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Malnutrition in postacute geriatric care: Basic ESPEN diagnosis and etiology based diagnoses analyzed by length of stay, in-hospital mortality, and functional rehabilitation indexes

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ABSTRACT

Objective: To determine the relationships between malnutrition and nutrition-related conditions according to the European Society of Clinical Nutrition and Metabolism (ESPEN) consensus and guidelines and clinical outcomes in postacute rehabilitation.

Methods: Of 102 eligible inpatients, 95 (84.5 years old, 63.2% women) fulfilled inclusion criteria: aged ≥70 years, body mass index <30 kg/m^2, admission for rehabilitation. Mini-Nutritional Assessment-Short Form (MNA-SF≤11) identified patients "at risk" and ESPEN basic and etiology based definitions were applied. Nutrition-related conditions (sarcopenia, frailty, overweight/obesity, micronutrient abnormalities) were determined. We assessed the relationship between these conditions and the clinical and rehabilitation outcomes (relative functional gain, rehabilitation efficiency) during hospitalization.

Results: All patients were "at risk" by MNA-SF criteria and 31 reported unintentional weight loss >5% in the last year or 2–3 kg in the last 6 months. Nineteen fulfilled the ESPEN basic definition, of which 10 had disease-related malnutrition with inflammation and 9 without inflammation, and 20 had cachexia. Sarcopenia (n = 44), frailty (n = 94), overweight/obesity (n = 59), and micronutrient abnormalities (n = 70) were frequent. Unintentional weight loss impaired all functional outcomes and increased length of stay [OR = 6.04 (2.87–9.22); p < 0.001]. In multivariate analysis, relationships between rehabilitation impact indices and the ESPEN basic and etiology-based definitions observed in univariate analysis persisted only (and marginally) for relative functional gain [OR = 13.24 (0.96–181.95); p = 0.005]. Infrequent in-hospital mortality prevented meaningful analysis of this outcome.

Conclusions: ESPEN basic and etiology-based definitions and nutrition related disorders were determined in postacute care. Malnutrition was associated with poor rehabilitation outcomes, mainly due to unintentional weight loss.

Abbreviations: BMI, body mass index; ESPEN, European Society of Clinical Nutrition and Metabolism; EWGSOP, European Working Group on Sarcopenia in Older People; FFMI, fat-free mass index; MNA, Mini-Nutritional Assessment; MNA-SF, Mini-Nutritional Assessment-Short Form; REI, Rehabilitation efficiency index; RFG, relative functional gain; SD, standard deviation; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; WHO, World Health Organization.

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1. Introduction

Malnutrition, a common condition in older adults, is associated with adverse medical consequences, contributing to frailty, morbidity, mortality, and use of health resources (Agarwal et al., 2013; Chen et al., 2010; Guyonnet, Secher, & Vellas, 2015; Marshall, 2016; Morley, 2015; Shen et al., 2011; Soysal et al., 2017). Although early identification and management of individuals at risk of malnutrition make it possible to reverse its adverse effects (Cederholm et al., 2015, 2017; Cruz-Jentoft, Kiesswetter, Drey, & Sieber, 2017; Deutz et al., 2014; Deutz et al., 2016; Lindegaard Pedersen, Pedersen, & Damsgaard, 2017; Shen et al., 2011), the condition often remains unrecognized and undermanaged, partly due to the lack of clear and consensual guidelines appropriate for all patients and settings (Cederholm & Jensen, 2017; Cederholm et al., 2015; Hamirudin, Charlton, & Walton, 2016; Lee & Tsai, 2012; Vischer et al., 2012).

The European Society of ClinicalNutrition and Metabolism (ESPEN) has proposed a consensus statement on nutrition for all age ranges and healthcare settings providing a unified, simple and reliable tool for malnutrition diagnosis, independently of etiology (Cederholm et al., 2015; Rojer et al., 2016). This consensus was further completed with the ESPEN Guidelines on Definition and Diagnoses of Malnutrition, with an etiology-based diagnostic tree including the identification of inflammatory markers, a crucial step for identifying and addressing malnutrition (Cederholm et al., 2017).

The ESPEN consensus has already shown appropriateness for the diagnosis of malnutrition, and engaging in corrective interventions, in a wide range of patients including acutely ill middle-aged patients and geriatric patients hospitalized with diabetes (Rojer et al., 2016; Sanz-Paris et al., 2016) and in postacute care (Sánchez-Rodríguez et al., 2016). However, the relationship of the ESPEN consensus with clinical outcomes during hospitalization in rehabilitation settings is not well established.

The post-acute care pathways are key moments in the patient's trajectory, reflecting their vulnerability, as illustrated by longer hospital stay (Kruizenga et al., 2016), increased inhospital mortality, or poor functional prognosis (Arinzon, Fidelman, Zuta, Peisakh, & Berner, 2005; Cerri et al., 2015; Cruz-Jentoft et al., 2017; Guyonnet et al., 2015; Landi et al., 2002; Nunes, Flores, Mielke, Thumé, & Facchini, 2016; Sánchez-Rodríguez et al., 2014). Thus, since nutritional status is recognized as the most potent prognostic factor in older adults (Sanz-París et al., 2016; Shen et al., 2011), we hypothesize that nutritional disorders according to the ESPEN consensus may be associated with worse post-acute care pathways. Moreover, as the ESPEN basic diagnostic tool is composed of various criteria, including unintentional weight loss, low body mass index (BMI) and low fat-free mass index (FFMI) (Cederholm et al., 2015), an assessment of the respective weight of each criterion and its potential to predict adverse health events seems to be warranted.

The main objective of this study was to determine the relationship, if any, between nutritional disorders diagnosed according to the ESPEN consensus and clinical and functional rehabilitation outcomes; a second objective was to determine if an etiology-based malnutrition diagnosis provides complementary information about the prognosis of older patients during post-acute rehabilitation care.

2. Methods

2.1. Design

Cross-sectional analysis of consecutive hospitalized older patients who participated in a larger prospective study on sarcopenia and functional outcomes (Sánchez-Rodríguez et al., 2014; Sánchez-Rodríguez, Marco et al., 2015). Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Guidelines for reporting observational research cohorts were followed (See file 1).

2.2. Setting

The study was carried out in a post-acute geriatric rehabilitation care unit in a university hospital in Barcelona (Catalonia, Spain). This post-acute hospitalization unit focuses on rehabilitation and recovery during a defined period of time, usually about two weeks before a scheduled home discharge.

2.3. Participants

The study population consisted of 102 consecutive patients who met inclusion criteria during a five-month period: age ≥70 years; admitted in the post-acute rehabilitation care unit for functional loss resulting from a non-disabling medical disease. Patients whose general and/or cognitive condition (Mini-Mental Status Examination ≤21) prevented completion of the diagnostic tests and an active physical rehabilitation program were excluded.

