



## Original article

# Prognostic implications of the global leadership initiative on malnutrition criteria as a routine assessment modality for malnutrition in hospitalized patients at a university hospital



Naoharu Mori <sup>a,\*</sup>, Keisuke Maeda <sup>a,b</sup>, Yasushi Fujimoto <sup>c</sup>, Tomoyuki Nonogaki <sup>a,d</sup>, Yuria Ishida <sup>a,e</sup>, Rie Ohta <sup>e</sup>, Akio Shimizu <sup>a,f</sup>, Junko Ueshima <sup>a,g</sup>, Ayano Nagano <sup>a,h</sup>, Ryoji Fukushima <sup>i</sup>

<sup>a</sup> Department of Palliative and Supportive Medicine, Graduate School of Medicine, Aichi Medical University, Nagakute, Aichi, Japan

<sup>b</sup> Department of Geriatric Medicine, Hospital, National Center for Geriatrics and Gerontology, Obu, Aichi, Japan

<sup>c</sup> Department of Otorhinolaryngology and Head and Neck Surgery, Aichi Medical University, Nagakute, Aichi, Japan

<sup>d</sup> Department of Pharmacy, Aichi Medical University Hospital, Nagakute, Aichi, Japan

<sup>e</sup> Department of Nutrition, Aichi Medical University Hospital, Nagakute, Aichi, Japan

<sup>f</sup> Department of Health Science, Faculty of Health and Human Development, University of Nagano, Nagano City, Nagano, Japan

<sup>g</sup> Department of Clinical Nutrition and Food Services, NTT Medical Center Tokyo, Shinagawa-ku, Tokyo, Japan

<sup>h</sup> Department of Nursing, Nishinomiya Kyoritsu Neurosurgical Hospital, Nishinomiya, Japan

<sup>i</sup> Department of Surgery, Teikyo University School of Medicine/Health and Dietetics Teikyo Heisei University, Tokyo, Japan

## ARTICLE INFO

## Article history:

Received 6 April 2022

Accepted 11 December 2022

## Keywords:

GLIM

Malnutrition

Nutritional assessment

Cachexia

Disease related malnutrition

Calf circumference

## SUMMARY

**Background & aims:** Few studies have examined the association between mortality and malnutrition diagnosed using the Global Leadership Initiative on Malnutrition (GLIM) criteria for routine nutritional assessment; thus, this association is not well known. We aimed to clarify the association between GLIM-defined malnutrition and mortality in a large population of hospitalized patients.

**Methods:** In this retrospective cohort study, we enrolled adult patients admitted to Aichi Medical University Hospital between April 2019 and March 2021, who underwent nutritional assessment using the GLIM criteria. In November 2021, we collected the following data from electronic medical records: demographic, clinical, and laboratory data upon admission; nutritional data assessed using GLIM criteria; and data on final patient outcomes.

**Results:** In this study, we included 9372 hospitalized patients who were identified to be at risk by the validated nutritional screening tools (50.6% men, median age 75.0 [67.0–82.0] years, 69.2% patients aged  $\geq 70$  years). The number of patients with no, moderate, and severe GLIM-defined malnutrition was 4145 (44.2%), 2799 (29.9%), and 2428 (25.9%), respectively. Kaplan–Meier survival curve analysis showed a significant increase in mortality with worsening nutritional status (log-rank test,  $P < 0.001$ ). After adjusting for age and sex, multivariable Cox regression analysis revealed that both moderate (Hazard ratio [HR] 2.0, 95% confidence interval [CI] 1.79–2.23,  $P < 0.001$ ) and severe malnutrition (HR 3.06, 95% CI 2.74–3.40,  $P < 0.001$ ) were independent risk factors for mortality. Moreover, multivariable analysis showed that four of the five GLIM sub-criteria (except low body mass index) were independently associated with prognosis.

**Conclusion:** Malnutrition and its severity, routinely assessed using the GLIM criteria, are associated with high mortality in hospitalized patients at nutritional risk. Further research is needed to evaluate the usefulness of the GLIM sub-criteria, including low body mass index, in these patients.

© 2022 The Author(s). Published by Elsevier Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

\* Corresponding author. Palliative Care Center, Aichi Medical University, 1-1 Yazakokarimata, Nagakute, Aichi 480-1195, Japan.

E-mail address: [nmori@aichi-med-u.ac.jp](mailto:nmori@aichi-med-u.ac.jp) (N. Mori).

## 1. Introduction

Malnutrition results from a combination of varying degrees of nutritional deficiencies and inflammatory activity, leading to

changes in body composition and decreased function [1,2]. It is associated with increased complication rates, longer hospital stays, increased mortality, higher costs, and increased readmission rates [3,4]. In addition, hospitalized patients often experience further deterioration of nutritional status after admission [5]. Therefore, it is increasingly being considered important to perform early screening and appropriate nutritional assessments in patients at risk of malnutrition [2,6].

