 Unadjusted and adjusted models for risk of incident sarcopenia in the study population.

	Univariate odds ratio (95% CI)	Adjusted model[a] odds ratio (95% CI)
Age, years	1.07 (1.02–1.11)	1.03 (0.98–1.09)
Gender (female)	0.84 (0.48–1.47)	0.86 (0.46–1.49)
Cognitive impairment (SPMSQ)	1.21 (1.08–1.35)	1.03 (0.97–1.32)
ADL impairment (number)	1.23 (1.08–1.41)	1.23 (1.01–1.49)
Body mass index (kg/m^2)	0.88 (0.82–0.94)	0.92 (0.86–0.98)
Skeletal muscle index (kg/m^2)	0.81 (0.68–0.96)	0.43 (0.29–0.61)
Emergency admission	2.03 (1.05–3.91)	1.25 (0.59–2.67)
Length of hospital stay (days)	1.03 (1.00–1.05)	0.99 (0.95–1.03)
Length of bed rest (days)	1.05 (1.00–1.09)	1.05 (1.01–1.12)

[a]Adjusted simultaneously for all the variables listed.
Age, SPMSQ score, ADL scale score, BMI, skeletal muscle index, emergency admission, length of hospital stay, and length of bed rest were treated as a continuous variable.

After multivariable adjustment, (Table 2) we found an increased and independent likelihood of developing sarcopenia during hospital stay with ADL disability (OR: 1.23; 95% CI 1.01–1.49) and length of bed rest (OR: 1.05; 95% CI 1.01–1.12). Conversely, a decreased probability of being sarcopenic at hospital discharge was detected with increasing BMI (OR: 0.92; 95% CI 0.86–0.98) and baseline SMI (OR: 0.43; 95% CI 0.29–0.61).

Discussion

The evaluation of the impact of hospitalization on the onset of sarcopenia among frail older patients is an important and intricate issue. In the present study, we explored the incidence of sarcopenia during hospital stay and the association of different domains with incident sarcopenia in a large sample of hospitalized older patients. Our data show that sarcopenia develops in approximately 15% of hospitalized elderly patients. Considering that, at the time of hospital admission, the prevalence of sarcopenia is around 35%;[9] this means that half of the patients present with sarcopenia at discharge. Furthermore, our findings show that the days of bed rest and baseline disability exert an important influence on the onset of sarcopenia, independent of age, gender, and other clinical and functional variables. Greater muscle mass and good nutritional status at hospital admission emerged as protective factors against incident sarcopenia.

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Sarcopenia is caused by the simultaneous reduction in the number of muscle fibres and atrophy of the remaining myocytes, likely as a result of lower rate of myofibrillar protein synthesis and enhanced myonuclear elimination via an apoptosis-like mechanism.[21,22] These phenomena reflect a progressive reduction of anabolism and increased catabolism, along with reduced muscle regeneration capacity. Histological sections of aged muscles have also shown increased infiltration of non-contractile tissue (i.e. collagen and fat).[23]

Muscle mass loss is linked, although not linearly, with reduced force generation and impaired muscle performance.[24] Many factors are involved in the age-dependent muscle decline: the aging processes itself, genetic susceptibility, behavioural factors (e.g. less-than-optimal diet, prolonged bed rest, sedentary lifestyle), chronic health conditions, and several drugs.[5] In this respect, it is important to highlight that our results show that the days of inactivity are an important risk factor for the onset of sarcopenia. On the other hand, in agreement with previous observations,[25] we found a significant association between baseline BMI and SMI value the incidence of sarcopenia, with patients with higher BMI and greater SMI having a lower likelihood of developing sarcopenia during hospital stay. Malnutrition per se is a powerful risk factor for sarcopenia and might well explain the increased prevalence and incidence of sarcopenia in patients with lower BMI.[26] Loss of appetite and/or reduction of food intake, usually observed during hospitalization, can lead to muscle wasting, decreased immunocompetence, and an increased rate of disease complications. In particular, a reduction in food intake along with physical inactivity leads to significant losses in muscle mass and strength.[27]