2.4. Procedure

Upon admission to the post-acute rehabilitation unit, patients were screened for risk of malnutrition using the Mini-Nutritional Assessment Short-Form (MNA-SF) (Camina-Martín et al., 2015; Kaiser et al., 2009; Lee & Tsai, 2012). The ESPEN consensus definition of malnutrition was later applied to all screened subjects with MNA-SF score ≤11. According to the ESPEN consensus (Cederholm et al., 2015), the variables that most accurately reflect malnutrition are weight loss, reduced BMI, and reduced FFMI. Unintentional weight loss was determined by patient and caregiver anamnesis and medical records, either by documented weight loss of at least 5% in the previous 12 months during an underlying illness (Evans et al., 2008) and/or by item 11 on the Kihon checklist: "Have you experienced more than 2–3 kg unintentional weight loss over the past 6 months? Yes = 1, No = 0." (Komai et al., 2016). BMI was calculated from weight and height (kg/m^2). Body weight was measured to the nearest 0.1 kg; height was measured in all patients who were able to stand and a knee height equation was applied in bedridden patients unable to stand safely. Fat-free mass (FFM), expressed in kg, was measured by bioimpedance (Bodystat 1500, Bodystat Ltd., Isle of Man British Isles) as previously described (Sánchez-Rodríguez et al., 2016). The FFM values were divided by height squared to obtain the fat-free mass index (FFMI), expressed in kg/m^2 and compared with those of the reference population (Schutz, Kyle, & Pichard, 2002).

Nutrition-related conditions (sarcopenia, frailty, overweight and obesity, and micronutrient abnormalities) were also considered. Sarcopenia was assessed following European Working Group on Sarcopenia in Older People (EWGSOP) criteria: low muscle mass and low muscle function or low physical performance assessed with bioimpedance analysis, isometric handgrip dynamometry and gait speed in a 4-m walk test as previously described (Cruz-Jentoft et al., 2010; Sánchez-Rodríguez et al., 2014). Gait speed was considered 0 m/s in bedridden patients unable to stand (Cereda, Bertoli, Vanotti, & Battezzati, 2010). Frailty was assessed by the Frailty Phenotype (Fried et al., 2001) when 3 of the following criteria were present: weight loss, weakness, exhaustion, slow walking speed, and low physical activity. Overweight and obesity were considered following World Health Organization recommendations: overweight, BMI 25–30 kg/m^2 and obesity, BMI ≥30 kg/m^2. Micronutrient abnormalities: Total proteins, total cholesterol, triglycerides, homocysteine-related markers (folic acid and B12 vitamin), thyroid-stimulating hormone, iron profile (serum iron, ferritin),

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ionogram (sodium, potassium), and renal profile (creatinine, urea and glomerular filtration rate from the equation developed by the Modification of Diet in Renal Diseases Study). Following an overnight fast, 10 ml of venous blood were collected under standardized conditions between 7 and 9 am, with the patient in a supine position. Blood handling and collection were carried out under strictly standardized conditions. For purpose of analysis, micronutrient abnormalities were considered as a dichotomous variable to determine whether one or more of the biomarkers of interest was altered.

Patients fulfilling basic diagnostic malnutrition criteria were further considered for the etiology-based diagnoses: Disease-related malnutrition (DRM), with and without inflammation, according to albumin serum levels (reference cut-off point 3.2 mg/dl) (Cederholm et al., 2017) and Malnutrition/undernutrition without disease. Cachexia (wasting disease) diagnostic criteria in adults were applied: weight loss of at least 5% in 12 months or less in the presence of underlying illness, plus three of the following criteria: decreased muscle strength, fatigue (defined as physical and/or mental weariness resulting from exertion), anorexia (total caloric intake <20 kcal/kg body weight/day; $<70\%$ of usual food intake), low fat-free mass index, or abnormal biochemistry (hemoglobin <12 g/dl or low serum albumin <3.2 g/dl) (Evans et al., 2008).

Main outcome variables were changes in the functional status assessed with the Rehabilitation Impact Indexes: Relative Functional Gain (RFG, the achieved percentage of potential gain), corrected with premorbid functional status [RFG = (Barthel index at discharge – Barthel index at admission)/(Barthel index premorbid – Barthel index at admission) × 100]; and the Rehabilitation Efficiency Index (REI), designed to incorporate the duration of therapy [REI = (Barthel index at discharge – Barthel index at admission)/(length of hospital stay)] (Koh, Chen, Petrella, & Thind, 2013; Sánchez-Rodríguez, Miralles et al., 2015). Cut points for these outcomes were RFG $<35\%$, and REI <0.50, respectively. Regarding RFG, for purposes of analysis, negative or indeterminate values resulting from calculations were converted to 0. Patients who died, lost functional capacity during their stay in the unit or were transferred to acute care hospitals for an acute event or worsening clinical status are included in this group (Sánchez-Rodríguez, Miralles et al., 2015). Intrahospital mortality and length of stay (days) were also considered for purpose of analysis.

2.5. Ethics

National and international research ethics guidelines were followed, including the Deontological Code of Ethics, Declaration of Helsinki, and Spain's confidentiality law concerning personal data (*Ley Orgánica* 15/1999, 13 December, *Protección de Datos de Carácter Personal*). Detailed, understandable oral and written information was provided to patients and family members, and informed consent to participate was signed by all participants. The study was approved by the local Clinical Ethics Committee (CEIC Parc de Salut Mar, ref. 4447/I).

2.6. Statistical analysis

Descriptive analysis of the sample used percentages and frequency distributions for categorical variables, and means (SD) for quantitative continuous variables. Univariate analysis was used to check clinical and functional characteristics of the study participants according to the presence of the basic definition of malnutrition. Qualitative variables were compared by Chi-square or Fisher exact test, as appropriate and quantitative variables by Student *t*-test. Changes in the Barthel index during the study period were assessed by analysis of variance using a repeated-measures mixed design (intrasubject) and a one-factor design (intersubject). As histogram and Q–Q plot showed that length of stay was not normally distributed, median regression was applied to check differences in medians (MD).

For categorical outcomes (RFG, REI), logistic regressions were used to determine Odds Ratios of poorer outcomes. Univariate and multivariate models were performed in order to determine which of the covariates were statistically significant. All covariates included in univariate analysis were also included in the corresponding multivariate model, with malnutrition considered as two distinct variables: disease-related malnutrition with and without inflammation. P values less than 0.05 were considered as statistically significant. Analysis was performed using SPSS 22 (IBM Corporation, SPSS, INC., Chicago, IL, USA).

