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The association between delirium and sarcopenia in older adult patients admitted to acute geriatrics units: Results from the GLISTEN multicenter observational study

Giuseppe Bellelli, Antonella Zambon, Stefano Volpato, Pasquale Abete, Lara Bianchi, Mario Bo, Antonio Cherubini, Francesco Corica, Mauro Di Bari, Marcello Maggio, Giovanna Maria Manca, Maria Rosaria Rizzo, Andrea Rossi, Francesco Landi, for the GLISTEN Group Investigators

Summary

Background & aims

To date, studies assessing the relationship between sarcopenia and delirium, two of the most common geriatric syndromes, are lacking. We sought to explore this association by investigating the co-occurrence of these two conditions and the independent association between them in a population of hospitalized older adults.

Methods

Cross-sectional multicenter analysis of older adults consecutively admitted to 12 acute geriatric units (AGUs). Sarcopenia was assessed upon admission by evaluating the presence of low skeletal mass index (kg/m^2), and either low handgrip strength or low walking speed (European Working Group on Sarcopenia in Older People, EWGSOP criteria). Skeletal muscle mass was estimated using bioimpedance analysis. Participants underwent a comprehensive geriatric assessment upon admission; information concerning demographics, cognition (Short Portable Status Mental Questionnaire, SPMSQ) functional (Instrumental Activities of Daily Living, IADL and Basic-Activities of Daily Living, BADL), and health status (Charlson Index and specific diseases) was evaluated. The presence of delirium upon admission was ascertained as an explicit clinical diagnosis recorded by the researcher of each centre on the data form. All association estimates were reported as Prevalence Ratios (PRs) and 95% confidence intervals (CIs), using a Cox hazard proportional regression model with robust variance and constant time.

Results

Of the 588 analyzed patients (mean age = 80.9 ± 6.8, 53.2% females), 199 (33.8%) had sarcopenia upon admission to the AGU. According to a multivariable Cox regression, delirium upon admission (PR 1.66, 95% CI: 1.12–2.45), IADL total score (PR 0.93, 95% CI: 0.87–0.98), Body Mass Index values (BMI) ranging from 18.5 to 25.0 (PR 1.70, 95% CI: 1.33–2.18), BMI values >18.5 (PR 2.53, 95% CI: 1.81–3.53), previous stroke (PR 1.51, 95% CI: 1.10–2.07) and chronic heart failure (CHF) (PR 1.31, 95% CI: 1.02–1.68) were significantly and independently associated with sarcopenia upon admission to the AGU.

Conclusion

The study, carried out in a population of hospitalized older patients, shows that a diagnosis of delirium upon admission to the AGU was more frequent in those with sarcopenia than in others. Furthermore, the study found that delirium was independently associated with the risk of being sarcopenic upon admission to the AGU. Future studies are needed to confirm this association.

Sarcopenia is a geriatric syndrome, defined as a loss of muscle mass and strength that occurs with advancing age [1]. It is an important public health issue in our society: indeed, epidemiological research demonstrates that the prevalence of sarcopenia is high in community dwelling, nursing home, and hospital-based studies [2], [3], [4], [5]. Additionally, because of the continuous aging of the elderly population, the prevalence of sarcopenia is expected to increase. Furthermore, because it is associated with an increased risk of disability, falls, and all-cause mortality, sarcopenia carries an important burden in terms of healthcare expenditure [2], [3], [4], [5], [6], [7].

Delirium is another geriatric syndrome that shares some commonalities with sarcopenia. Defined as a neuropsychiatric disorder, delirium is characterized by prominent cognitive and behavioural abnormalities that are triggered by acute underlying organic causes [8]. Like sarcopenia, delirium is relevant from an epidemiological perspective—about one in five patients in acute hospital wards currently suffer from this condition [9], [10], and there is an expected increase in its global prevalence in the coming decades. Moreover, delirium is associated with various negative outcomes, including worsening of functional and cognitive status, nursing home placement, and death in the medium to long term [9], [11], [12], [13], [14], [15].

Several studies have shown that geriatric syndromes tend to co-occur in older people [16], complicating the clinical course of hospitalized patients [17]. However, studies assessing a potential relationship between sarcopenia and delirium in older people have not been carried out so far.