With the recognition of the importance of nutritional assessment, several diagnostic criteria for malnutrition have been published [1,7]; although, none of them are hitherto well-established. The Global Leadership Initiative on Malnutrition (GLIM) criteria have been newly developed by representatives of the world's leading clinical nutrition societies [8]. In diagnosing malnutrition using the GLIM criteria, the first step is to identify patients at risk for malnutrition using a validated nutritional screening tool. Nutritional assessment is then performed to diagnose malnutrition and determine its severity [8]. At the time of publication of the GLIM criteria, several measurable criteria did not have established reference values. For example, no reference values were available for body mass index (BMI) in grading the severity of malnutrition among Asians, and thus, we previously conducted a study to establish BMI cutoff values in hospitalized patients, shortly after the publication of the GLIM criteria [9]. Owing to the necessity of validating the GLIM criteria on a global scale [8,10], validation studies are being conducted in various healthcare facilities and on various patient populations; these validation studies range from prospective studies to retrospective analyses using existing nutritional data. However, at present, the findings of these validation studies are insufficient [11].

The GLIM criteria are primarily used in hospitalized patients at high risk for disease-related malnutrition. Nevertheless, most validation studies of the GLIM criteria have been conducted in patients with specific diseases or elderly patients, and few studies have been conducted on the general hospitalized patient population in acute-care hospitals [11]. In addition, no study has validated the outcome of malnutrition using the GLIM criteria as a routine nutritional assessment for hospitalized patients, and the association between GLIM-defined malnutrition and mortality in these patients remains unknown. Therefore, the main objective of this study was to determine the association between malnutrition, diagnosed using the GLIM criteria as a routine nutritional assessment, its severity, and overall survival. The secondary objective was to identify the effect of each GLIM criterion on mortality.

## 2. Materials & methods

### 2.1. Participants

This retrospective cohort study included adult patients aged  $\geq 18$  years who were admitted to the Aichi Medical University Hospital between April 2019 and March 2021. The study site was a 900-bed, acute-care university hospital. All newly admitted patients were screened for malnutrition on admission in accordance with the Japanese health insurance system's regulations for basic hospitalization charges. Nutrition screening was performed using the Malnutrition Universal Screening Tool (MUST) [12] and Mini-Nutritional Assessment-Short Form (MNA-SF) [13] for young and elderly patients, respectively. Patients with a MUST score  $\geq 2$  were considered at risk for malnutrition and required referral to a nutrition support team (NST) [12]; an MNA-SF score  $\leq 11$  was also recognized as a criterion for subsequent nutritional assessment [13]. Nutritional assessment by the NST was conducted within 5 days of admission of patients at nutritional risk. Under the Japanese health insurance system, when an NST, comprising a qualified physician, nurse, pharmacist, and dietitian, works to improve the

nutritional status of malnourished patients or patients at high risk of malnutrition in an acute care ward, the team can obtain 200 points (about 14 USD) per patient per week in reimbursement (named "Additional Medical Fee for the Nutrition Support Team Activity"). The NST in the study hospital comprised four qualified professionals and conducted nutrition assessments. Therefore, the patients in this study were eligible for the additional medical fee. The NST visited all patients at nutritional risk and attempted to perform the nutritional assessment. However, during several NST visits, patients were often absent owing to engagement in other medical procedures or other reasons, and about one-third of the patients were discharged without a nutritional assessment, with a short stay in an acute care hospital. The exclusion criteria for cases with nutritional assessment in this study were missing nutritional assessment data related to GLIM criteria, including height and weight. This study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Review Committee of Aichi Medical University Hospital (No. 2021–136). Owing to the retrospective nature of the study, written informed consent could not be obtained. However, the participants were guaranteed the right to withdraw from the study through an opt-out procedure by posting a notice on the hospital's website.

### 2.2. Data collection

Data were obtained retrospectively from the patients' medical records. The variables collected included age, sex, height, weight, BMI, calf circumference (CC), hemoglobin levels, serum albumin levels, C-reactive protein (CRP) levels, MUST score, MNA-SF score, malnutrition diagnosed using the GLIM criteria and sub-criteria, length of hospital stay, patient status on discharge (alive or dead), and final outcome as documented in the electronic medical record at the end of November 2021. The GLIM sub-criteria included phenotypic criteria, such as weight loss, low BMI, and reduced muscle mass, as well as etiologic criteria, such as reduced food intake or assimilation and disease burden/inflammation.