3. Results

Of the 102 patients hospitalized in the rehabilitation unit during the study period, 95 met inclusion criteria (mean age, 84.5 years, standard deviation [SD] 6.5 years; 63.2% women). Two of these patients were excluded from the analysis because they died within the first 48 h of admission, before geriatric assessment was performed. Table 1

Table 1
Clinical and functional characteristics of the study participants according to basic malnutrition status (n = 95).

	Total sample (n = 95)	Malnutrition (n = 19)	No malnutrition (n = 76)	p
Age (years)	84.5 (6.5)	84.3 (5.3)	84.6 (6.8)	0.479
Sex (M:W)	35:60	6:13	29:47	0.595
Body mass index (Kg/m^2)	25.5 (4.3)	21.7 (4.3)	26.3 (3.9)	**0.005**
Fat-free mass index (FFMI, Kg/m^2)	14.9 (2.9)	12.7 (1.7)	15.4 (2.9)	**0.007**
Fat-free mass (Kg)	38.4 (10.3)	32.4 (6.6)	39.7 (10.5)	**0.069**
Charlson comorbidity index	2.4 (1.8)	2.5 (2.2)	2.3 (1.7)	0.466
Short Portable Mental Status Questionnaire	4.2 (3.1)	5.1 (3.4)	4.0 (3.0)	0.265
Lawton index	2.6 (2.6)	2.5 (2.9)	2.6 (2.5)	0.577
Barthel index:				
-Prior	71.4 (21.6)	66.4 (25.3)	72.5 (20.8)	**0.005**[a]
-At admission	27.0 (15.4)	19.1 (14.8)	28.7 (15.1)	
-At discharge	54.3 (26.2)	38.9 (29.1)	57.7 (24.5)	
Length of stay (days):				
-In acute care unit	15.0 (12.1)	18.3 (17.0)	15.2 (11.5)	0.805
-In post-acute care unit	14.9 5.8)	18.3 (8.1)	14.1 (4.9)	**0.009**
Rehabilitation efficiency index	0.4 (0.3)	0.2 (0.2)	0.4 (0.3)	**0.008**
Relative functional gain (RFG, %)	56.8 (40.7)	33.7 (36.9)	62.7 (39.8)	**0.002**

Data are expressed as numbers for sex distribution and as mean and standard deviation (SD) for continuous variables.
[a] Changes in Barthel index during the study period were asssessed by analysis of variance using both a repeated-measures mixed design and a one-factor design.

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shows the baseline general and geriatric assessment of the participants. Fig. 1 shows the sample distribution according to nutritional disorders and nutrition-related conditions, after applying ESPEN basic diagnoses. In these deconditioned patients, frailty was confirmed in the whole sample by Fried phenotype. Fig. 2 depicts the malnutrition diagnostic tree. All patients were identified as at risk of malnutrition (MNA-SF scores ≤11); 19 patients fulfilled the basic criteria for a diagnosis of malnutrition. Etiology-based malnutrition diagnoses completed this tree. Ten of the 19 patients had disease-related malnutrition (DRM) with inflammation due to acute disease and 9 patients had DRM without inflammation. Unintentional weight loss was present in 31 patients. Table 2 shows distribution of weight loss, reduced BMI, and reduced fat-free mass index (FFMI) in patients fulfilling criteria of ESPEN basic diagnosis and malnutrition-related conditions. Reduced FFMI was the most prevalent feature in the total sample and in all the subgroups, including the overweight and obese subgroup of patients.

Clinical characteristics, nutritional disorders according to the ESPEN consensus (basic diagnoses), nutrition-related conditions, and etiology-based malnutrition diagnosis were further related to poor functional rehabilitation and clinical outcomes, as shown in Table 3 (univariate analysis) and Table 4 (multivariate analysis). Univariate analysis showed that poorer RFG results were associated with unintentional weight loss (OR = 0.16; 95% CI: 0.06–0.42; $p < 0.001$) and basic diagnosis of malnutrition (OR = 0.12; 95% CI: 0.04–0.37; $p < 0.001$). The association between RFG and the etiology-based diagnoses was significant for DRM with inflammation (OR = 0.14; 95% CI: 0.03–0.63; $p = 0.01$) and without inflammation (OR = 0.19; 95% CI: 0.05–0.76; $p = 0.019$). The same associations were observed in the multivariate analysis for unintentional weight loss (OR = 4.25; 95% CI: 1.08–16.75; $p = 0.039$) and DRM with inflammation (OR = 13.24; 95% CI: 0.96–181.95; $p = 0.05$). Finally, a poor REI score was highly associated with unintentional weight loss (OR = 5.06; 95% CI: 1.58–16.19; $p = 0.006$) and with basic diagnosis of malnutrition (OR = 5.36; 95% CI: 1.15–24.92; $p = 0.032$). Only the relationship with unintentional weight loss persisted after multivariate analysis (OR = 4.49; 95% CI: 0.99–20.31; $p = 0.051$).

Length of stay (Table 5) was associated with unintentional weight loss in univariate (median difference [MD] = 7; 95% CI: 4.29–9.71; $p < 0.001$) and multivariate analysis (MD = 6.04; 95% CI: 2.87–9.22;

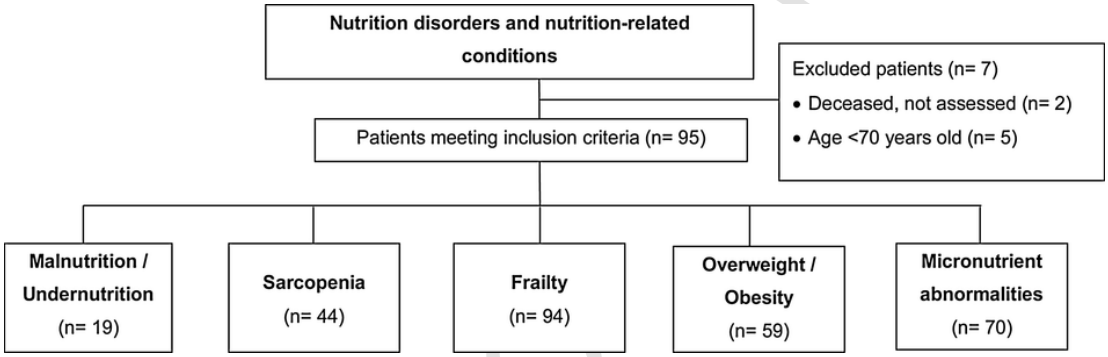

Fig. 1. Overview of nutrition disorders and nutrition-related conditions in postacute care population (Cederholm et al., 2016).

