RESEARCH
Research Brief

Evaluation of the Validity and Feasibility of the GLIM Criteria Compared with PG-SGA to Diagnose Malnutrition in Relation to One-Year Mortality in Hospitalized Patients

Vera IJmker-Hemink, MSc; Samantha Heerschop, MSc; Geert Wanten, MD, PhD; Manon van den Berg, PhD

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ABSTRACT

Background The Global Leadership Initiative on Malnutrition (GLIM) approach to diagnose malnutrition was published in 2018. An important next step is to use the GLIM criteria in clinical investigations to assess their validity and feasibility.

Objective To compare the validity and feasibility of the GLIM criteria with Patient-Generated Subjective Global Assessment (PG-SGA) in hospitalized patients and to assess the association between malnutrition and 1-year mortality.

Design Post hoc analysis of a prospective cohort study.

Participants/setting Hospitalized patients (n = 574) from the Departments of Gastroenterology, Gynecology, Urology, and Orthopedics at the Radboudumc academic facility in Nijmegen, The Netherlands, were enrolled from July 2015 through December 2016.

Main outcome measures The GLIM criteria and PG-SGA were applied to identify malnourished patients. Mortality rates were collected from electronic patient records. Feasibility was assessed by evaluating the amount of and reasons for missing data.

Statistical analyses performed Concurrent validity was evaluated by assessing the sensitivity, specificity, and Cohen's kappa coefficient for the GLIM criteria compared with PG-SGA. Cox regression analysis was used for the association between the GLIM criteria and PG-SGA and mortality.

Results Of 574 patients, 160 (28%) were classified as malnourished according to the GLIM criteria and 172 (30.0%) according to PG-SGA ($\kappa = 0.22$, low agreement). When compared with PG-SGA, the GLIM criteria had a sensitivity of 43% and a specificity of 79%. Mortality of malnourished patients was more than two times higher than for non-malnourished patients according to the GLIM criteria (hazard ratio [HR], 2.68; confidence interval [CI], 1.33-5.41). Data on muscle mass was missing in 454 of 574 (79%) patients because of practical problems with the assessment using bioimpedance analysis (BIA).

Conclusions Agreement between GLIM criteria and PG-SGA was low when diagnosing malnutrition, indicating that the two methods do not identify the same patients. This is supported by the GLIM criteria showing predictive power for 1-year mortality in hospitalized patients in contrast to PG-SGA. The assessment of muscle mass using BIA was difficult to perform in this clinical population.
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INTERNATIONALLY, SEVERAL ATTEMPTS HAVE BEEN made to achieve consensus on diagnosing malnutrition, but the results were never globally accepted nor implemented. In 2018, the Global Leadership Initiative on Malnutrition (GLIM) comprising representatives of four clinical nutrition societies from different parts of the world reached a new global consensus on criteria for diagnosing malnutrition.[1] These new criteria are based on phenotypic (unintentional weight loss, low body mass index, or low Fat Free Mass Index (FFMI)) and etiologic criteria (reduced food intake or disease burden/inflammation). Cederholm et al[1] state that it is necessary to start using the GLIM criteria in clinical investigations to assess the relevance and feasibility of the criteria in clinical practice.[1] Because the GLIM consensus approach to diagnose malnutrition has been released recently, validation studies have not been performed yet, but a guidance paper was published describing how to perform such studies.[2] The best form of validation is

concurrent validity by comparing a tool with a gold standard.[2] Because there is no gold standard for malnutrition, a semi-gold standard such as the Patient-Generated Subjective Global Assessment (PG-SGA) can be used to assess the validity of the GLIM criteria.[3]

The primary aim of this study was to compare the prevalence of malnutrition according to the GLIM criteria and PG-SGA and to assess the concurrent validity of the GLIM criteria based on the data from a previous prospective cohort study. To determine the predictive validity of the GLIM criteria, secondary aims were to compare the association of malnutrition according to the GLIM criteria and PG-SGA with 1-year mortality. Finally, the aim was to assess the feasibility of the GLIM criteria in clinical practice by determining those criteria that were not possible to obtain.