### 2.3. GLIM criteria

The GLIM criteria consist of three phenotypic and two etiologic criteria; at least one phenotypic and one etiologic criterion are required for the diagnosis of malnutrition [8]. Table 1 shows the parameters of the GLIM criteria and their thresholds used in the present study. To evaluate weight loss, participants were asked to self-report their weight change over the past 3–6 months. BMI was calculated as body weight (kg) divided by the square of the patient height (m). Reduced muscle mass was determined based on the CC (cm) of the right leg, with the patient in the supine position with 90° knee flexion. In this study, we used the validated reduced muscle mass cutoff values of CC for Japanese patients (30 cm in men and 29 cm in women), as previously reported [9,14]. The criterion for reduced food intake or assimilation was determined by interviewing the patient during the nutrition assessment visit and checking the patient's medical record, and if the reduction in oral intake exceeding 50% of the energy requirement lasted more than one week, any reduction exceeding two weeks, or if the patient had a chronic gastrointestinal condition that adversely affects food assimilation or absorption, such as short bowel syndrome, pancreatic insufficiency, esophageal strictures, gastroparesis or chronic diarrhea, was determined to be applicable. Disease burden/inflammation criterion was defined as the presence of acute inflammatory diseases, such as major infection; burns; trauma or closed head injury; comorbidity of chronic or recurrent mild to moderate inflammation, such as malignant disease, chronic obstructive pulmonary disease, congestive heart failure, chronic renal disease, or C-

**Table 1**  
Parameters of the GLIM criteria and their thresholds used in the present study.

Grade	Phenotypic criteria			Etiologic criteria	
	Non-volitional weight loss	Low BMI	Reduced muscle mass	Reduced food intake or assimilation	Disease burden/inflammation
Moderate malnutrition	5%–10% within the past 6 months, or 10%–20% beyond 6 months	BMI <18.5 kg/m <sup>2</sup> for age <70 years, BMI <20 kg/m <sup>2</sup> for age ≥70 years	CC < 30.0 cm for men, CC < 29.0 cm for women	50% of energy requirements >1 week or any reduction in energy requirement for >2 weeks	Acute disease/injury or Chronic inflammatory disease or CRP level >5 mg/L
Severe malnutrition	>10% within the past 6 months, or >20% beyond 6 months	BMI <17.0 kg/m <sup>2</sup> for age <70 years, BMI <17.8 kg/m <sup>2</sup> for age ≥70 years	CC < 27.0 cm for men, CC < 26.0 cm for women	any chronic gastrointestinal condition that adversely impacts food assimilation or absorption	

GLIM, The Global Leadership Initiative on Malnutrition; BMI, body mass index; CC, calf circumference; CRP, C-reactive protein.

reactive protein levels >5 mg/L. For patients diagnosed with malnutrition, three phenotypic criteria were used to assess the severity of malnutrition, in accordance with the diagnostic flow of the GLIM criteria [8]: (i) weight loss >10%, (ii) severely low BMI, or (iii) a severe deficit in muscle mass. The GLIM criteria do not provide specific cutoff values for BMI that distinguish between moderate and severe malnutrition in Asians [8]. We identified and used 17.0 and 17.8 kg/m<sup>2</sup> as cutoff values for severely low BMI in the younger and older adult populations, respectively, as previously reported in our institution [9]. Additionally, specific reference values for CC, which assesses severe loss of muscle mass, are not provided in the GLIM criteria. In our institution, the CC values indicating severe muscle mass loss were defined as < 27 cm for men and <26 cm for women; these values are >10% lower than the corresponding values indicating muscle mass loss in the sarcopenia diagnostic criteria [9]. Using these cutoff values, we conducted a study in our institution to investigate the prevalence of GLIM-defined malnutrition that showed similar frequencies of patients with severely reduced muscle mass and other phenotypic criteria [9]. Therefore, these values were considered reasonable as cutoff values for severely reduced muscle mass and continued to be employed.

#### 2.4. Statistical analysis

Continuous data are presented as medians [interquartile ranges] and categorical data as numbers and percentages. Differences in continuous variables were analyzed using the Mann–Whitney U test. Categorical data were expressed as numbers and percentages, and differences were analyzed using the chi-square test. Multi-group comparisons were performed using the Bonferroni method. Kaplan–Meier survival curves were used to evaluate malnutrition-related mortality. Differences were confirmed using the log-rank test, followed by crude and adjusted Cox regression analysis. Age and sex, which are clinical factors that are not included in the GLIM criteria and sub-criteria, were included as covariates in the Cox regression model. Age was stratified (<70 or ≥ 70 years) according to the characteristics of the GLIM criteria. Multivariable analysis was also performed to identify the effect of each GLIM criterion on mortality, and hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated. For all statistical tests, a *p*-value <0.05 was considered statistically significant. All statistical analyses were performed using R (version 4.0.4; The R Foundation for Statistical Computing, Vienna, Austria).

### 3. Results

During the study period, 14,934 patients were found to be at risk for malnutrition via nutritional screening performed on admission.

Nutritional assessment was performed by the nutrition support team in 9520 patients. We included 9372 patients in the final analysis, after excluding patients who did not undergo nutritional assessment using the GLIM criteria or who did not have related documented data. Of these, 50.6% (*n* = 4746) were men. The median age of the patients was 75.0 [67.0–82.0] years, and 69.2% (*n* = 6485) of patients were aged ≥70 years. Major reasons for hospital admission, based on the ICD-10, were neoplasms (*n* = 2604, 27.8%) as well as cardiovascular (*n* = 1403, 15.0%), digestive (*n* = 1275, 13.6%), and respiratory (*n* = 842, 9.0%) diseases.