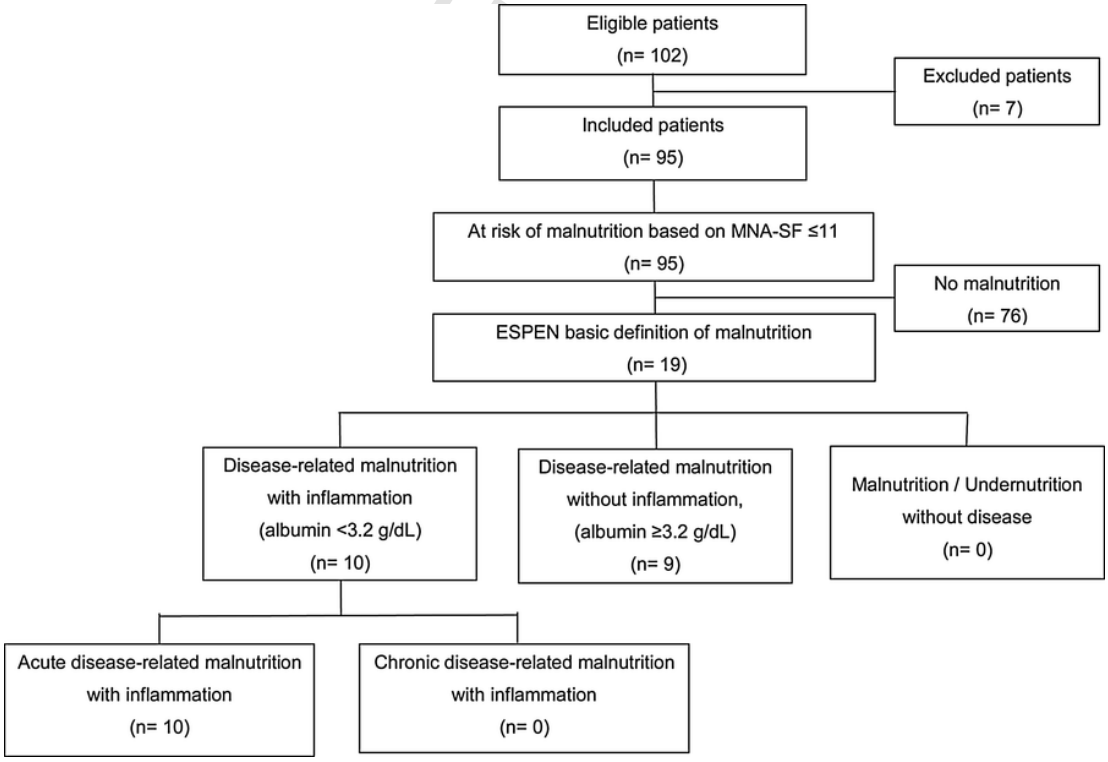

Fig. 2. Diagnostic tree of malnutrition, from identification of risk to basic definition of malnutrition and etiology-based diagnoses (Cederholm et al., 2016).

Table 2
Unintentional weight loss, reduced body mass index, and reduced fat-free mass index according to malnutrition basic diagnosis and malnutrition-related conditions.(*) Data are expressed as numbers and percentages.

	Malnutrition (ESPEN) (n = 19)	Cachexia (Evans) (n = 20)	Malnutrition-related conditions			Total sample (n = 95)
			Sarcopenia (EWGSOP) (n = 44)	Frailty (Fried) (n = 94)	Overweight-Obesity (WHO) (n = 59)	
Unintentional weight loss	14 (73.7%)	12 (60%)	13 (29.5%)	31 (33%)	17 (28.8%)	31 (32.6%)
Reduced body mass index (<18.5 kg/m^2)	4 (21.1%)	3 (15%)	3 (6.8%)	4 (4.3%)	0 (0%)	4 (4.2%)
Reduced fat-free mass index (<15 kg/m^2 in women, <17 kg/m^2 in men)	19 (100%)	20 (100%)	43 (97.7%)	59 (62.8%)	29 (49.2%)	60 (63.2%)

Abbreviations;: European Society of Clinical Nutrition and Metabolism (ESPEN), European Working Group on Sarcopenia in Older People (EWGSOP), World Health Organization (WHO). (*) Data are expressed as numbers and percentages.

Table 3
Factors affecting poor rehabilitation outcomes, according to clinical characteristics, components of the basic definition of malnutrition, and etiology-based diagnoses of malnutrition. Univariate analysis.

	Relative functional gain		Rehabilitation efficiency index	
	Odds ratio (95%CI)	p	Odds ratio (95%CI)	p
Clinical characteristics				
Age	1.01 (0.94–1.08)	0.853	1 (0.94–1.07)	0.997
Sex	1.25 (0.49–3.20)	0.642	0.96 (0.39–2.34)	0.923
Comorbidity (Charlson > 2)	1.08 (0.83–1.41)	0.559	0.89 (0.70–1.13)	0.339
Unintentional weight loss	**0.16 (0.06–0.42)**	**<0.001**	**5.06 (1.58–16.19)**	**0.006**
Albumin <3.2g/dL	1.02 (0.40–2.60)	0.96	1.11 (0.46–2.68)	0.812
Basic definition of malnutrition and nutrition-related conditions				
Malnutrition	**0.12 (0.04–0.37)**	**<0.001**	**5.36 (1.15–24.92)**	**0.032**
Sarcopenia	0.71 (0.28–1.78)	0.465	1.26 (0.53–2.30)	0.603
Overweight-obesity	1.38 (0.55–3.50)	0.494	0.84 (0.34–2.04)	0.694
Micronutrient abnormalities	0.87 (0.34–2.26)	0.783	0.54 (0.22–1.37)	0.198
Etiology-based diagnoses				
Disease-related malnutrition with inflammation	**0.14 (0.03–0.63)**	**0.01**	4.364 (0.521–36.57)	0.174
Disease-related malnutrition without inflammation	**0.19 (0.05–0.76)**	**0.019**	5 (0.604–41.392)	0.136
Cachexia	0.40 (0.14–1.16)	0.093	1.08 (0.37–3.19)	0.884

Table 4
Factors affecting poor rehabilitation outcomes, according-clinical characteristics, components of the basic definition of malnutrition, and etiology-based diagnoses of malnutrition. Multivariate analysis.