RESEARCH SNAPSHOT

Research question: What is the validity and feasibility of the GLIM criteria compared with PG-SGA to diagnose malnutrition in hospitalized patients and what is the association with 1-year mortality?

Key findings: Agreement between the GLIM criteria and PG-SGA was low when diagnosing malnutrition, indicating that GLIM criteria and PG-SGA do not identify the same patients. The assessment of muscle mass using bioimpedance analysis was difficult to perform in this clinical population.

MATERIALS AND METHODS

Study Population and Design

This study was a post hoc analysis of a cohort study in which a traditional three meals per day food service was compared with a novel 6 times per day food service containing protein-rich food items, called FoodforCare.[4] The cohort study was performed between July 2015 and May 2016. The Medical Ethics Committee of the Radboud University Medical Center (Radboudumc) decided that a formal approval of the cohort study was not required (clinicaltrials.gov: NCT03195283). The study population (n = 637) comprised patients from the departments of Gastroenterology, Gynecology, Urology, and Orthopedics. All subjects were Dutch speaking, older than 18 years, and able to adequately respond to questions. Patients with tube or parenteral feeding, or those who were unable to adequately answer questions were excluded from the study. Potential participants were identified and approached through screening of electronic medical records on the day of admission. All participants provided written informed consent.[4]

Primary Outcome

Primary study outcome was the validity of the GLIM criteria in hospitalized patients compared with PG-SGA. The guidance paper by Keller et al[2] was followed to assess concurrent and predictive validity. Malnutrition was assessed according to the GLIM criteria and PG-SGA to compare malnutrition prevalence associated with each of these sets of criteria. Additionally, the association of malnutrition based on GLIM criteria and PG-SGA with 1-year mortality was assessed. The electronic patient database of the Radboudumc was used to determine the date of death, which was assessed 1 year after admission to the hospital.

Secondary Outcome

As a secondary outcome, the GLIM criteria responsible for the diagnosis of malnutrition were identified, and the number of and reasons for missing data were assessed to evaluate the feasibility of the GLIM criteria. This identification was performed by investigating whether data were present and by listing the experiences of those who collected the data.

GLIM Criteria

The GLIM criteria describe the assessment for diagnosis and severity grading of malnutrition. The assessment for diagnosis is based on three phenotypic and two etiologic criteria and was performed for all patients.[1] Malnutrition is diagnosed when at least one phenotypic and one etiologic criterion are present. Severity grading of malnutrition was beyond the scope of this analysis.

Measurements

The GLIM criteria were applied to all patients, and measurements were taken on the first full day of oral intake during admission to the hospital regardless of their risk of malnutrition according to the Malnutrition Universal Screening Tool (MUST). Measurements were performed by nutritionists or dietitians trained with standard operating procedures before the start of the study to avoid variance. For phenotypic criteria, data on weight loss were obtained from step 2 of the MUST, which means that patients had 5% to 10% weight loss during the prior 3 to 6 months.[5] Body mass index (BMI) was calculated as weight, measured on a calibrated digital sitting scale, divided by height in meters squared (kg/m^2). The cutoff values indicated by Cederholm et al[1] were applied for BMI: <20 for patients younger than 70 years or <22 for patients older than 70 years (Table 1). Bioimpedance analysis (BIA) (Bodystat 1500 MDD) was used to calculate FFMI. The Kyle formula was used for this calculation except for chronic obstructive pulmonary disease patients (Rutten formula) and patients with a BMI > 30 (Horie formula).[6] Cutoff values of <17 for men and <15 for women were used to assess muscle mass.[1] For etiologic criteria, step 2 of the PG-SGA about food intake during the past month was used to determine reduced food intake or assimilation.[3] Disease burden or inflammation was assessed based on patients' medical records: here no laboratory markers were used. This variable was categorized as an emergency case, oncological, infectious disease at baseline, or when any other disease burden or chronic inflammation–related condition was mentioned in the medical history, such as chronic obstructive pulmonary disease, pneumonia, or diabetes. PG-SGA was also applied to all patients to diagnose malnutrition to compare with the GLIM criteria. PG-SGA is an instrument to diagnose malnutrition and has been used in oncology, acute medical, surgical, and elderly patients.[3,7-10] Scores range from 0 to 52, and patients were considered malnourished with a score ≥9.[3]