Table 2 shows the characteristics of patients by GLIM-defined nutritional status. The number of patients with no, moderate, and severe malnutrition was 4145 (44.2%), 2799 (29.9%), and 2428 (25.9%), respectively. Compared with patients without malnutrition, those with moderate and severe malnutrition were older; predominantly women; had significantly lower BMIs, CCs, and hemoglobin levels; and had higher CRP levels.

In-hospital mortality increased with worsening nutritional status (*P* < 0.001); the mortality rates were 2.1%, 4.9%, and 9.2% for patients with no, moderate, and severe malnutrition, respectively. During the follow-up period, 2085 patients (22.2%) were confirmed dead. The median observation period for surviving patients was 345 [72–599] days. The Kaplan–Meier survival curves shown in Fig. 1 differed significantly by GLIM-defined nutritional status (log-rank test; *P* < 0.001). The 1-year survival rates for patients with no, moderate, and severe malnutrition were 85.9% (95% CI, 84.6–87.1), 72.6% (95% CI, 70.6–74.4), and 62.1% (95% CI, 59.8–64.4), respectively; moreover, the 2-year survival rates were 78.1% (95% CI, 46.2–79.9), 63.8% (95% CI, 61.3–66.2), and 51.5% (95% CI, 48.6–54.2), respectively.

Table 3 shows the results of the Cox regression analysis of the relationship between GLIM-defined malnutrition and mortality. After adjusting for age and sex, multivariable Cox regression analysis showed that both moderate (HR 2.0, 95% CI 1.79–2.23, *P* < 0.001) and severe malnutrition (HR 3.06, 95% CI 2.74–3.40, *P* < 0.001) were independent risk factors for mortality.

Table 4 shows the results of the Cox regression analysis for mortality associated with six combinations of three phenotypic and two etiologic criteria. After adjusting for age, all six combinations were associated with mortality.

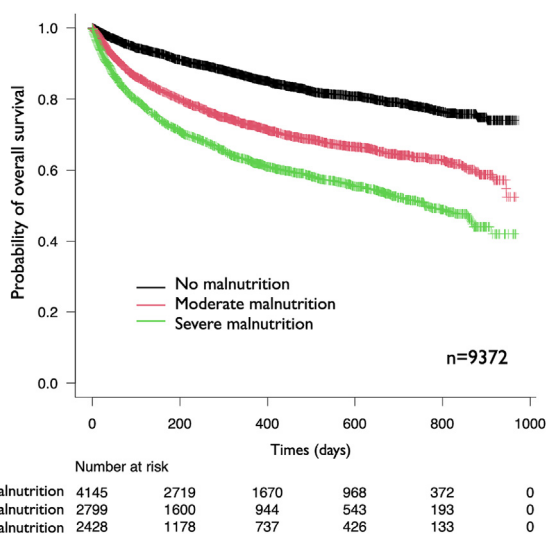
Results of the multivariable analysis of the relationship between each GLIM sub-criterion and mortality are presented in Supplementary Table S1. After adjusting for age, four sub-criteria (except low BMI) were independently associated with mortality. The disease burden/inflammation criterion showed the highest HR among all sub-criteria (HR 4.32, 95% CI 3.65–5.12).

Figure 2 shows Kaplan–Meier curves for the nutritional status for different age groups. The median age of patients aged <70 years

**Table 2**  
Characteristics of patients classified based on the GLIM criteria.

	No malnutrition n = 4145	Moderate malnutrition n = 2799	Severe malnutrition n = 2428	P-value
Age, years median [IQR]	73.0 [65.0–80.0]	76.0 [68.0–82.0]	77.0 [69.0–84.0]	<0.001
Age ≥70 years, n (%)	2652 (64.0)	2016 (72.0)	1817 (74.8)	<0.001
Men, n (%)	2202 (53.1)	1390 (49.7)	1154 (47.5)	<0.001
Body mass index, kg/m <sup>2</sup> , median [IQR]	21.9 [19.8–24.2]	19.5 [18.3–21.4]	17.2 [16.0–19.1]	<0.001
Calf circumference, cm, median [IQR]				
Men	33.0 [31.1–35.0]	29.8 [28.5–31.8]	27.0 [25.0–29.6]	<0.001
Women	31.2 [29.7–33.2]	28.7 [27.4–30.6]	26.0 [24.0–28.2]	<0.001
Hemoglobin level, g/dL, median [IQR]	12.4 [10.8–13.7]	11.4 [9.8–12.9]	11.0 [9.5–12.3]	<0.001
Albumin level, g/dL, median [IQR]	3.6 [3.2–4.1]	3.4 [2.9–3.8]	3.2 [2.7–3.7]	<0.001
C-reactive protein level, mg/L, median [IQR]	3.8 [1.0–34.4]	13.3 [2.3–57.7]	15.4 [2.7–57.2]	<0.001

GLIM, The Global Leadership Initiative on Malnutrition; IQR, interquartile range.