	Relative functional gain		Rehabilitation efficiency index	
	Odds ratio (95%CI)	p	Odds ratio (95%CI)	p
Clinical characteristics				
Age	1.00 (0.92–1.09)	0.987	1.01 (0.93–1.09)	0.859
Sex	0.64 (0.21–1.99)	0.445	0.78 (0.27–2.27)	0.647
Comorbidity (Charlson > 2)	0.86 (0.62–1.18)	0.349	0.88 (0.66–1.17)	0.367
Unintentional weight loss	**4.25 (1.08–16.75)**	**0.039**	**4.49 (0.99–20.31)**	**0.05**
Basic definition of malnutrition and nutrition-related conditions				
Malnutrition	–	–	–	–
Sarcopenia	0.86 (0.49–7.02)	0.362	2.02 (0.62–6.62)	0.245
Overweight-obesity	1.01 (0.29–3.55)	0.983	0.78 (0.22–2.70)	0.691
Micronutrient abnormalities	0.81 (0.26–2.50)	0.709	0.46 (0.16–1.34)	0.156
Etiology-based diagnoses				
Disease-related malnutrition with inflammation	**13.24 (0.96–181.95)**	**0.053**	6.82 (0.38–122.08)	0.192
Disease-related malnutrition without inflammation	5.47 (0.73–40.95)	0.098	4.23(0.29–60.51)	0.289
Cachexia	0.22 (0.02–2.37)	0.211	0.17 (0.02–1.26)	0.083

p < 0.001). The association between length of stay and DRM without inflammation observed in univariate analysis (MD = 4; 95% CI: 0.39–7.61; p = 0.030) was not maintained after multivariate analysis.

Finally, although intrahospital mortality (Table 6) was an unfrequented event (n = 11), it was related to sex in both univariate analysis (OR = 0.07; 95% CI:0.01–0.46; p = 0.006) and multivariate analysis (OR = 0.24; 95% CI: 0.07–0.89; p = 0.032) and with unintentional weight loss in both univariate (OR = 0.003; 95% CI: 0.00–0.31; p = 0.014) and multivariate analysis (OR = 0.16; 95% CI: 0.02 –1.28; 0 = 0.084).

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Table 5
Factors affecting length of stay in postacute care, according-clinical characteristics, components of the basic definition of malnutrition, and etiology-based diagnoses of malnutrition. Univariate and multivariate analysis.

	Length of stay in postacute care			
	Univariate analysis		Multivariate analysis	
	MD[a] (95%CI)	p	MD[a] (95%CI)	p
Clinical characteristics				
Age	−0.06 (−0.22 to 0.10)	0.446	−0.03 (−0.21 to 0.15)	0.747
Sex	1 (−1.17 to 3.17)	0.362	0.54 (−1.88 to 2.97)	0.656
Comorbidity (Charlson > 2)	0 (−0.62 to 0.62)	1	0.10 (−0.55 to 0.76)	0.755
Unintentional weight loss	**7 (4.29–9.71)**	**< 0.001**	**6.04 (2.87–9.22)**	**< 0.001**
Basic definition of malnutrition and nutrition-related conditions				
Malnutrition	–	–	–	–
Sarcopenia	0 (−2.40 to 2.40)	1	0.07 (−2.74 to 2.89)	0.959
Overweight-obesity	1 (−1.64 to 3.64)	0.454	0.82 (−1.97 to 3.61)	0.559
Micronutrient abnormalities	0 (−2.77 to 2.77)	1	−0.54 (−2.98 to 1.89)	0.658
Etiology-based diagnoses				
Disease-related malnutrition with inflammation	0 (−3.77 to 3.77)	1	−2.10 (−7.49 to 3.29)	0.440
Disease-related malnutrition without inflammation	**4 (0.39–7.61)**	**0.03**	4.18 (−0.49 to 8.84)	0.079
Cachexia	0 (−3.43 to 3.43)	1	−2.34 (−6.52 to 1.85)	0.270

[a] Median difference.

Table 6
Factors affecting intrahospital mortality in postacute care, according to clinical characteristics, components of the basic definition of malnutrition, and etiology-based diagnoses of malnutrition. Univariate and multivariate analysis.

Intrahospital mortality in postacute care				
	Univariate analysis		Multivariate analysis	
	Odds ratio (95%CI)	P	Odds ratio (95%CI)	p
Clinical characteristics				
Age	1.11 (0.97–1.27)	0.135	1.1 (0.99–1.22)	0.063
Sex	**0.07 (0.01–0.46)**	**0.006**	**0.24 (0.07–0.89)**	**0.032**
Comorbidity (Charlson > 2)	1.49 (0.91–2.43)	0.108	1.21 (0.88–0.68)	0.238
Unintentional weight loss	**0.003 (0.00–0.31)**	**0.014**	**0.16 (0.02–1.28)**	**0.084**
Basic definition of malnutrition and nutrition-related conditions				
Malnutrition	–	–	–	–
Sarcopenia	9.19 (0.98–68.11)	0.052	2.69 (0.75–9.64)	0.130
Overweight-obesity	0.69 (0.14–18.86)	0.689	0.85 (0.25–2.91)	0.797
Micronutrient abnormalities	0.59 (0.12–3.0)	0.527	0.85 (0.25–2.91)	0.797
Etiology-based diagnoses				
Disease-related malnutrition with inflammation	23.79 (0.41–1380.89)	0.126	0.84 (0.10–7.39)	0.876
Disease-related malnutrition without inflammation	**175.91 (1.80–17153.45)**	**0.027**	0.74 (0.08–6.40)	0.782
Cachexia	0.767 (0.04–16.58)	0.87	1.27 (0.31–5.23)	0.736

4. Discussion

Our study applied both the ESPEN consensus and guidelines to describe the influence of basic and etiology-based diagnoses of malnutrition on clinical outcomes during hospitalization for postacute care. As malnutrition and disability are linked bidirectionally to mobility and disability (Landi et al., 2017), an early identification of malnourished patients would help the multidisciplinary care team to set realistic aims, plan therapeutic strategies, and provide the patient and caregivers with more precise information. The influence of the ESPEN consensus on clinical outcomes was recently reported in geriatric patients with diabetes in acute care (Sanz-París et al., 2016), but its influence on clinical and rehabilitation outcomes during hospitalization in postacute care has not previously been described

In our study, malnutrition and nutritional disorders are associated with worse functional prognosis in older patients during postacute rehabilitation care. This association is probably explained by weight loss prior to admission, which has been the most powerful predictor of poor functional outcomes in postacute care in our study and in previous findings (Lee & Tsai, 2012; Morley, 2015). Unintentional weight loss has been proposed as a key indicator to assess formal nutrition because of its validity, feasibility, efficiency, and availability for every population and level of healthcare assistance (Cederholm & Jensen, 2017). Nevertheless, our results highlight that reduced FFMI is the most powerful indicator of malnutrition, sarcopenia, frailty, and cachexia.

Although the influence of BMI on mortality is still a controversial issue, most authors agree that a protective optimal BMI range of 25–30 kg/m^2 provides better nutritional status and protects older individuals from diseases and the malnutrition caused by diseases (Chang, Beason, Hunleth, & Colditz, 2012). In our sample, overweight and obese patients were analyzed as one group because no significant differences in age, functional and cognitive status, comorbidity, length of stay, rehabilitation impact indexes, or survival were observed between them.