To fill this gap, the aim of this study was to assess the co-occurrence and the independent association between sarcopenia and delirium in a population of older patients upon admission to acute hospitals. The demonstration of such a co-occurrence could be particularly relevant from a practical perspective, since it may help clinicians identify subjects with increased levels of frailty and subjects most at risk for the development of adverse health outcomes.

1. Methods

This is a cross-sectional study embedded within the framework of the Gruppo di Lavoro Italiano Sarcopenia Trattamento E Nutrizione (GLISTEN) study, on behalf of the Italian Society of Gerontology and Geriatrics (SIGG). The methodology of the GLISTEN project has been described in detail elsewhere [18]. In brief, the study involved twelve Acute Geriatric Units (AGUs) in Italy, and it was designed to investigate the prevalence and the clinical correlates of sarcopenia in older hospitalized adults, as well as its incidence at hospital discharge. All participating centres obtained ethical approval from their institutions.

All patients 70 years of age and above, consecutively admitted to the hospital wards between May and July 2014 consenting to participation in this study were enrolled.

Informed consent was obtained either from patients or their legal representatives. Furthermore, in order to limit the exclusion of patients with cognitive impairment, we accepted "deferred" consent from patients who presented with delirium upon admission. Deferred consent refers to consent obtained after treatment or intervention has commenced and when the patient has regained capacity. A proxy was engaged to give deferred consent if the patient did not regain his/her mental capacity after one week. In the case that either the patient or the proxy denied consent, the patient was excluded from the study [19].

1.1. Data collection

Data were collected from patients and recorded on a standardized form, which was initially filled out within the first 24 h following admission and then completed at discharge by fellows working in the Geriatrics ward who received specific training to perform this task during a 2-day course occurring before the start of this study.

All eligible patients underwent a comprehensive geriatric assessment (CGA), involving the evaluation of demographics and of each patient's cognitive, affective, functional, health, and nutritional status. Cognitive status was assessed using the Short Portable Mental Status Questionnaire (SPMSQ) [20]and by ascertaining the presence of delirium. The SPMSQ is a 10-item test used to investigate the presence and the degree of cognitive impairment in the elderly with a series of questions testing orientation, memory function related to capacity for self-care, remote memory, and the capacity to perform several mental operations. One or two errors indicate normal cognitive status; 3–4 errors indicate mild; 5–7 errors indicate moderate; and 8–10 errors indicate severe cognitive impairment [19]. The diagnosis of delirium was performed by each researcher immediately upon patient admission, in accordance with criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM) 5th edition [8]. Depressive symptoms were evaluated using the 15-item Geriatric Depression Scale (GDS) [21]. The 15-item GDS is commonly used to assess depressive symptoms in elderly patients: a GDS score between 0 and 5 denotes the absence of depressive symptoms; scores between 6 and 9 indicate mild depressive symptoms; while scores between 10 and 15 denote the presence of moderate to severe depressive symptoms [2]. Functional status was assessed with Katz's activity of daily living (ADL) index [22] and Lawton's instrumental activities of daily living (IADL) scale [23]. The first evaluates the ability to perform six basic ADL: feeding, transferring, toileting, dressing, bathing, continence. 1 point is assigned if the subject is able to perform the activity independently, and 0 if he or she is unable; thus, the total score can range from 0 (worst) to 6 (best). Lawton's scale assesses eight tasks providing information about functional skills necessary to live independently in the community: i.e. the ability to use the telephone, shop, prepare food, handle finances, do housework, take medication, do laundry, and travel. Each activity can be scored as either 1 (can perform task independently) or 0 (not able to do) [23]. Both the ADL index and Lawton's scale were

completed based on interviews with caregivers or with family members concerning the patients' functional status two weeks prior to admission. Comorbidity was assessed with the Charlson Comorbidity Index, a weighted index that considers a total of 22 conditions and assigns each a score from 1 to 6, depending on the associated relative risk of mortality [24]. Nutritional status was assessed by determinating the Body mass Index (BMI). The BMI was calculated upon hospital admission by measuring the height and weight of each patient. If height was not measurable, the estimated knee height was then calculated according to a standardized method [25]. Furthermore, we also collected the number of falls occurred in the past 12 months and the number and types of medications upon admission.