Statistical Analysis

Characteristics of participants were described by frequencies and percentages in case of dichotomous or ordinal data. With

Table 1. Descriptive characteristics of 574 hospitalized patients included in a post hoc analysis on the validity and feasibility of the GLIM[a] criteria compared with PG-SGA[b] displayed as malnourished and non-malnourished

		GLIM Criteria		PG-SGA	
	Total n = 574	Malnourished n = 160	Non-malnourished n = 414	Malnourished n = 172	Non-malnourished n=402
Male, n (%)	278 (48.4)	80 (50.0)	198 (47.8)	71 (41.3)	207 (51.5)
Age, years, mean ± SD[c]	59.6 ± 16.3	60.4 ± 17.7	59.2 ± 15.7	61.4 ± 17.7	58.8±15.6
MUST,[d] n (%)					
0	429 (74.7)	30 (18.8)	399 (96.4)	100 (58.1)	329 (81.8)
1	77 (13.4)	69 (43.1)	8 (1.9)	35 (20.3)	42 (10.4)
≥2	68 (11.8)	61 (38.1)	7 (1.7)	37 (21.5)	31 (7.7)
Admission, n (%)*					
Emergency	234 (40.8)	93 (58.1)	141 (34.1)	115 (66.9)	119 (29.6)
Elective	340 (59.2)	67 (41.9)	273 (65.9)	57 (33.1)	283 (70.4)
Oncological disease, n (%)	129 (22.5)	48 (30.0)	81 (19.6)	41 (23.8)	88 (21.9)
Surgical procedure, n (%)*	352 (61.3)	72 (45.0)	280 (67.6)	55 (32.0)	297 (73.9)
(Suspected) infection, n (%)	117 (20.4)	32 (20.0)	78 (18.8)	49 (28.5)	61 (15.2)
Complications, n (%)	84 (14.6)	26 (16.3)	58 (14.0)	21 (12.2)	63 (15.7)
Cause of admission, n (%)*					
Gastrointestinal	125 (21.8)	49 (30.6)	76 (18.4)	69 (40.1)	56 (13.9)
Hepatic	49 (8.5)	24 (15.0)	25 (6.0)	29 (16.9)	20 (5.0)
Urogenital	125 (21.8)	31 (19.4)	94 (22.7)	22 (12.8)	103 (25.6)
Genital	62 (10.8)	16 (10.0)	46 (11.1)	18 (10.5)	44 (10.9)
Musculoskeletal	206 (35.9)	38 (23.8)	175 (38.9)	30 (17.4)	176 (43.8)
Respiratory	2 (0.003)	1 (0.6)	1 (0.2)	1 (0.6)	1 (0.2)
Internal medicine	3 (0.005)	1 (0.6)	2 (0.5)	1 (0.6)	2 (0.5)
Dermatological	4 (0.007)	1 (0.6)	3 (0.7)	2 (1.2)	2 (0.5)
Department, n (%)*					
Gastroenterology and Hepatology	179 (31.2)	76 (47.5)	103 (24.9)	102 (59.3)	77 (19.2)
Orthopedics	207 (36.0)	37 (23.1)	170 (41.1)	30 (17.4)	177 (44.0)
Urology	130 (22.6)	30 (18.8)	100 (24.2)	23 (13.4)	107 (26.6)
Gynecology	48 (10.1)	17 (10.6)	41 (9.9)	17 (19.9)	41 (10.2)

(*continued on next page*)