**Fig. 1.** Kaplan–Meier curves for overall survival based on GLIM-defined nutritional status. GLIM, Global Leadership Initiative on Malnutrition.

was 57.0 [44.0–66.0] years, and the median age of patients aged ≥70 years was 79.0 [74.0–84.0] years. Patients aged <70 years and ≥70 years showed increased mortality with an increase in malnutrition severity. Based on the Cox regression analysis findings, the HRs for moderate and severe malnutrition were 2.0 (95% CI 1.52–2.66) and 3.97 (95% CI 3.17–4.97), respectively, in patients <70 years, and 1.73 (95% CI 1.52–1.96) and 2.70 (95% CI 2.39–3.05), respectively, in patients ≥70 years.

Supplementary Table S2 shows the frequency of phenotypic and etiologic criteria in patients with different GLIM-defined nutritional statuses. The frequency of each sub-criterion increased with worsening nutritional status. Cancer was found to impose the highest disease burden in all the different nutritional status categories, followed by chronic kidney disease (CKD), congestive heart failure, and major infections.

**Table 3**  
Cox regression analysis of the association between GLIM-defined malnutrition and mortality.

	Univariable analysis			Multivariable analysis		
	HR	95% CI	P-value	HR	95% CI	P-value
Age ≥70 years	1.56	1.41–1.73	<0.001	1.41	1.27–1.56	<0.001
Sex, Male	1.38	1.26–1.50	<0.001	1.41	1.29–1.54	<0.001
GLIM-defined malnutrition						
No malnutrition	1.00 (reference)			1.00 (reference)		
Moderate malnutrition	2.02	1.81–2.26	<0.001	2.00	1.79–2.23	<0.001
Severe malnutrition	3.04	2.73–3.39	<0.001	3.06	2.74–3.40	<0.001

GLIM, The Global Leadership Initiative on Malnutrition; HR, hazard ratio; CI, confidence interval.

**Table 4**  
Cox regression analysis of each combination of GLIM sub-criteria for mortality.

Factors	HR	95% CI	P-value
<b>Non-volitional weight loss</b>			
+Reduced food intake/Assimilation	2.10	1.89–2.32	<0.001
+Disease burden/Inflammation	2.27	2.08–2.48	<0.001
<b>Low body mass index</b>			
+Reduced food intake/Assimilation	1.88	1.71–2.07	<0.001
+Disease burden/Inflammation	1.86	1.71–2.03	<0.001
<b>Reduced muscle mass</b>			
+Reduced food intake/Assimilation	2.30	2.10–2.52	<0.001
+Disease burden/Inflammation	2.35	2.15–2.56	<0.001

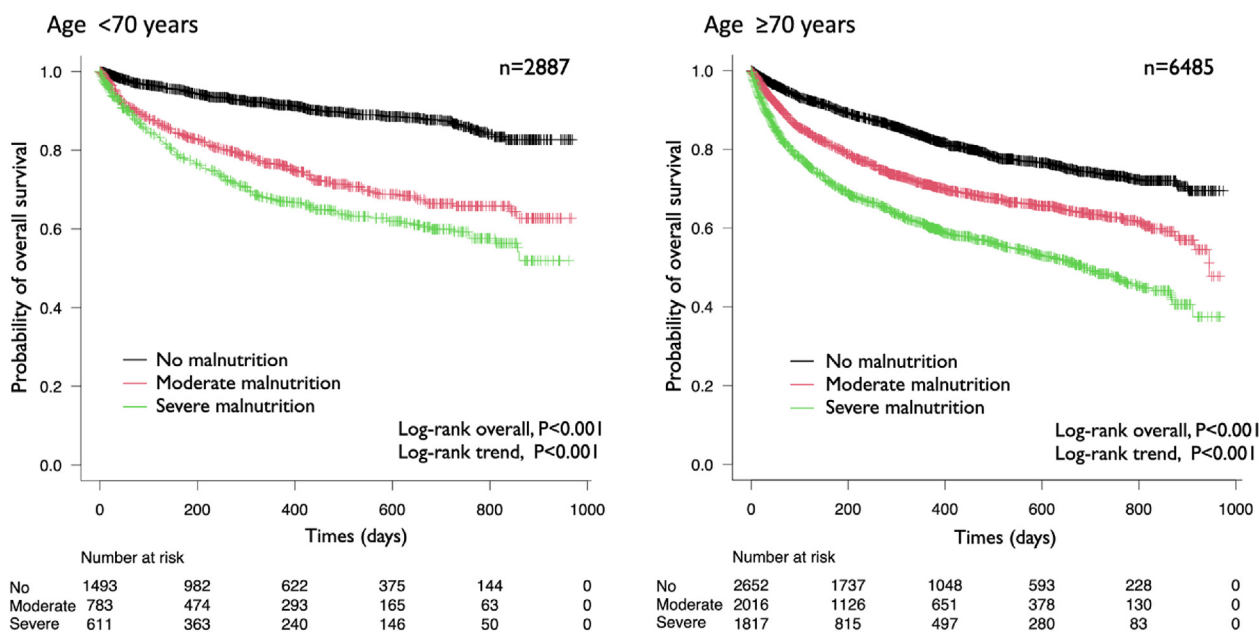
Each combination of GLIM sub-criteria was adjusted for age group (≥70 or <70 years).