The researchers used a variety of information sources, such as direct observation, interviews with the patients, family, or formal service providers, in addition to the review of clinical records, and of the care administered by both medical and nursing staff in order to improve the quality of data collection.

1.2. Sarcopenia

According to the European Working Group on Sarcopenia in Older People (EWGSOP) criteria, sarcopenia is defined as low muscle mass plus either low muscle strength or low physical performance [1]. Walking speed was evaluated measuring usual gait speed (metres per second) of participants over a 4-m course; low physical performance was indicated by a speed of less than or equal to 0.8 m/s [26] and muscle strength was assessed by measuring handgrip strength using a hand-held dynamometer (JAMAR hand dynamometer Model BK-7498, Fred Sammons Inc., Brookfield, IL) with the patient seated, with the wrist in a neutral position, and with the elbow flexed at 90°. Three trials for the dominant hand were performed, with a 1-min resting interval between tests, and the best result was used for the present analyses. Using cut-off points indicated in the EWGSOP consensus, low muscle strength was classified as handgrip strength less than 30 kg and 20 kg in men and women, respectively [3]. Muscle mass was measured with bioimpedance analysis (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 the subject in a supine position. Muscle mass was calculated using the BIA equation of Janssen and colleagues [27]: Skeletal muscle mass (kg) = [(height^2/BIA resistance x 0.401) + (gender x 3.825) + (age x − 0.071)] + 5.102, where height is measured in centimetres, BIA resistance is measured in ohms, for gender men = 1 and women = 0, and 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 after standardization by metres squared (kg/m^2). Using the cut-off points indicated in the EWGSOP consensus, low muscle mass was classified as a skeletal muscle index of less than 8.87 and 6.42 kg/m^2 in men and women, respectively.

1.3. Statistical analysis

Continuous variables were expressed as means ± standard deviation and categorical data as proportions. The Student's t test and the chi-square testwere used to compare clinical characteristics between patients with or without sarcopenia on admission. We also used the Satterthwaite correction for the degrees of freedom of t-test where appropriate. We adopted a Cox proportional hazards regression model with Breslow's modification by using a constant time and robust variance estimates proposed by Lin [28] because the logistic regression models can lead to poor estimates of the effect of covariates on prevalence ratios when data are from cross-sectional studies and the outcome is not rare [29], [30]. All variables with $p < 0.10$ were eligible for multivariate Cox proportional regressions. Three different models were created: model 1, including delirium as the only risk factor; model 2, including delirium and socio-demographic covariates in addition to delirium; and model 3 including delirium and all socio-demographic and clinical covariates. All models were adjusted for the different settings of hospital admission. The association estimates were reported as Prevalence Ratios (PRs) and 95% confidence intervals (CIs).

Additionally, we conducted three other analyses to verify the robustness of our findings. The first analysis was run to assess whether a different method to evaluate delirium, potentially more effective at capturing a broader proportion of patients with this condition, was able to confirm our findings. Indeed, not all the centres participating in this study used a screening tool to fulfill the DSM-5criteria for the diagnosis of delirium. This is important because a lack of delirium screening tools is associated with a high risk of under-recognition of delirium, as shown by several studies [31], [32]. Without the support of such tools, a risk of misdiagnosis is elevated; a misinterpretation of DSM items may occur as well. Accordingly, we decided to provide an additional analysis to control for a possible delirium misdetection among centres. To do this, we used an approach (i.e., a classification of delirium using the SPSMQ item combination) that, though not specific for the diagnosis of delirium, certainly does not depend upon the rater's expertise. We defined "probable delirium" as a condition in which the patient had either delirium defined on a clinical basis or as a cognitive disorder. The responses to items 1, 2, and 3 were used as a measure of spatial/temporal disorientation; the responses to items 5, 6, and 9 as a measure of personal disorientation; the responses to items 4/4a, 7, and 8 as a measure of episodic memory deficit; and the response to item 10 as a measure of inattention. Errors in response to each item were used to define and establish the presence of corresponding deficits. Since delirium is an acute neuropsychiatric condition characterized by disordered attention, awareness, along with other cognitive deficits (including spatial and temporal orientation and episodic memory) [8], we think that our approach is appropriate for the scope of this study.