Our study also evaluates micronutrient abnormalities and albumin serum levels, and sheds light on the updated role of these biomarkers, which have been commonly used as markers of malnutrition in clinical settings (Cabrerizo et al., 2015) even though their relation with malnutrition was controversial (Reijnierse et al., 2015). Evidence-based medicine agrees on considering serum albumin and C-reactive protein as markers of inflammation (Bano et al., 2017; Cederholm et al., 2017; Reijnierse et al., 2015; Schaap et al., 2009), but not as useful tools for basic diagnosis of malnutrition. Nevertheless, they have become a part

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of the etiology-based diagnoses of malnutrition since the ESPEN diagnostic tree was proposed as the gold standard for nutritional assessment in Europe.

Although unintentional weight loss and malnutrition with and without inflammation was associated with the rehabilitation outcomes in the univariate analysis, only unintentional weight loss emerged as a significant risk factor of poor rehabilitation outcomes, longer hospital stay, and 2-year mortality. In a large multicenter study in a cohort of older diabetic patients hospitalized for acute care (Sanz-París et al., 2016), malnutrition as defined by the ESPEN consensus statement was the only factor associated within hospital mortality. In our postacute care sample, the impact of malnutrition on mortality could not be determined because mortality was a rare event. Further research is needed on this issue in larger samples or in a follow-up after hospital discharge.

Our results support calls for simplified diagnostic tools that connect clinical and basic sciences and act bidirectionally, summarized as the 'Action Research' philosophy: from bedside to bench to bedside again, providing both meaningful challenges and new answers for clinicians and researchers (Beauchet, Fantino, & Annweiler, 2012). The findings in our postacute care unit may contribute to efforts to reach an international unified definition of malnutrition for application in all geriatric settings (Cederholm & Jensen, 2017).

4.1. Limitations of the study

There was an initial selection bias, given that patient selection was based on the potential to pursue rehabilitation therapy. Those who were unable to walk or needed help from two or more persons prior to their hospitalization, as well as patients who do not require rehabilitation after the acute medical process, are not admitted to the post-acute care unit. The relatively small number of patients is also a potential limitation. The use of the MNA-SF as a screening tool is valid (Kaiser et al., 2009; Lee & Tsai, 2012) and has been recommended by the Spanish Geriatrics and Gerontology Society (Camina-Martín et al., 2015), but using the full MNA might have improved specificity. Other potential limitations of the study are related to the REI; this index is highly conditioned by the mean length of stay, which could be influenced by multiple factors that do not depend on the rehabilitation process (Sánchez-Rodríguez, Miralles et al., 2015). Anthropometric measurements, such as the use of demispan or knee height in patients unable to stand (12 patients) without taking into account possible kyphosis or vertebral osteoporotic degenerative changes, might interfere with an accurate BMI, FFMI, basic diagnosis of malnutrition, and sarcopenia or cachexia diagnosis (Bahat et al., 2012; Sánchez-Rodríguez et al., 2016). Limitations for determining weight loss in older populations have been well described (Robbins, 1989), and could be avoided by systematic measurement and recording as part of the comprehensive geriatric assessment. Regarding the etiology-based diagnoses, only albumin levels were considered as markers of inflammation, when C-reactive protein is likely a more specific marker. Last, but not least, the observational design of the study might be considered a limitation; further studies should be designed to assess causality and associations related with postdischarge and follow-up events.

4.2. Conclusions and future lines of clinical research

The key point of this study is to discuss practical implications of malnutrition assessment. Further research is urgently needed to assess the value of a basic diagnosis of malnutrition, according to the ESPEN consensus statement and its subscores, as a predictor of adverse outcomes after hospital discharge, including institutionalization, unexpected hospital readmissions, and mortality.

Conflict of interest

None.

Author contributions

DS, EM conceived and designed the experiments; DS, EM, NR, AT performed the experiments; DS, EM, XD, CA analyzed and interpreted the data; DS, EM, CA, NR, OVI, FE, JMM contributed reagents, materials, analysis tools or data; DS, EM, CA wrote the paper.

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Landi et al. (2015).

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References

Agarwal, E., Ferguson, M., Banks, M., Batterham, M., Bauer, J., Capra, S., Isenring, E., 2013. Malnutrition and poor food intake are associated with prolonged hospital stay, frequent readmissions, and greater in-hospital mortality: Results from the Nutrition Care Day Survey 2010. Clinical Nutrition (Edinburgh, Scotland) 32 (5), 737–745. https://doi.org/10.1016/j.clnu.2012.11.021.

Arinzon, Z., Fidelman, Z., Zuta, A., Peisakh, A., Berner, Y.N., 2005. Functional recovery after hip fracture in old–old elderly patients. Archives of Gerontology and Geriatrics 40 (3), 327–336. https://doi.org/10.1016/j.archger.2004.10.003.

Bahat, G., Tufan, F., Saka, B., Akin, S., Ozkaya, H., Yucel, N., … Karan, M.A., 2012. Which body mass index (BMI) is better in the elderly for functional status?. Archives of Gerontology and Geriatrics 54 (1), 78–81. https://doi.org/10.1016/j.archger.2011.04.019.

Bano, G., Trevisan, C., Carraro, S., Solmi, M., Luchini, C., Stubbs, B., … Veronese, N., 2017. Inflammation and sarcopenia: A systematic review and meta-analysis. Maturitas 96, 10–15. https://doi.org/10.1016/j.maturitas.2016.11.006.

Beauchet, O., Fantino, B., Annweiler, C., 2012. The action-research philosophy: From bedside to bench, to bedside again. International Journal of Clinical Practice 66 (5), 517. https://doi.org/10.1111/j. 1742-1241.2012.02909.x.

Cabrerizo, S., Cuadras, D., Gomez-Busto, F., Artaza-Artabe, I., Marín-Ciancas, F., Malafarina, V., 2015. Serum albumin and health in older people: Review and meta analysis. Maturitas 81 (1), 17–27. https://doi.org/10.1016/j.maturitas.2015.02.009.

Camina-Martín, M.A., de Mateo-Silleras, B., Malafarina, V., Lopez-Mongil, R., Niño-Martín, V., López-Trigo, J.A., Redondo-del-Río, M.P., 2015. Nutritional status assessment in geriatrics: Consensus declaration by the Spanish society of geriatrics and gerontology nutrition work group. Maturitas 81 (3), 414–419. https://doi.org/10.1016/j.maturitas.2015.04.018.