Table 1. Descriptive characteristics of 574 hospitalized patients included in a post hoc analysis on the validity and feasibility of the GLIM[a] criteria compared with PG-SGA[b] displayed as malnourished and non-malnourished (*continued*)

		GLIM Criteria		PG-SGA	
	Total n = 574	Malnourished n = 160	Non-malnourished n = 414	Malnourished n = 172	Non-malnourished n=402
Comorbidities, n (%)					
Hypertension	136 (23.7)	42 (26.3)	94 (22.7)	38 (22.1)	98 (24.4)
Diabetes mellitus	64 (11.1)	26 (16.3)	38 (9.2)	28 (16.3)	36 (9.0)
Cerebrovascular	23 (4.0)	9 (5.6)	14 (3.4)	6 (3.5)	17 (4.2)
Cardiovascular	99 (17.2)	27 (16.9)	72 (17.4)	31 (18.0)	68 (16.9)
Other	192 (33.4)	64 (40.0)	128 (30.9)	70 (40.7)	122 (30.3)

[a]GLIM = Global Leadership Initiative on Malnutrition.
[b]PG-SGA = Patient-Generated Subjective Global Assessment.
[c]SD = standard deviation.
[d]MUST = Malnutrition Universal Screening Tool.
*Statistically significant difference between groups, $P < 0.05$.

normally distributed continuous data, mean and standard deviation were used. Baseline characteristics between groups were analyzed using *t* tests and χ^2 tests.

Patient data were included if at least two or more phenotypic criteria were scored and excluded if two phenotypic criteria were not scored and the third criterion was missing. The same strategy was applied for missing data on cause.

Concurrent validity was evaluated by comparison of the GLIM criteria with PG-SGA by sensitivity, specificity, and Cohen's kappa coefficient for the GLIM criteria compared with PG-SGA. Sensitivity and specificity should be higher than 80%.[2] A kappa coefficient between 0 and 0.20 reflects weak agreement; 0.21–0.4, low agreement; 0.41–0.6, moderate agreement; 0.61–0.8, good agreement; and 0.81-1.00, excellent agreement.[2] Malnutrition according to the GLIM criteria and 1-year mortality were defined as dichotomous variables. Kaplan-Meier curves and Cox regression analysis were used to assess the association between malnutrition and 1-year mortality for the GLIM criteria and the PG-SGA. Potential confounders were based on the significant differences between well-nourished and malnourished patients and an assumed association with malnutrition and 1-year mortality. These potential confounders (sex, age, planned or emergency admission, oncological disease, surgical procedure, [suspected] infection, primary diagnosis, department, and comorbidities) were added to the regression model one by one. Covariates with a significant impact, a difference of >10% on the beta coefficient, or those with an assumed effect were included in the final model, because the sample size was sufficient. For all statistical tests, a two-tailed $P < 0.05$ was considered to be statistically significant. All data were analyzed with the software package SPSS (version 25, IBM Corp.).[11] Sample size calculation is described in the article about this cohort study.[4]

RESULTS

Patient Characteristics

Of the 637 patients in the study, 63 were excluded because of missing data of the GLIM criteria (n = 13) and PG-SGA (n = 50). Therefore, 574 patients were included in the analysis, of whom 48% were male, with a mean age of 59.5 ± 16.4 years (Table 1). The MUST score indicated that 145 (25%) patients were at risk for malnutrition. Furthermore, 58% of the malnourished patients according to PG-SGA were not malnourished according to MUST compared with 19% according to the GLIM criteria (Table 1).

Concurrent Validity

The prevalence of malnutrition was 28% using the GLIM criteria and 30% using PG-SGA. When compared with PG-SGA, malnutrition according to the GLIM criteria had a sensitivity of 43% and a specificity of 79%, which is lower than the required 80%. There was a low agreement between the GLIM criteria and PG-SGA in diagnosing malnutrition (κ = 0.22, $P = 0.00$). This indicates that the two methods do not identify the same patients, as is shown in Figure 1. There was an overlap of 77 patients, but 95 patients were not malnourished according to GLIM criteria, and 83 patients were not malnourished according to PG-SGA.

