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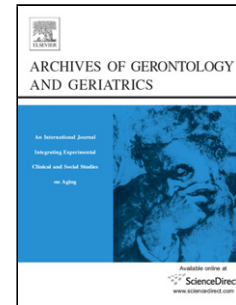
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Clinical application of the basic definition of malnutrition proposed by the European Society for Clinical Nutrition and Metabolism (ESPEN): comparison with classical tools in geriatric care

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Highlights

- Malnutrition was twice as prevalent when diagnosed by the ESPEN consensus, compared to classical assessment methods.
- Classical methods showed fair validity and poor agreement with the ESPEN consensus in assessing malnutrition in geriatric postacute care.
- Further studies incorporating the ESPEN consensus definition are needed to assess nutrition-related longitudinal outcome measures, effects by nutritional treatment, impact on functional status, and survival.
- Determining the most current gold standard for nutritional assessment could improve delivery of geriatric care.

Abstract: Background: Malnutrition is a prevalent condition related to adverse outcomes in older people. Our aim was to compare the diagnostic capacity of the malnutrition criteria of the European Society of Parenteral and Enteral Nutrition (ESPEN) with other classical diagnostic tools.

Methods: Cohort study of 102 consecutive in-patients ≥ 70 years admitted for postacute rehabilitation. Patients were considered malnourished if their Mini-Nutritional Assessment-Short Form (MNA-SF) score was ≤ 11 and serum albumin $< 3\text{mg/dL}$ or MNA-SF ≤ 11 , serum albumin $< 3\text{mg/dL}$, and usual clinical signs and symptoms of malnutrition. Sensitivity, specificity, positive and negative predictive

values, accuracy likelihood ratios, and kappa values were calculated for both methods and compared with ESPEN consensus.

Results: Of 102 eligible in-patients, 88 fulfilled inclusion criteria and were identified as "at risk" by MNA-SF. Malnutrition diagnosis was confirmed in 11.6% and 10.5% of the patients using classical methods, whereas 19.3% were malnourished according to the ESPEN criteria. Combined with low albumin levels, the diagnosis showed 57.9% sensitivity, 64.5% specificity, 85.9% negative predictive value, 0.63 accuracy (fair validity, low range), and kappa index of 0.163 (poor ESPEN agreement). The combination of MNA-SF, low albumin, and clinical malnutrition showed 52.6% sensitivity, 88.3% specificity, 88.3% negative predictive value, and 0.82 accuracy (fair validity, low range), and kappa index of 0.43 (fair ESPEN agreement).

Conclusions: Malnutrition was almost twice as prevalent when diagnosed by the ESPEN consensus, compared to classical assessment methods. Classical methods showed fair validity and poor agreement with the ESPEN consensus in assessing malnutrition in geriatric postacute care.

Abbreviations

AND: Academy of Nutrition and Dietetics

ASPEN: American Society of Parenteral and Enteral Nutrition

BMI: Body mass index

ESPEN: European Society for Clinical Nutrition and Metabolism

FFMI: Fat-Free mass index

GLIM: Global Leadership Initiative on Malnutrition meeting

ICD: International Classification of Diseases

k: kappa statistics

LR+: Positive likelihood ratio

MNA-SF: Mini-Nutritional Assessment-Short Form

NPV: Negative predictive value

PPV: Positive predictive value

SD: Standard deviation

WHO: World Health Organization

Keywords: ESPEN; malnutrition; older people; postacute; sensitivity; Specificity

INTRODUCTION

Malnutrition is highly frequent in older in-patients, with a prevalence ranging from 49% to 67% (Campos del Portillo et al., 2015) (Marshall, Young, Bauer, & Isenring, 2016) (Strakowski, Strakowski, & Mitchell, 2002); the highest prevalence was observed in postacute care settings (Strakowski et al., 2002). Malnutrition and related syndromes, such as sarcopenia and frailty (Cederholm et al., 2015) are associated with longer hospital stays (Agarwal et al., 2013) (Correia, Perman, & Waitzberg, 2017) (Sanz-París et al., 2016), infectious and non-infectious clinical complications (Carlsson, Haglin, Rosendahl, & Gustafson, 2013) (Nunes, Flores, Mielke, Thumé, & Facchini, 2016), poor

functional outcomes (Arinzon, Fidelman, Zuta, Peisakh, & Berner, 2005)(Cerri et al., 2015)(Goisser et al., 2015)(Luk, Chiu, Tam, & Chu, 2011)(Wakabayashi & Sashika, 2014), lack of recovery during three-month follow-up(Sánchez-Rodríguez et al., 2014), and increased risk of adverse outcomes following discharge, institutionalization, use of health care resources, readmissions, mortality, and costs (Agarwal et al., 2013)(Correia et al., 2017)(Curtis et al., 2017)(Hamirudin, Charlton, & Walton, 2016).