GLIM, The Global Leadership Initiative on Malnutrition; HR, hazard ratio; CI, confidence interval.

Supplementary Fig. S1 shows Kaplan–Meier curves for the abovementioned four conditions having the highest disease burdens. In all disease subgroups, mortality tended to worsen with worsening GLIM-defined nutritional status (all log-rank trend tests, P < 0.001).

#### 4. Discussion

In this study, we examined participant nutritional status and its association with all-cause mortality in a university hospital that uses the GLIM criteria as a routine nutritional assessment modality for the diagnosis of malnutrition in hospitalized patients with nutritional risks; we obtained the following findings. First, GLIM-defined malnutrition was associated with high mortality in hospitalized patients, and the mortality increased with the severity of malnutrition. Second, of the three phenotypic criteria and two etiologic criteria used in the GLIM criteria, four criteria (except low BMI) were independently associated with mortality. A trend toward an increase in mortality with the severity of GLIM-defined malnutrition was observed in different age groups and patients with conditions constituting major burden diseases. Although this



**Fig. 2. Kaplan–Meier curves based on GLIM-defined nutritional status for different age groups.** P values for overall log-rank tests examine whether the three different Kaplan–Meier curves differ. P values for log-rank trend tests examine whether increased severity of malnutrition is associated with worsening of overall survival. GLIM, Global Leadership Initiative on Malnutrition.

was a retrospective cohort study, the assessment of the three phenotypic and two etiologic GLIM sub-criteria and the diagnosis of malnutrition based on these sub-criteria were performed by the nutrition support team at admission. Therefore, data on the assessment of nutritional status and the presence of each sub-criterion were available in the medical records, unlike in many other large-scale retrospective studies wherein the GLIM criteria were retrospectively applied for malnutrition diagnosis. To the best of our knowledge, this is the first study to examine the association between nutritional status and all-cause mortality in a large sample population, using the GLIM criteria for routine nutritional assessment.

GLIM-defined malnutrition was associated with high mortality in hospitalized patients, and the mortality increased with malnutrition severity. Compared with nutritionally at-risk patients without malnutrition, the HRs for mortality were approximately twice and thrice as high as those of patients with moderate and severe malnutrition, respectively. The association between GLIM-defined malnutrition and mortality in the general adult population in acute-care hospitals was examined in four previous studies. In a prospective cohort study of 601 adult hospitalized patients, Brito et al. reported that GLIM-defined malnutrition was associated with a 5.1-fold increased risk of in-hospital mortality and high 6-month mortality [15]. Moreover, Martín et al., in a prospective observational study of 1015 adult patients admitted to the general ward of a university hospital, reported that in-hospital mortality increased with the severity of GLIM-defined malnutrition [16]. In addition, Ijmker-Hemink et al. conducted a post hoc analysis of a prospective cohort study of 574 patients admitted in an academic hospital and found that GLIM-defined malnutrition showed good predictive power for 1-year mortality [17]. Furthermore, Balci et al., in a retrospective analysis of 231 patients admitted to a medical or surgical ward, showed that moderate or severe GLIM-defined malnutrition effectively predicted 5-year mortality [18]. These previous study findings corroborated with our findings that GLIM-defined malnutrition was associated with worse prognosis in hospitalized patients. Our study revealed the abovementioned

association in a larger sample population and over a relatively longer observation period for adult hospitalized patients with nutritional risks; we also demonstrated the association between the severity of malnutrition and mortality in hospitalized patients.

The effects on mortality associated with the six combinations of three phenotypic and two etiologic criteria used to diagnose malnutrition in GLIM generally did not appear to be markedly different, although the two with low BMI had slightly lower hazard ratios. Contrarily, in examining the association of each of the five sub-criteria with mortality, with the exception of low BMI, the four GLIM sub-criteria of non-volitional weight loss, loss of muscle mass, decreased food intake/assimilation, and disease burden/inflammation were independently associated with mortality. The combination and importance of the GLIM sub-criteria for the diagnosis of malnutrition have not been adequately examined in previous studies [11]. Among the aforementioned studies examining the association between each sub-criterion and mortality in acute-care hospitalized patients, only Martín et al. reported that reduced muscle mass and the presence of inflammation were independently associated with in-hospital mortality [16]. Among the four sub-criteria found to be associated with mortality in our study, disease burden/inflammation was an independent factor with a HR more than twice as high as that of the other sub-criteria. This may suggest the importance of this sub-criterion on the outcome of disease-related malnutrition, which is common in hospitalized patients. In contrast, low BMI was not an independent prognostic factor in our study. Some studies have questioned the adoption of BMI for nutritional diagnosis as it may not reflect muscle mass; therefore, depleted muscle mass may be missed using BMI alone [19]. In recent years, several problems have been encountered with the use of BMI for the diagnosis of malnutrition [20,21]. Chaar et al. recently conducted a single-center prospective study of 121 patients that met the GLIM criteria and reported that the use of low BMI may not be effective in diagnosing malnutrition in a hospital setting [22]. Our findings may also prompt a reconsideration of the use of the low BMI sub-criterion in the diagnosis of malnutrition among hospitalized patients.