The second analysis was conducted to evaluate the extent to which the choice of the Cox regression model as a statistical method may have influenced the final model estimates.

We applied the approach proposed by Wilcosky and implemented by Bastos et al. [33]; accordingly, we used the marginal method because the obtained estimates were internally adjusted measures. The third analysis was conducted to evaluate the impact of missing values on our estimates, considering the sample of patients for whom a measurement of sarcopenia was available. We used a multiple imputation approach for missing data, by creating 1000 copies of the original dataset, with the missing values replaced by imputed values, sampled from their predictive distribution based on the observed data. Then, we fitted the Cox model to each of the imputed datasets, and we estimated their associations after taking into account the variability introduced by the imputation of the missing values. As a result, an overall estimated association was finally obtained [34].

The analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC) and R Statistical Software (Foundation for Statistical Computing, Vienna, Austria). All calculated p-values were two-tailed, with values less than 0.05 considered statistically significant.

2. Results

Among the 655 patients consecutively admitted to the participating wards during the study period and assessed for the presence of sarcopenia on admission, 67 had incomplete data, leaving a final sample of 588 participants.

Of these, 199 (33.8%) had sarcopenia upon admission to the AGUs. The characteristics of the participants (mean age 80.9 ± 6.8, 53.2% females) are shown in Table 1, according to the presence of sarcopenia upon admission. In comparison to non-sarcopenic participants, those with sarcopenia were significantly older (83.0 ± 6.9 vs. 79.7 ± 6.5 years, $p < 0.0001$), more frequently unmarried (13.0% vs. 5.7%, $p = 0.008$), and malnourished, as suggested by significantly lower BMI values ($p < 0.0001$). They more frequently had a previous diagnosis of stroke (15.6% vs. 10.0 %, $p = 0.0492$) and less frequently a diagnosis of diabetes (23.6% vs. 32.9%, $p = 0.0198$). Moreover, in comparison to their counterparts, sarcopenic participants were more impaired in both the ADL Index ($4.1 + 2.2$ vs. $4.8 + 1.7$, $p < 0.0002$) and the IADL total score ($3.7 + 2.8$ vs. $4.7 + 2.5$, $p < 0.0001$). Sarcopenic participants also had more severe cognitive impairment (SPMSQ total score $= 3.1 \pm 2.7$ vs. 2.49 ± 2.4, $p = 0.0009$) and a higher prevalence of delirium upon admission (7.0% vs. 2.3%, $p = 0.005$). There was no significant difference with regards to the Charlson index score, sources of admission (more than 90% came from home in both groups), history of falls occurring in the year prior to AGU admission, and presence of chronic heart failure (CHF); length of hospital stay was also comparable between the two groups.

Table 1. Participant characteristics by diagnosis of sarcopenia on admission.

Characteristics	Sarcopenia (*n* = 199)	No sarcopenia (*n* = 389)	*p*-Value
Age (years), *n* (%)			
<80	61 (30.65)	198 (50.90)	<0.0001
80–85	58 (29.15)	107 (27.51)	
>85	80 (40.20)	84 (21.59)	
Female gender, *n* (%)	102 (51.26%)	211 (54.24%)	0.4924
Marital status, *n* (%)			
Unmarried	26 (13.07)	22 (5.66)	0.0080
Married	90 (45.23)	216 (55.53)	
Widowed	78 (39.20)	142 (36.50)	
Divorced	5 (2.51)	9 (2.31)	
Sources of admission, *n* (%)			
Home	182 (91.5)	363 (93.3)	0.4126
Health and nutritional status			
Body mass index (kg/m^2)			
<18.5	15 (7.54)	7 (1.80)	<0.0001
18.5–25	106 (53.27)	130 (33.42)	
≥25	78 (39.20)	252 (64.78)	
Charlson Comorbidity index (mean ± SD)	3.32 (2.25)	3.31 (2.38)	0.9486
Previous stroke, *n* (%)	31 (15.58)	39 (10.03)	0.0492
Previous CHF, *n* (%)	42 (21.11)	58 (14.91)	0.0585
Diabetes, *n* (%)	47 (23.62)	128 (32.90)	0.0198
Functional and cognitive status			
IADL total score (mean ± SD)	3.71 (2.79)	4.74 (2.56)	<0.0001
ADL total score (mean ± SD)	4.10 (2.22)	4.78 (1.74)	0.0002[a]
SPMSQ (mean ± SD)	3.12 (2.74)	2.40 (2.36)	0.0016[a]
Formal diagnosis of delirium on admission,[b] *n* (%)	14 (7.04)	9 (2.31)	0.0052
History of falls, *n* (%)	58 (29.15)	108 (27.76)	0.7246
Length of hospital stay, days (mean ± SD)	9.80 (6.13)	10.27 (9.26)	0.4323[a]