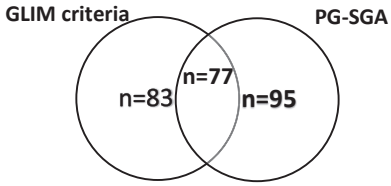

Figure 1. Overlap of malnourished patients between the GLIM[a] criteria (n = 160) and PG-SGA[b] (n = 172) for 574 hospitalized patients included in a post hoc analysis on the validity and feasibility of the GLIM criteria compared with PG-SGA. [a]GLIM = Global Leadership Initiative on Malnutrition. [b]PG-SGA = Patient-Generated Subjective Global Assessment.

Predictive Validity

Overall, 34 of 574 patients (6%) died during a mean follow-up period of 350 days. Based on the GLIM criteria and PG-SGA, significantly fewer malnourished patient were alive 1 year after admission compared with their non-malnourished counterparts (88% vs 97%, 90% vs 96%, $P < 0.01$). The 1-year mortality of malnourished patients was more than two times higher than non-malnourished patients after adjusting for age, department, and planned or emergency admission (unadjusted hazard ratio [HR], 3.89, 1.96–7.70; adjusted HR, 2.68, 1.33–5.41) (Fig 2A). However, malnutrition according to PG-SGA was not significantly associated with 1-year mortality after adjusting for age, department, and planned or emergency admission (unadjusted HR, 2.40, 1.23–4.71; adjusted HR, 1.36, 0.65–2.83) (Fig 2B).

Feasibility

For phenotypic criteria, unintentional weight loss occurred in 69% of the malnourished patients and in 2% of the non-malnourished. Reduced muscle mass occurred in 18% of the malnourished patients and in 1% of the non-malnourished. For the etiologic criteria, 59% of the malnourished and 40% of the non-malnourished patients scored on the disease burden item. Data on muscle mass using bioimpedance analysis was missing in 454 of 574 (79%) patients because of an abnormal hydration status and patients not having fasted at least 8 hours before the measurement. The combinations of criteria on which the diagnosis was based can be found in Table 2.

DISCUSSION

Twenty-eight percent of patients were malnourished based on the diagnostic GLIM criteria for malnutrition and 30% based on PG-SGA. When compared with PG-SGA, the GLIM criteria had a sensitivity of 43%, specificity of 79%, and a low agreement ($\kappa = 0.22$). One-year mortality of malnourished patients was more than two times higher than non-malnourished patients according to the GLIM criteria, but no association with mortality was found for malnutrition according to PG-SGA. Reduced muscle mass, necessary for the GLIM criteria, was missing in 79% of the patients.

The low agreement between the GLIM criteria and PG-SGA indicates that the two methods do not identify the same patients. This is supported by the finding that the GLIM criteria seem to have better predictive power for mortality than PG-SGA. This discrepancy might be attributable to several differences between PG-SGA and the GLIM criteria. First, PG-SGA includes nutrition-related symptoms as part of the diagnosis and a subjective judgment of body composition. The latter suggests that the assessment can be influenced by the assessor, unlike the GLIM criteria that are developed as an objective tool. Second, the time frame used for unintentional weight loss is 1 month in PG-SGA and within or beyond 6 months in the GLIM criteria. Third, the diagnosis of PG-SGA is based on a continuous score of all components together, whereas the GLIM criteria result in a dichotomous outcome. Finally, the weighing of each component summing up to the total score is different in PG-SGA, whereas each component in the GLIM criteria has the same contribution. For example, disease burden in PG-SGA is scored as 1 point per disease or risk factor, which could inflate the total score diagnosing patients as malnourished based on this item alone.