The assessment of malnutrition is a 2-step approach. The first step is to screen for malnutrition, mainly with the Mini-Nutritional Assessment questionnaire(Hamirudin et al., 2016)(Kaiser et al., 2009), as recommended by several Societies of Gerontology and Geriatrics(Camina-Martín et al., 2015), especially in postacute rehabilitation care settings (Marshall, Craven, Kelly, & Isenring, 2017)(Sánchez-Rodríguez et al., 2017).In the absence of an internationally standardized diagnostic method, the second step is to arrive at a diagnosis with a combination of clinical anamnesis, physical examination, and/or biochemical measurements(Camina-Martín et al., 2015)(Campos del Portillo et al., 2015)(Reuben, Greendale, & Harrison, 1995). For instance, clinical manifestations may include unintentional weight loss (Cederholm et al., 2015)(Evans et al., 2008)(Reuben et al., 1995)(Wirth et al., 2016)(White et al., 2012), reduced anthropometry (body mass index [BMI], calf circumference)(Bahat et al., 2012)(Rolland et al., 2014), and changes in behavior (i.e. reduced food intake, anorexia) (Agarwal et al., 2013)(Goisser et al., 2015)(Reuben et al., 1995)(White et al., 2012).

Biochemical markers, such as serum albumin concentration, which has been used for years as a marker of malnutrition (Cabrerizo et al., 2015)(Camina-Martín et al., 2015)(Reuben et al., 1995), are no longer recommended as diagnostic markers because

they are also influenced by inflammation (Cederholm et al., 2015)(Cederholm et al., 2017). This heterogeneity of definitions and tools has hindered the development of a best-practice approach to the diagnosis of malnutrition, at least until the recent consensus statement from the European Society for Clinical Nutrition and Metabolism (ESPEN)(Cederholm et al., 2015).

The ESPEN Consensus on malnutrition diagnosis is valid for all adults and healthcare settings, independently of etiology. The definition includes only weight loss, reduced BMI, and reduced fat-free-mass index (FFMI) as clinical criteria(Cederholm et al., 2015). Despite the growing literature reporting benefits of using the ESPEN consensus tool in older adults(Sánchez-Rodríguez et al., 2018)(Sánchez-Rodríguez et al., 2017)(Sanz-París et al., 2016)(Jiang et al., 2017), no comparison with previous diagnostic methods has been made available to date. The aim of the present study was to compare the diagnostic properties of the previous methods with the ESPEN basic definition of malnutrition in a postacute care setting.~

METHODS

Design

Cross-sectional analysis of older hospitalized patients participating in a larger prospective study on sarcopenia and functional outcomes(Sánchez-Rodríguez et al., 2014).

Setting

The study was conducted in a postacute geriatric rehabilitation care unit in a university

hospital in Barcelona (Catalonia, Spain), focused on comprehensive geriatric assessment and rehabilitation during a defined period of time, usually about two weeks before a scheduled home discharge. The data were recorded between January and August 2011 (Sánchez-Rodríguez et al., 2014). ESPEN basic diagnosis was applied retrospectively.

Participants

The study population consisted of 102 consecutive in-patients who met inclusion criteria: age ≥ 70 years, admitted to the postacute rehabilitation care unit for functional loss due to a non-disabling medical disease. Patients whose general and/or cognitive condition (Mini-Mental State Examination score $< 21/30$) prevented completion of the diagnostic tests and those who were participating in an active physical rehabilitation program were excluded from analysis.

Main outcomes

The main outcomes for analysis were the metrological assessments that determine the diagnostic properties and the overall value of an assessment method: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy index, and positive likelihood ratio (LR+). Results of the ESPEN definition of malnutrition were compared with two frequently used diagnostic approaches: a) the Mini-Nutritional Assessment (MNA-SF) (Kaiser et al., 2009) plus serum albumin levels and b) the MNA-SF, serum albumin levels, and the presence of clinical signs or symptoms of malnutrition, as detailed below.