CHF = chronic heart failure; ADL: activities of daily living. IADL: instrumental activities of daily living; SPMSQ: short portable status mental questionnaire, GDS = geriatric depression scale; *p*-value = significance on *t*-test or chi-square test for categorical variables.

[a]Satterthwaite correction.

[b]Included the diagnosis of delirium as recorded by the researcher of each centre on the data form.

In Appendix B, the characteristics of our participants according to the diagnosis of delirium are reported.

The multivariable Cox regression model estimates (PRs of sarcopenia on AGU admission) are shown in Table 2. All models showed an important effect on delirium. In particular, after adjusting for both clinical and socio-demographic covariates (model 3), factors independently associated with the presence of sarcopenia were delirium on admission (PR 1.66, 95% CI: 1.12–2.45), IADL total score (PR 0.93, 95% CI: 0.87–0.98), BMI values ranging from 18.5 to 25.0 (PR 1.70, 95% CI: 1.33–2.18), BMI values <18.5 (PR 2.53, 95% CI: 1.81–3.53), previous stroke (PR 1.51, 95% CI: 1.10–2.07) and CHF (PR 1.31, 95% CI: 1.02-1.68).

Table 2. Adjusted Cox regression model estimates of the Prevalence Ratios of sarcopenia on admission to acute geriatric wards.

	Model 1		Model 2		Model 3	
	PR	*p*	PR	*p*	PR	*p*
Delirium on admission (yes/no)	**1.76**	**0.0031**	**1.78**	**0.0020**	**1.66**	**0.0114**
Age, years						
≤80	–	–	**0.57**	**0.0003**	0.76	0.0634
80-85	–	–	0.84	0.2581	0.96	0.8122
>85	–	–	1		1	(Ref.)
Marital status						
Unmarried	–	–	1.30	0.5069	1.23	0.5825
Married	–	–	0.84	0.6267	0.81	0.5301
Widowed	–	–	0.87	0.7020	0.88	0.6959
Divorced	–	–	1	(Ref.)	1	(Ref.)
ADL total score	–	–	–	–	0.98	0.5754
IADL total score	–	–	–	–	**0.93**	**0.0060**
SPMSQ, total score	–	–	–	–	0.95	0.0640
Body mass index						
<18.5	–	–	–	–	**2.53**	**<0.0001**
18.5-25	–	–	–	–	**1.70**	**<0.0001**
≥25	–	–	–	–	1	(Ref.)
Previous stroke	–	–	–	–	**1.51**	**0.0098**
Chronic heart failure	–	–	–	–	**1.31**	**0.0371**
Diabetes	–	–	–	–	0.93	0.6228

PR: prevalence ratio. 95% CI: 95% confidence interval. *p*: *p*-value. The prevalence ratios are adjusted for the hospital centres of admission. ADL: activities of daily living. IADL: instrumental activities of daily living; SPMSQ: short portable status mental questionnaire.
Significant values are reported in bold.

The results of the analyses conducted to check the robustness of our findings are as follows: there were 152 participants (25.8%) who met the criteria for the diagnosis of "probable delirium". Of these, 74 (37.2%) had sarcopenia while 78 (20.0%) did not. In the fully adjusted Cox regression, using "probable delirium" as an independent variable, the PR of sarcopenia was 1.48 ($p = 0.001$), a modest change from the model using the clinically based diagnosis of delirium.

Regarding the analysis based on the Wilcosky marginal approach, we did not find substantial changes in comparison to the original Cox regression. In particular, the PR (95% CI) estimates were 1.73 (1.21–2.47) for delirium, 0.94 (0.90–0.98) for the IADL total score, 2.82 (2.40–3.31) for BMI values <18.5, 1.64 (1.30–2.07) for BMI values 18.5–25, and 1.40 (1.08–1.83) for stroke. Only CHF failed to show a statistically significant association estimate.