The GLIM criteria suggest that unintentional weight loss, low BMI, and reduced muscle mass can be used interchangeably whenever these occur in combination with an

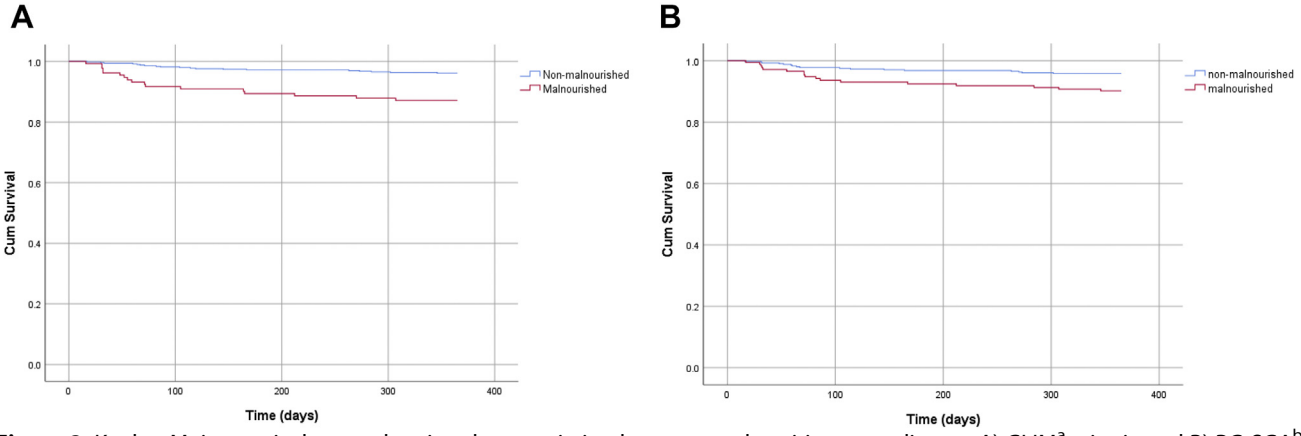

Figure 2. Kaplan-Meier survival curve showing the association between malnutrition according to: A) GLIM[a] criteria and B) PG-SGA[b] and 1-year survival of 574 hospitalized patients included in a post hoc analysis on the validity and feasibility of the GLIM criteria compared to PG-SGA. [a]GLIM = Global Leadership Initiative on Malnutrition. [b]PG-SGA = Patient-Generated Subjective Global Assessment.

Table 2. Presence of GLIM phenotypic and etiologic criteria[a,b,5] in malnourished patients in a post hoc analysis on the validity and feasibility of the GLIM criteria compared with PG-SGA[c] (n = 160)

	Etiologic Criteria, n (%)		
Phenotypic criteria, n (%)	Reduced food intake[d]	Disease burden[e]	Reduced food intake and disease burden
Weight loss[f]	5 (3)	26 (16)	51 (32)
Low BMI[g]	3 (2)	17 (11)	7 (4)
Reduced muscle mass[h]	1 (0.6)	8 (5)	7 (4)
Weight loss and low BMI	0	9 (6)	9 (6)
Weight loss and reduced muscle mass	0	0	4 (2.5)
Low BMI and reduced muscle mass	1 (0.6)	6 (4)	1 (0.6)
Weight loss and low BMI and reduced muscle mass	0	1 (0.6)	4 (2.5)

[a]According to the GLIM definition, malnutrition is diagnosed when at least one phenotypic and one etiologic criterion are present.
[b]GLIM = Global Leadership Initiative on Malnutrition.
[c]PG-SGA = Patient-Generated Subjective Global Assessment.
[d]Reduced food intake was assessed by asking patients whether their food intake was changed during the past month; no missing data.
[e]Disease burden was categorized as an emergency case, oncological, infectious disease at baseline, or any other disease burden or chronic inflammation-related condition in the medical history; no missing data.
[f]Weight loss was defined as 5%–10% weight loss during the past 3–6 months; no missing data.
[g]BMI = body mass index; low BMI was defined as a BMI < 20 for patients younger than 70 years or <22 for patients older than 70 years; no missing data.
[h]Muscle mass was measured using bioimpedance analysis (BIA), and reduced muscle mass was defined as <17 kg/m^2 for men and <15 kg/m^2 for women. Missing in 111/160 malnourished patients.