Cederholm, T., Jensen, G.L., 2017. To create a consensus on malnutrition diagnostic criteria: A report from the Global Leadership Initiative on Malnutrition (GLIM) meeting at the ESPEN Congress 2016. Clinical Nutrition 36 (1), 7–10. https://doi.org/10.1016/j.clnu.2016.12.001.

Cederholm, T., Bosaeus, I., Barazzoni, R., Bauer, J., Van Gossum, A., Klek, S., … Singer, P., 2015. Diagnostic criteria for malnutrition—An ESPEN consensus statement. Clinical Nutrition (Edinburgh, Scotland) 34 (3), 335–340. https://doi.org/10.1016/j.clnu.2015.03.001.

Cederholm, T., Barazzoni, R., Austin, P., Ballmer, P., Biolo, G., Bischoff, S.C., … Singer, P., 2017. ESPEN guidelines on definitions and terminology of clinical nutrition. Clinical Nutrition (Edinburgh, Scotland) 36 (1), 49–64. https://doi.org/10.1016/j.clnu.2016.09.004.

Cereda, E., Bertoli, S., Vanotti, A., Battezzati, A., 2010. Estimated height from knee-height in Caucasian elderly: Implications on nutritional status by mini nutritional assessment. The Journal of Nutrition, Health & Aging 14 (1), 16–22.

Cerri, A.P., Bellelli, G., Mazzone, A., Pittella, F., Landi, F., Zambon, A., Annoni, G., 2015. Sarcopenia and malnutrition in acutely ill hospitalized elderly: Prevalence and outcomes. Clinical Nutrition (Edinburgh, Scotland) 34 (4), 745–751. https://doi.org/10.1016/j.clnu.2014.08.015.

Chang, S.-H., Beason, T.S., Hunleth, J.M., Colditz, G.A., 2012. A systematic review of body fat distribution and mortality in older people. Maturitas 72 (3), 175–191. https://doi.org/10.1016/j.maturitas.2012.04.004.

Chen, Y.-M., Chuang, Y.-W., Liao, S.-C., Lin, C.-S., Yang, S.-H., Tang, Y.-J., … Chen, D.-Y., 2010. Predictors of functional recovery (FR) for elderly hospitalized patients in a geriatric evaluation and management unit (GEMU) in Taiwan. Archives of Gerontology and Geriatrics 50, S1–S5. https://doi.org/10.1016/S0167-4943(10)00041-5.

Cruz-Jentoft, A.J., Baeyens, J.P., Bauer, J.M., Boirie, Y., Cederholm, T., Landi, F., … Zamboni, M., 2010. Sarcopenia: European consensus on definition and diagnosis. Age and Ageing 39 (April), 412–423. https://doi.org/10.1093/ageing/afq034.

UNCORRECTED PROOF

Cruz-Jentoft, A.J., Kiesswetter, E., Drey, M., Sieber, C.C., 2017. Nutrition, frailty, and sarcopenia. Aging Clinical and Experimental Research 29 (1), 43–48. https://doi.org/10.1007/s40520-016-0709-0.

Deutz, N.E.P., Bauer, J.M., Barazzoni, R., Biolo, G., Boirie, Y., Bosy-Westphal, A., … Calder, P.C., 2014. Protein intake and exercise for optimal muscle function with aging: Recommendations from the ESPEN Expert Group. Clinical Nutrition (Edinburgh, Scotland) 33 (6), 929–936. https://doi.org/10.1016/j.clnu.2014.04.007.

Deutz, N.E., Matheson, E.M., Matarese, L.E., Luo, M., Baggs, G.E., Nelson, J.L., … Ziegler, T.R., 2016. Readmission and mortality in malnourished, older, hospitalized adults treated with a specialized oral nutritional supplement: A randomized clinical trial. Clinical Nutrition (Edinburgh, Scotland) 35 (1), 18–26. https://doi.org/10.1016/j.clnu.2015.12.010.

Evans, W.J., Morley, J.E., Argilés, J., Bales, C., Baracos, V., Guttridge, D., … Anker, S.D., 2008. Cachexia: A new definition. Clinical Nutrition 27 (6), 793–799. https://doi.org/10.1016/j.clnu.2008.06.013.

Fried, L.P., Tangen, C.M., Walston, J., Newman, A.B., Hirsch, C., Gottdiener, J., … Cardiovascular Health Study Collaborative Research Group, 2001. Frailty in older adults: Evidence for a phenotype. The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences 56 (3), M146–M156.

Guyonnet, S., Secher, M., Vellas, B., 2015. Nutrition, frailty, cognitive frailty and prevention of disabilities with aging. Nestle Nutrition Institute Workshop Series 82, 143–152. https://doi.org/10.1159/000382011.

Hamirudin, A.H., Charlton, K., Walton, K., 2016. Outcomes related to nutrition screening in community living older adults: A systematic literature review. Archives of Gerontology and Geriatrics 62, 9–25. https://doi.org/10.1016/j.archger.2015.09.007.

Kaiser, M.J., Bauer, J.M., Ramsch, C., Uter, W., Guigoz, Y., Cederholm, T., … Sieber, C.C., 2009. Validation of the mini nutritional assessment short-form (MNA-SF): A practical tool for identification of nutritional status. The Journal of Nutrition, Health & Aging 13 (9), 782–788.

Koh, G.C.-H., Chen, C.H., Petrella, R., Thind, A., 2013. Rehabilitation impact indices and their independent predictors: A systematic review. BMJ Open 3 (9), e003483. https://doi.org/10.1136/bmjopen-2013-003483.

Komai, S., Watanabe, Y., Fujiwara, Y., Kim, H., Edahiro, A., Kawai, H., … Hirano, H., 2016. Association between the nutritional status and the severity of sarcopenia among community-dwelling elderly Japanese people. Nihon Ronen Igakkai Zasshi. Japanese Journal of Geriatrics 53 (4), 387–395. https://doi.org/10.3143/geriatrics.53.387.

Kruizenga, H., van Keeken, S., Weijs, P., Bastiaanse, L., Beijer, S., Huisman-de Waal, G., … Thijs, A., 2016. Undernutrition screening survey in 564,063 patients: Patients with a positive undernutrition screening score stay in hospital 1.4 d longer. American Journal of Clinical Nutrition 103 (4), 1026–1032. https://doi.org/10.3945/ajcn.115.126615.

Landi, F., Bernabei, R., Russo, A., ZuccalÃ, G., Onder, G., Carosella, L., … Cocchi, A., 2002. Predictors of rehabilitation outcomes in frail patients treated in a geriatric hospital. Journal of the American Geriatrics Society 50 (4), 679–684. https://doi.org/10.1046/j.1532-5415.2002.50162.x.