Finally, in the multiple imputation analysis, none of the significant estimates (point estimates of PR and relative p-value of model 3) substantially changed.

3. Discussion

This multicentre observational study, conducted in a population of older patients consecutively admitted to twelve Italian AGUs, shows that delirium was significantly more frequent in patients with sarcopenia than in those without. The association between sarcopenia and delirium remained significant even after adjusting for important clinical and functional covariates. The study also showed that other four variables (i.e., IADL impairment, BMI values <25, previous stroke and previous CHF) were independently associated with sarcopenia upon admission to the AGU.

The association between delirium and sarcopenia is a novel finding in the literature. Despite the fact that geriatric syndromes frequently co-exist in hospitalized older people [11], [17] and that they may share risk factors and pathophysiological mediators [35], [36], studies focussing on a potential association between delirium and sarcopenia, among two of the most common geriatric syndromes in hospitalized patients, are lacking so far. Our study therefore contributes valuable knowledge to this field. Since sarcopenia may be considered a marker of and possibly even a biological substrate for frailty [37], it can be hypothesized that sarcopenic patients are at increased risk of developing delirium because they are frailer than non-sarcopenic ones. Elevated concentrations of inflammatory markers in blood serum have been found in sarcopenic patients [38], as well as in the serum and in the cerebrospinal fluid of delirious patients [39], [40], [41], [42], suggesting that abnormal inflammatory responses might mediate the co-existence of both delirium and sarcopenia. It could even be postulated that inflammatory stimulation of sarcopenic patients [43] may lead to activation of brain microglia and the overproduction of proinflammatory cytokines and inflammatory

modulators, leading to neurocognitive changes characteristic of delirium [40]. However, whether sarcopenia comes before or after brain neuroinflammation is yet to be clarified.

In previous studies, sarcopenia has also been found to be strongly associated with IADL impairment [6], [44]. For example, in a prospective study of 478 non-disabled community-dwelling older individuals, sarcopenia was significantly associated with IADL disability at the 4-year follow-up, after controlling for several covariates [45]. The relationship between sarcopenia and IADL is interesting to note because IADL dependence reflects an impairment in cognitive status and/or dementia. Indeed, there is evidence that specific IADL items (namely "shopping" and "telephone use") [45] and total IADL score [46]can be used as screening questions and/or proxies for cognitive impairment by clinicians assessing an older individual. The finding that delirium and IADL impairment in our population were both independently associated with the risk of being sarcopenic indirectly supports this view, since dementia and delirium are pathophysiologically linked in a reciprocal manner, i.e., dementia is a risk factor for delirium [9] and delirium is a risk factor for worsening dementia [14]. The relationship between sarcopenia and cognitive impairment in community-dwelling individuals is controversial, with some studies finding a positive association [47], [48] and with others not [49]. To date, only one study has been conducted on this topic in hospitalized patients, and it found that cognitive impairment was associated with a diagnosis of definitive and possible sarcopenia, independent of other covariates [50]. However, a limit of that study was that the authors did not evaluate cognitive impairment using a single definitive method, so its evaluation was dependent on the accuracy of clinical hospital records and caregivers' reports [49]. To address this issue in our study, we conducted a sensitivity analysis to evaluate the impact of dementia on our association estimates, including only those patients without dementia ($n = 520$), and, consistently, we found a significant association (PR = 2.05; p-value = 0.0303).

The role of BMI as marker of malnutrition is well-known [51], as well as its association with sarcopenia in elderly people [2], [52]. It is therefore not surprising that low BMI values, especially below 18.5 kg/m^2, predicted the risk of being sarcopenic in our sample. However, this finding clearly suggests that the combined assessment of sarcopenia and nutritional status are key in the evaluation and management of geriatric inpatients, and it provides further support to the hypothesized existence of a "malnutrition-sarcopenia syndrome" [53]. Similarly, the association of sarcopenia with both stroke and CHF is consistent with previous studies in community-dwelling individuals and hospitalized patients [54], [55], [56]. A stroke-specific sarcopenia has been recently described [54]. Its underlying pathophysiological mechanisms are probably multifactorial, including the alterations of structural and functional muscle capacity, neurovegetative control, systemic and local metabolic imbalance, feeding difficulties, and inflammation [54]. In CHF, the mechanisms leading to sarcopenia may include a generalized metabolic myopathy, developing early in the course of the disease, with replacement of muscle tissueby non-

functional tissue [56]. These skeletal muscle metabolic abnormalities may be more relevant in explaining major CHF symptoms such as fatigue, exercise limitation, and dyspnoea than central haemodynamic parameters.