Muscle composition and function are regulated by muscle protein turnover rate. Impaired muscle protein synthesis may be due to many factors including inadequate nutritional intake, deficit in post-absorptive protein synthesis, and reduced anabolic response to nutrient ingestion, especially amino acids.[28,29] It has been shown that physical exercise and targeted oral nutritional supplementation may improve muscle health through various mechanisms.[30]

Our findings have potentially relevant clinical implications. Physical inactivity during in-hospital bed rest and malnutrition can have a negative synergistic effect on muscle protein synthesis, favouring the subsequent onset of sarcopenia. The preservation of muscle mass and function is increasingly recognized as a crucial factor for promoting healthy aging and better outcomes in different healthcare settings. As such, sarcopenia represents an ideal target for interventions aimed at preventing or postponing the occurrence of negative health-related events in late life. At present, multicomponent interventions, involving the combination of physical activity and nutrition (in particular adequate protein intake) are the only 'interventions' to prevent negative outcomes.[30] In particular, an adequate nutritional support and an early mobilization program during hospital stay are essential for preventing sarcopenia. For this reason, it is very important to promptly arrange rehabilitation services for frail older inpatients to avoid bed immobilization and treat potentially disabling conditions. Programs that meet these needs can reduce the number of severely disabled persons, or at least delay their entering a critically disabled state.

In interpreting our findings, some limitations should be considered. First, as in all observational studies, results may be confounded by unmeasured factors. However, our homogeneous population of hospitalized older people minimizes the possibility that patients without sarcopenia at hospital discharge had substantially better healthcare or health knowledge than those with incident sarcopenia. However, because of the use of an extensive multidimensional assessment approach, the present study could comprehensively investigate the different domains influencing the incidence of sarcopenia. This made it possible to control for a large number of potential confounders. Despite this effort, it is still possible that differences between study groups may have biased the results and conclusions. For example, biomarkers that potentially correlate with sarcopenia (i.e. vitamin D and inflammatory markers) were not considered. Second, the use of BIA for muscle mass assessment presents some drawbacks mainly due to hydration problems frequently observed in older persons that may result in underestimation of body fat and 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.[31,32] As such, its standardized use may favour the widespread assessment of body composition in everyday clinical practice.[33] Another important limitation that needs to be considered in the interpretation of the results is the lack of data about daily food intake. Even though the days of fasting did not significantly differ between patients who developed sarcopenia and those who did not, it is possible that the intake of specific nutrients (e.g. protein intake or oral supplementation) might be different. Finally, we were not able to formally differentiate cases of sarcopenia from cases of cachexia, a condition highly prevalent in acute care wards. Although after the exclusion of cases with very low BMI (< 20 kg/m^2), the prevalence of sarcopenia at hospital admission was not substantially modified (31.9%), the possibility cannot be ruled out that we overestimated the true prevalence of sarcopenia.[9]

Despite these limitations, our data support the concept that there is an urgent need to screen for sarcopenia at

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an early stage—for example, at hospital admission and/or during hospital stay—to initiate prevention and specific interventions to avoid the debilitating consequences of this condition. For the construction of a practical conceptual model, sarcopenia may be considered the central element of the physical frailty syndrome.[34,35] By establishing a specific biological basis (i.e. skeletal muscle decline) of physical frailty, new approaches may be determined for the development of interventions designed to reduce or reverse this disorder.[36,37]

In conclusion, the results of this study show that the number of patients who develop sarcopenia during hospitalization is relatively high. The onset of sarcopenia is directly related to the nutritional status and the number of days of bed rest. This is of particular interest considering that during a period of acute illness, the loss of lean body mass can both affect the patient's recovery outcomes and treatment plans. Preventing the loss of muscle mass during hospitalization, through specific nutritional programs and early mobilization, might improve disease-specific and functional outcomes.[38,39]

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The authors certify that they comply with the ethical guidelines for publishing in the Journal of Cachexia, Sarcopenia and Muscle: update 2015.[40]

Conflict of interest

Anna Maria Martone, Lara Bianchi, Pasquale Abete, Giuseppe Bellelli, Mario Bo, Antonio Cherubini, Francesco Corica, Mauro Di Bari, Marcello Maggio, Giovanna Maria Manca, Emanuele Marzetti, Maria Rosaria Rizzo, Andrea P. Rossi, Stefano Volpato, and Francesco Landi declare that they have no conflict of interest.

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