The cut-off points for validity of an assessment method have been set as follows:

sensitivity **and** specificity >80%, good validity; sensitivity **or** specificity <80% but both values >50%, fair validity; if sensitivity or specificity <50%, poor validity (Baek & Heo, 2015)(Van Bokhorst-de van der Schueren, Guaitoli, Jansma, & de Vet, 2014). Concordance between the ESPEN consensus and previous diagnostic methods was determined with kappa (k) statistics: k <0, no agreement; 0.00-0.20, poor agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80 substantial agreement; 0.81-1, almost perfect agreement(Baek & Heo, 2015)(Landis & Koch, 1977).

Screening for malnutrition

Upon admission to the postacute rehabilitation unit, patients were screened for malnutrition using the short form of the Mini-Nutritional Assessment (MNA-SF): score 12-14, normal; 8-11, risk of malnutrition; and 0-7, malnourished(Camina-Martín et al., 2015)(Kaiser et al., 2009). A 10-ml venous blood sample was collected from all patients under standardized conditions between 7 and 9 am, at rest, and following an overnight fast to determine serum albumin level.

Procedure for ESPEN basic diagnosis

The ESPEN basic diagnosis was applied to all screened subjects with MNA-SF score ≤ 11 . **Unintentional weight loss** was determined by patient and caregiver anamnesis and medical records documenting at least 5% unintentional weight loss 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).**Body mass index (BMI)** was calculated (kg/m^2) from weight and height. 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**, expressed in kg, was measured by bioimpedance (Bodystat 1500, Bodystat Ltd., Isle of Man British Isles) as previously described (Sánchez-Rodríguez et al., 2014) and values were divided by height squared to obtain the **FFMI** value, expressed in kg/m^2 , and compared with those of the reference population (Schutz, Kyle, & Pichard, 2002).

Procedure for malnutrition assessment according to previous methods

A positive diagnosis of malnutrition was considered using two approaches: a combination of MNA-SF score ≤ 11 , indicating risk of malnutrition (Camina-Martín et al., 2015) (Kaiser et al., 2009), and serum albumin ≤ 3 mg/dL (Cabrerizo et al., 2015) (Reuben et al., 1995); and a second method consisting of both of the previous assessments combined with evidence of at least one of the following clinical signs or symptoms of malnutrition (Reuben et al., 1995): **unintentional weight loss**, determined as described above; low **BMI**, according to World Health Organization (WHO) recommendations (underweight cut-off value $\text{BMI} < 18.5 \text{ kg}/\text{m}^2$); **calf circumference** < 31 cm); **reduced food intake**, estimated by plate waste (%) during hospital stay, as part of the daily usual care by trained nurses (24-h food intake: 0, 25, 50, 75, 100% intake) (Agarwal et al., 2013), categorized as “yes” when food intake was $< 50\%$ and “no” otherwise; **anorexia** (total caloric intake < 20 kcal/kg body weight/day; $< 70\%$ of usual food intake) was also recorded as a dichotomous variable (Evans et al., 2008).

Other clinical and demographic characteristics recorded were age, sex, comorbidity (Charlson index), cognitive status (Short Portable Mental Status Questionnaire), and

functional status at admission (Lawton and Barthel indexes), as previously published (Sánchez-Rodríguez et al., 2014).

Ethics

National and international research ethics guidelines were followed (Muller & Soares, 2017), including the Deontological Code of Ethics, Declaration of Helsinki, and Spain's confidentiality law concerning personal data. Detailed, understandable oral and written information was provided to patients and family members, and informed consent to participate was signed by all participants. The institution's Clinical Ethics Committee approved the study and the informed consent process used.

Statistical analysis

Sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, accuracy likelihood ratios, and kappa values were calculated for both methods and compared with ESPEN consensus. Other descriptive categorical variables were shown as absolute values and percentages, and quantitative variables were presented with mean and standard deviation (SD). Contingency tables were used to calculate the reliability indexes of the two previously described clinical assessment methods for malnutrition compared with ESPEN malnutrition basic diagnosis. Each 2×2 contingency table contains two rows for malnutrition (according to method 1 or 2) and two columns for ESPEN basic diagnosis (yes or no). P value of $p < 0.05$ was considered statistically significant ($p < 0.05$). Analysis was performed using IBM SPSS Statistics 22 (IBM Corporation, SPSS, INC., Chicago, IL, USA).