There are some theoretical and practical implications of the present study. Firstly, patients with delirium upon hospital admission could be regarded as potential candidates for subsequent sarcopenia assessment. Such an assessment could be obtained once delirium has resolved, if not possible immediately upon admission. Indeed, it might be possible that patients with both delirium and sarcopenia may have different health trajectories, in terms of clinical outcomes, than those with none or only one. Second, the finding that another four variables (i.e., IADL impairment, low BMI scores, history of stroke/TIA and history of CHF), in addition to delirium, were independently associated with a diagnosis of sarcopenia upon hospital admission suggests that these four variables may aid physicians in targeting a population for sarcopenia assessment in an acute hospital. Previous studies have proposed screening tools to diagnose sarcopenia and obviate the need for the measurement of muscle mass [57], [58]. However, these methods have been created and validated only for patients in primary care, and may therefore overestimate the prevalence of sarcopenia in hospitalized patients.

The current study has several notable strengths. First, to our knowledge, this is the first study to evaluate delirium as a factor associated with the risk of being sarcopenic upon hospital admission. Second, this is a large multicenter prospective cohort study involving twelve acute geriatric hospital units. Based on the results of previous studies in Italy and other European countries [2], [52], [59], we believe that our findings should be at least considered when treating all the hospitalized patients of our continent. Third, we used a validated method to diagnose sarcopenia, and we performed an accurate geriatric assessment on all eligible patients. Fourth, we evaluated the strength of our findings by considering three different possibilities: the possibility that the clinical diagnosis of delirium may have underestimated the true prevalence; the possibility that the PRs may have been influenced by the statistical method used; and the possibility that missing values may have biased the final results. As a result, we achieved consistent findings concerning the effect of delirium in all models.

A limitation of this study is the lack of an inter-rater reliability measure in performing CGA among researchers. Indeed, while we are confident that the assessment used to evaluate sarcopenia was performed in a similar way on every patient, we cannot exclude that some CGA tools may have been administered by researchers with different degrees of sensitivity and expertise, potentially altering some results. However, in the multivariable Cox regression, we controlled for the variability among centres. Another important limitation is the method used to detect delirium in our population. Ideally, formal delirium testing should have been performed using screening tools (such as Confusion Assessment Method [60] or the 4AT [61]) to fulfill the DSM-5th edition criteria [8]. This was not the case

in our study, with the exception of a few centres, which may explain the lower delirium prevalence in comparison to previous studies [9]. However, it should also be considered that many patients, due to delirium, were excluded from the study upon admission because they were unable to give informed consent or to perform functions comprising the evaluation for sarcopenia. Accordingly, we can hypothesize that many delirious patients did not meet such criteria, since delirium is frequent among critical patients [10], [15], [62], [63]. Furthermore, we also assessed the prevalence of delirium using another sensitive approach, leading to results which are consistent with the other analyses. However, future studies may confirm this association using standardized methods to diagnose delirium. A third limitation is that we did not assess psychomotor subtypes nor the severity or the duration of delirium. Accordingly, we can only speculate that most delirium cases were of mild severity and lasted no more than a few days after AGU admission.

4. Conclusions

The results of this prospective multicentre study show that delirium and other four variables (i.e., IADL impairment, BMI values <25, previous stroke and previous CHF) are all independently associated with the risk of being sarcopenic upon admission to hospital wards. Since this is the first study showing such an association (i.e., between delirium and sarcopenia), future research is needed to confirm our data. It can be hypothesized that sarcopenia may precede delirium, suggesting that sarcopenia should be assessed systematically in older patients in order to identify those at risk of developing delirium.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.clnu. 2017.08.027

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