GLIM-defined malnutrition was significantly associated with mortality in both younger (<70 years) and older adults ( $\geq 70$  years). Several studies have reported an association between GLIM-defined malnutrition and mortality in older adults. Xu et al. reported that GLIM-defined malnutrition increased the odds of in-hospital mortality in hospitalized patients aged  $\geq 70$  years [23]. Sobestiansky examined 56 geriatric inpatients and reported that GLIM-defined malnutrition was associated with increased 1-year mortality [24]. These findings are generally consistent with our study findings. Nevertheless, to our knowledge, no previous study has investigated mortality-related outcomes in the hospitalized non-elderly adult population, such as those aged under 70 years. We found that malnutrition in hospitalized patients was significantly associated with mortality, even in patients aged <70 years, although HRs differed by age group. The exacerbation of the HR due to malnutrition may have been greater in patients aged <70 years because of the longer life expectancy of non-malnourished patients aged <70 years compared to that of patients aged  $\geq 70$  years.

In a subgroup analysis of patients with cancer, CKD, heart failure (HF), and major infections—the most frequent diseases in the disease burden criteria—a trend toward increased mortality was also observed with worsening GLIM-defined nutritional status. Previous studies have reported the association between GLIM-defined malnutrition and mortality in disease-specific cohorts, especially in patients with cancer, HF, and severe infections, as well as in patients undergoing dialysis [25–29]. Of the four diseases examined in this study, three were classified as chronic wasting diseases and one as acute disease, which clearly demonstrates that the association between GLIM-defined malnutrition and high mortality is maintained in patients with each of these inflammation-inducing diseases.

The present study had several limitations. First, this was a single-center retrospective study; hence, the findings may not be generalizable to patients in different healthcare settings. Second, although the patient prognosis was evaluated over an observation period of  $\geq 6$  months, approximately 20% of the included patients had an actual observation period of <3 months. This is because our study was a large-scale retrospective cohort study, and therefore, it was difficult to contact each patient for prognosis assessment. We took advantage of the characteristics of the study hospital, wherein most inpatients continue to receive follow-up after discharge; thus, we obtained data on patient outcomes from the last medical examination findings available in the electronic medical records. Due to the nature of this study, it was also not possible to retrospectively collect data on the severity of individual cases. Therefore, this study could not be adjusted for disease severity, which may affect mortality. Third, the assessment of skeletal muscle mass was not based on an accurate and reproducible method using validated methods of body composition assessment. The GLIM criteria state that physical measurements, such as the CC measurement employed in this study, are acceptable and feasible in clinical practice [8]. A recent study reviewed the findings of GLIM-related studies and reported that almost half of the tools used for assessing low muscle mass in the literature were based on anthropometry, with CC measurement performed in most of the studies [11]. In the evaluation of muscle mass during routine nutritional assessment, the measurement of CC is more acceptable in clinical practice, and our results may support its usefulness. Finally, one-third of the patients at nutritional risk were discharged without having undergone a nutritional assessment. The NST visited all patients at nutritional risk and attempted to perform the nutritional assessment. However, because the study hospital was an acute care hospital and many patients had a short hospital stay, patients were often not present at the time of the NST visit as they were receiving other medical treatment or due to other reasons, resulting in a nutrition

assessment implementation rate of less than 70%. Therefore, if all cases had undergone nutritional assessment, it could have influenced the outcome.

## 5. Conclusions

We examined the prognostic impact of malnutrition diagnosed using the GLIM criteria as a routine nutritional assessment of a large sample of patients hospitalized in a university hospital; we found that GLIM-defined malnutrition and its severity were associated with a worse prognosis. We found similar trends in patients of different age groups as well as in patients with conditions constituting major disease burdens. Further research is needed to investigate the abovementioned association in different healthcare settings, for the universal standardization of the GLIM criteria for malnutrition diagnosis. In addition, future studies should evaluate the reference values and combinations of each GLIM criterion.

## Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Author contributions

NM, KM, and RF contributed to the conception of the study. YF, YI, RO, NM, and KM contributed to the acquisition of data. NM, KM, AS, JU, and AN contributed to the analysis and interpretation of data. NM, KM, and AS drafted the manuscript. All authors critically revised the manuscript, provided their final approval, and agreed to be accountable for all aspects of the work, ensuring its integrity and accuracy.