RESULTS

From the 102 eligible in-patients, 88 fulfilled study inclusion criteria. **Table 1** shows the general and geriatric assessment results. The entire sample (95 in-patients, 100%) was identified as being “at risk” due to MNA-SF scores ≤ 11 and 69 patients were considered “malnourished”; therefore, the malnutrition assessment according to previous assessment methods and the ESPEN criteria were applied to all participants. Unintentional weight loss was reported by 31 patients (32.6%). **Tables 2 and 3** compare the contingency tables for the prevalent clinical assessment methods for malnutrition with the ESPEN basic diagnosis frequency distribution. Prevalence of malnutrition was 19.3% (19 patients) using ESPEN criteria, 11.6% if determined by MNA-SF and low albumin levels and 10.5% if determined by a combination of MNA-SF, low albumin, and clinical signs and symptoms of malnutrition.

Table 3 summarizes the values of sensitivity, specificity, PPV, NPV, accuracy, LR+ and k statistics for the two most prevalent clinical assessment methods. Method 1 achieved values of 57.9%, 64.5%, 85.9%, and 0.63 (low range of fair validity), respectively. Method 2 values were 52.6%, 88.3%, 88.3%, and 0.82 (low range of fair validity), respectively. In addition, method 1 showed poor agreement with the gold-standard ESPEN consensus ($k = 0.163$, $p = 0.075$) and method 2 reached moderate agreement ($k = 0.430$, $p < 0.001$).

DISCUSSION

Malnutrition was almost twice as prevalent when diagnosed by the ESPEN consensus, compared to classical assessment methods. Our results show poor-to-moderate agreement and a rather low validity of previous methods for the diagnosis of malnutrition in older in-patients compared to the ESPEN consensus.

Before attempting any further discussion of these findings, it should be clear that, to date, we cannot assure that the ESPEN definition is the best tool to identify malnutrition. Proper validation would require nutrition-related longitudinal outcomes. However, the ESPEN consensus presents the first unified malnutrition criteria for Europe, provides an evidence-based approach with objective measurements, and minimizes the subjectivity and corresponding bias of health professionals. Moreover, it has been found to be a reliable and appropriate tool with predictive value for functional outcomes (Sánchez-Rodríguez et al., 2011), length of stay (Sanz-Paris et al., 2016), and long-term mortality (Jiang et al., 2017) in geriatric populations. For these reasons, for purposes of analysis, our study used the ESPEN consensus as if it were the gold standard. The primary aim of the authors was to provide insight about the applicability of this definition in geriatric care, considering both clinical implications and the challenges for researchers.

The aim of the Global Leadership Initiative on Malnutrition (GLIM)(Cederholm & Jensen, 2017b) is to develop a universal diagnostic tool; geriatricians and gerontologists should be involved in this process to provide better care in Geriatrics. The extended use of an international consensus would help to establish prevalence, allow comparisons

between settings, and support coding purposes, as a diagnosis admitted for the World Health Organization and the International Classification of Diseases (ICD)(Cederholm& Jensen, 2017a)(Cederholm & Jensen, 2017b).To improve quality of care for geriatric patients, it is essential that this definition be appropriate for use in the ageing population.

In addition to the ESPEN consensus and guidelines, clinical tools for malnutrition assessment have been proposed by the American Society of Parenteral and Enteral Nutrition (ASPEN) and Academy of Nutrition and Dietetics (AND) (White et al., 2012) and the Canadian Nutrition Society (Jeejeebhoy et al., 2015)(Cederholm & Jensen, 2017b), among others (Visser et al., 2017). To the best of our knowledge, comparisons between ESPEN consensus and other approaches are scarce (Poulia et al., 2017).Despite expert recommendations to introduce evidence-based criteria to diagnose malnutrition(Cederholm et al., 2015)(Cederholm & Jensen, 2017a)(Cederholm & Jensen, 2017b), there are not data of their implementation in clinical settings, partially due to resistance to change in clinical practice(Grace, 2018), and to the continued use of albumin as a malnutrition marker (Camina-Martín et al., 2015)(Raynaud-Simon, Revel-Delhom, Hébuterne, & French Nutrition and Health Program, 2011).