Landi, F., Calvani, R., Cesari, M., Tosato, M., Martone, A.M., Bernabei, R., … Marzetti, E., 2015. Sarcopenia as the biological substrate of physical frailty. Clinics in Geriatric Medicine 31 (3), 367–374. https://doi.org/10.1016/j.cger.2015.04.005.

Landi, F., Calvani, R., Ortolani, E., Salini, S., Martone, A.M., Santoro, L., … Marzetti, E., 2017. The association between sarcopenia and functional outcomes among older patients with hip fracture undergoing in-hospital rehabilitation. Osteoporosis International: A Journal Established as Result of Cooperation Between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA https://doi.org/10.1007/s00198-017-3929-z.

Lee, L.-C., Tsai, A.C., 2012. Mini-nutritional-assessment (MNA) without body mass index (BMI) predicts functional disability in elderly Taiwanese. Archives of Gerontology and Geriatrics 54 (3), e405–e410. https://doi.org/10.1016/j.archger.2011.12.006.

Lindegaard Pedersen, J., Pedersen, P.U., Damsgaard, E.M., 2017. Nutritional follow-up after discharge prevents readmission to hospital—A randomized clinical trial. The Journal of Nutrition, Health & Aging 21 (1), 75–82. https://doi.org/10.1007/s12603-016-0745-7.

Marshall, S., 2016. Protein-energy malnutrition in the rehabilitation setting: Evidence to improve identification. Maturitas 86, 77–85. https://doi.org/10.1016/j.maturitas.2016.01.014.

Morley, J.E., 2015. Novel approaches to nutrition in older persons. Preface. Clinics in Geriatric Medicine 31 (3), xiii–xiv. https://doi.org/10.1016/j.cger.2015.05.001.

Nunes, B.P., Flores, T.R., Mielke, G.I., Thumé, E., Facchini, L.A., 2016. Multimorbidity and mortality in older adults: A systematic review and meta-analysis. Archives of Gerontology and Geriatrics 67, 130–138. https://doi.org/10.1016/j.archger.2016.07.008.

Reijnierse, E.M., Trappenburg, M.C., Leter, M.J., Sipilä, S., Stenroth, L., Narici, M.V., … Maier, A.B., 2015. Serum albumin and muscle measures in a cohort of healthy young and old participants. Age (Dordrecht, Netherlands) 37 (5), 9825. https://doi.org/10.1007/s11357-015-9825-6.

Robbins, L.J., 1989. Evaluation of weight loss in the elderly. Geriatrics 44 (4), 31–34, 37.

Rojer, A.G.M., Kruizenga, H.M., Trappenburg, M.C., Reijnierse, E.M., Sipilä, S., Narici, M.V., … de van der Schueren, M.A.E., 2016. The prevalence of malnutrition according to the new ESPEN definition in four diverse populations. Clinical Nutrition (Edinburgh, Scotland) 35 (3), 758–762. https://doi.org/10.1016/j.clnu.2015.06.005.

Sánchez-Rodríguez, D., Marco, E., Miralles, R., Fayos, M., Mojal, S., Alvarado, M., … Muniesa, J.M., 2014. Sarcopenia, physical rehabilitation and functional outcomes of patients in a subacute geriatric care unit. Archives of Gerontology and Geriatrics 59 (1), 39–43. https://doi.org/10.1016/j.archger.2014.02.009.

Sánchez-Rodríguez, D., Marco, E., Ronquillo-Moreno, N., Miralles, R., Vázquez-Ibar, O., Escalada, F., Muniesa, J.M., 2016. Prevalence of malnutrition and sarcopenia in a post-acute care geriatric unit: Applying the new ESPEN definition and EWGSOP criteria. Clinical Nutrition (Edinburgh, Scotland) https://doi.org/10.1016/j.clnu.2016.08.024.

Sánchez-Rodríguez, D., Marco, E., Miralles, R., Guillén-Solà, A., Vázquez-Ibar, O., Escalada, F., Muniesa, J.M., 2015. Does gait speed contribute to sarcopenia case-finding in a postacute rehabilitation setting?. Archives of Gerontology and Geriatrics 61 (2), 176–181. https://doi.org/10.1016/j.archger.2015.05.008.

Sánchez-Rodríguez, D., Miralles, R., Muniesa, J.M., Mojal, S., Abadía-Escartín, A., Vázquez-Ibar, O., 2015. Three measures of physical rehabilitation effectiveness in elderly patients: A prospective, longitudinal, comparative analysis. BMC Geriatrics 15, 142. https://doi.org/10.1186/s12877-015-0138-5.

Sanz-París, A., Gómez-Candela, C., Martín-Palmero, , García-Almeida, J.M., Burgos-Pelaez, R., Matía-Martin, P., … Study VIDA group, 2016. Application of the new ESPEN definition of malnutrition in geriatric diabetic patients during hospitalization: A multicentric study. Clinical Nutrition (Edinburgh, Scotland) 35 (6), 1564–1567. https://doi.org/10.1016/j.clnu.2016.02.018.

Schaap, L.A., Pluijm, S.M.F., Deeg, D.J.H., Harris, T.B., Kritchevsky, S.B., Newman, A.B., Visser, M., 2009. Higher inflammatory marker levels in older persons: Associations with 5-year change in muscle mass and muscle strength. The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences 64 (11), 1183–1189. https://doi.org/10.1093/gerona/glp097.

Schutz, Y., Kyle, U.U.G., Pichard, C., 2002. Fat-free mass index and fat mass index percentiles in Caucasians aged 18–98 y. International Journal of Obesity and Related Metabolic Disorders: Journal of the International Association for the Study of Obesity 26 (7), 953–960. https://doi.org/10.1038/sj.ijo.0802037.

Shen, H.-C., Chen, H.-F., Peng, L.-N., Lin, M.-H., Chen, L.-K., Liang, C.-K., Hwang, S.-J., 2011. Impact of nutritional status on long-term functional outcomes of post-acute stroke patients in Taiwan. Archives of Gerontology and Geriatrics 53 (2), e149–e152. https://doi.org/10.1016/j.archger.2010.08.001.

Soysal, P., Isik, A.T., Carvalho, A.F., Fernandes, B.S., Solmi, M., Schofield, P., … Stubbs, B., 2017. Oxidative stress and frailty: A systematic review and synthesis of the best evidence. Maturitas 99, 66–72. https://doi.org/10.1016/j.maturitas.2017.01.006.

Vischer, U.M., Frangos, E., Graf, C., Gold, G., Weiss, L., Herrmann, F.R., Zekry, D., 2012. The prognostic significance of malnutrition as assessed by the Mini Nutritional Assessment (MNA) in older hospitalized patients with a heavy disease burden. Clinical Nutrition (Edinburgh, Scotland) 31 (1), 113–117. https://doi.org/10.1016/j.clnu.2011.09.010.

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