etiological criterion. Data on muscle mass was present in only 21% of patients because of practical problems with the assessment of BIA. This was mostly caused by an abnormal hydration status and patients not having fasted at least 8 hours before the measurement, both of which are important prerequisites for reliable data.[12,13] This abnormal hydration status is also present in most critically ill patients, which emphasizes the need for consensus for the diagnosis of malnutrition in this patient group.[14] Besides BIA, other validated body composition measures, such as dual-energy absorptiometry, ultrasound, computed tomography, or magnetic resonance imaging, can be used, but these are not used for medical care in many clinical settings.[1] However, the importance of assessing FFMI in the diagnosis of malnutrition has been described because of its association with mortality rates, the additional value in obese patients, and its role in the assessment of sarcopenia.[15-17] In comparison, the American Society for Parenteral and Enteral Nutrition proposed to identify two or more of the following characteristics: insufficient energy intake, weight loss, loss of muscle mass, loss of subcutaneous fat, localized or generalized fluid accumulation, or diminished functional status as measured by handgrip strength.[18] Also, more simple methods such as calf or arm muscle circumference can serve as alternatives until more validated composition measures become widely available. The findings from this study might contribute to the discussion on the feasibility of assessing FFMI.

This is one of the first studies reporting on both the validity and the feasibility of the GLIM criteria. Feedback and recommendations for optimizing the criteria were provided, because it is important that these criteria are easy to perform in both clinical and research settings to obtain global adoption. A limitation of this study is the relatively high number of missing data on FFMI because of the complexity of assessing BIA measurements in a clinical setting. This indicates a concern with regard to the feasibility of using the GLIM criteria in clinical practice. Given the large amount of missing FFMI data, some malnourished patients may not have been identified, and the prevalence of malnutrition might actually have been higher. However, likely the number of additional patients with reduced muscle mass but without weight loss or low BMI is minimal, considering that only 16 of 120 patients that had BIA measured had reduced muscle mass without weight loss or low BMI and that weight loss and low BMI are usually present in malnutrition. Also, the study population might be somewhat healthier compared with the general hospital population because of the exclusion of patients on tube or parenteral feeding and the relatively low age with a relatively low malnutrition prevalence.

CONCLUSIONS

Agreement between GLIM criteria and PG-SGA was low when diagnosing malnutrition, indicating that the two methods do not identify the same patients. This is supported by the GLIM criteria showing predictive power for 1-year mortality in hospitalized patients in contrast to PG-SGA. The assessment of muscle mass using bioimpedance analysis was difficult to perform in this clinical population.

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AUTHOR INFORMATION

V. IJmker-Hemink is a PhD student, Department of Gastroenterology and Hepatology—Dietetics and Intestinal Failure, Radboud University Medical Centre, Nijmegen, The Netherlands. S. Heerschop is a research intern, Department of Gastroenterology and Hepatology—Dietetics and Intestinal Failure, Radboud University Medical Centre, Nijmegen, The Netherlands. G. Wanten is a gastroenterologist and assistant professor, Department of Gastroenterology and Hepatology, Radboudumc, Nijmegen, The Netherlands. M. van den Berg is a research dietitian, Department of Gastroenterology and Hepatology—Dietetics and Intestinal Failure, Radboud University Medical Centre, Nijmegen, The Netherlands.

Address correspondence to: Vera IJmker-Hemink, MSc, Department of Gastroenterology and Hepatology—Dietetics and Intestinal Failure, Radboud University Nijmegen Medical Center, PO Box 9101, 6500 HB Nijmegen, The Netherlands. E-mail: Vera.IJmkerHemink@radboudumc.nl

STATEMENT OF POTENTIAL CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

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AUTHOR CONTRIBUTIONS

VIJ, SH, and MB designed the structure of the article; VIJ and SH wrote the first draft. All authors reviewed and commented on subsequent drafts of the manuscript).