Some characteristics of the study setting could have influenced our results and should be acknowledged as potential limitations. The unit's admission criteria based on capacity to participate in a short-term rehabilitation program is an initial selection bias for studies carried out in postacute care. Three groups of patients are generally excluded from postacute care units: those with good initial recovery in an acute care ward, with

no need for in-patient rehabilitation therapy and willing to be discharged home; those who require a rehabilitation program longer than two weeks and are referred to intermediate-care settings, and those admitted to long-term care because their acute physical, cognitive, or functional recovery prevents them from following a geriatric rehabilitation program. The use of the full-length nutritional questionnaire to detect malnutrition might have increased specificity; nevertheless, the MNA-SF has high sensitivity, which is desirable for a screening tool (Baek & Heo, 2015). To minimize bias, no subjective evaluation was incorporated as an assessment tool and criteria based on “subjectivity of professionals” were discarded, as these were discussed and discarded during the ESPEN consensus in a Delphi process. Obtaining an objective and accurate measurement of weight loss is often a challenge in clinical practice (Robbins, 1989). Moreover, the amount of weight and time period to be considered remain unclear, which could be considered a limitation of our study because weight loss should be measured systematically as part of the geriatric assessment in all geriatric settings.

Further studies incorporating the ESPEN consensus definition are needed to assess nutrition-related longitudinal outcome measures, effects by nutritional treatment, impact on functional status, and survival. Our study highlights the need to apply emerging research findings in clinical settings to improve geriatric care.

Conclusions

Malnutrition was almost twice as prevalent when diagnosed by the ESPEN consensus, compared to classical assessment methods. Malnutrition diagnosis based on previous

classical methods (MNA-SF screening combined with lower albumin concentrations and clinical signs or symptoms) remained in the low range of fair validity and showed only poor agreement with the ESPEN consensus in a geriatric postacute care setting.

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Conflict of interest

All authors declare they do not have any financial and personal relationships with other people or organizations that could inappropriately influence their work.

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Table 1. General characteristics of the study participants (n= 95)

Age (years)	84.7 (\pm 6.6)
Sex (female)	60 (63.2%)
Charlson comorbidity index (max score 43 points)	2.3 (\pm 1.8)
Short Portable Mental Status Questionnaire [10-point scale, mean (SD)]	4.2 (\pm 2.9)
Lawton index, [8-point scale, mean (SD)]	2.5 (\pm 2.5)
Barthel index [100-point scale, mean (SD)]	
Prior	70.5 (\pm 21.4)
At admission	26.6 (\pm 15.4)
At discharge	51.6 (\pm 26.7)
Body mass index (kg/m ²)	25.5 (\pm 4.2)
Unintentional weight loss	31 (32.6%)

*Data are given as numbers (percentages) for sex distribution and unintentional weight loss. SD: standard deviation

Table 2. Contingency table showing frequency distribution of clinical assessment of malnutrition based on Mini-Nutritional Assessment-Short Form (MNA-SF) combined with lower serum albumin concentration, and based on European Society of Parenteral and Enteral Nutrition (ESPEN) basic diagnosis.

		ESPEN BASIC DIAGNOSIS		
		Positive	Negative	
MNA-SF combined with lower albumin concentration	Positive	11	27	38
	Negative	8	49	57
		19	76	95

Table 3. Contingency table showing the frequency distribution of clinical assessment of malnutrition based on Mini-Nutritional Assessment-Short Form (MNA-SF) combined with lower serum albumin concentration and clinical signs or symptoms of malnutrition, and based on European Society of Parenteral and Enteral Nutrition (ESPEN) basic diagnosis.

	ESPEN BASIC DIAGNOSIS			
		Positive	Negative	
MNA-SF combined with lower albumin concentration and clinical signs and symptoms	Positive	10	9	19
	Negative	9	68	77
		19	76	95

Table 4. Metrological properties of the methods based on Mini-Nutritional Assessment-Short Form (MNA-SF), serum albumin concentration, and clinical signs and symptoms for the diagnosis of malnutrition according to European Society of Parenteral and Enteral Nutrition (ESPEN) basic diagnosis.

ESPEN BASIC DIAGNOSIS							
	Se (%)	Sp (%)	PPV (%)	NPV (%)	Accuracy (%)	LR+	Kappa
Malnutrition assessment by MNA-SF and low albumin levels	57.89	64.47	28.95	85.96	63.16	1.63	0.16
Malnutrition assessment by MNA-SF, low albumin levels, and clinical signs and symptoms	52.63	89.47	52.63	88.31	82.10	4.44	0.43

Se: sensitivity; Sp: specificity; PPV: positive predictive value; NPV: negative predictive value