## Conflicts of interest

Naoharu Mori: Grants outside the submitted work and speaking honoraria from Daichi Sankyo Co., LTD, Otsuka Pharmaceutical Factory, Inc., Abbott Nutrition and Shionogi & Co., Ltd., and speaking honoraria from Ono Pharmaceutical Co., LTD, and Kyowa Kirin Co., Ltd.

Ryoji Fukushima: Grants outside the submitted work from Ono Pharmaceutical Co., LTD, and Taiho Pharmaceutical Co., LTD, and speaking honoraria from Otsuka Pharmaceutical Factory, Inc., Terumo Corporation, and EA Pharma Co., Ltd.

The other authors declare that they have no conflicts of interest.

## Acknowledgement

The authors wish to express appreciation to the doctors, nurses, pharmacists, and all other professionals working at Aichi Medical University Hospital for all the time and attention they have devoted to our study.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnu.2022.12.008>.

## References

- [1] White JV, Guenter P, Jensen G, Malone A, Schofield M, Academy Malnutrition Work Group, A.S.P.E.N. Board of Directors. Consensus statement of the academy of nutrition and dietetics/American society for parenteral and enteral nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). *J Acad Nutr Diet* 2012;112: 730–8. <https://doi.org/10.1016/j.jand.2012.03.012>.

- [2] Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr* 2017;36:49–64. <https://doi.org/10.1016/j.clnu.2016.09.004>.
- [3] Sorensen J, Kondrup J, Prokopowicz J, Schiesser M, Krähenbühl L, Meier R, et al. EuroOOPS: an international, multicentre study to implement nutritional risk screening and evaluate clinical outcome. *Clin Nutr* 2008;27:340–9. <https://doi.org/10.1016/j.clnu.2008.03.012>.
- [4] Lim SL, Ong KCB, Chan YH, Loke WC, Ferguson M, Daniels L. Malnutrition and its impact on cost of hospitalization, length of stay, readmission and 3-year mortality. *Clin Nutr* 2012;31:345–50. <https://doi.org/10.1016/j.clnu.2011.11.001>.
- [5] Dupertuis YM, Kossovsky MP, Kyle UG, Raguso CA, Genton L, Pichard C. Food intake in 1707 hospitalised patients: a prospective comprehensive hospital survey. *Clin Nutr* 2003;22:115–23. <https://doi.org/10.1054/clnu.2002.0623>.
- [6] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M, Educational and Clinical Practice Committee, European Society of Parenteral and Enteral Nutrition (ESPEN). ESPEN guidelines for nutrition Screening. *Clin Nutr* 2003;22:415–21. [https://doi.org/10.1016/s0261-5614\(03\)00098-0](https://doi.org/10.1016/s0261-5614(03)00098-0).
- [7] Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, et al. Diagnostic criteria for malnutrition – an ESPEN consensus statement. *Clin Nutr* 2015;34:335–40. <https://doi.org/10.1016/j.clnu.2015.03.001>.
- [8] Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition – a consensus report from the global clinical nutrition community. *Clin Nutr* 2019;38:1–9. <https://doi.org/10.1016/j.clnu.2018.08.002>.
- [9] Maeda K, Ishida Y, Nonogaki T, Mori N. Reference body mass index values and the prevalence of malnutrition according to the Global Leadership Initiative on Malnutrition criteria. *Clin Nutr* 2020;39:180–4. <https://doi.org/10.1016/j.clnu.2019.01.011>.
- [10] De van der Schueren MAE, Keller H, Cederholm T, Barazzoni R, Compher C, Correia M, et al. Global Leadership Initiative on Malnutrition (GLIM): guidance on validation of the operational criteria for the diagnosis of protein-energy malnutrition in adults. *Clin Nutr* 2020;39:2872–80. <https://doi.org/10.1016/j.clnu.2019.12.022>.
- [11] Correia MITD, Tappenden KA, Malone A, Prado CM, Evans DC, Sauer AC, et al. Utilization and validation of the global leadership initiative on malnutrition (GLIM): a scoping review. *Clin Nutr* 2022;41:687–97. <https://doi.org/10.1016/j.clnu.2022.01.018>.
- [12] Stratton RJ, Hackston A, Longmore D, Dixon R, Price S, Stroud M, et al. Malnutrition in hospital outpatients and inpatients: prevalence, concurrent validity and ease of use of the ‘malnutrition universal screening tool’ (“MUST”) for adults. *Br J Nutr* 2004;92:799–808. <https://doi.org/10.1079/bjn20041258>.
- [13] Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B. Screening for under-nutrition in geriatric Practice Developing the short-form mini-nutritional assessment (MNA-SF). *Journals Gerontology Ser J Gerontol A Biol Sci Med Sci* 2001;56:M366–72. <https://doi.org/10.1093/gerona/56.6.m366>.
- [14] Maeda K, Koga T, Nasu T, Takaki M, Akagi J. Predictive accuracy of calf circumference measurements to detect decreased skeletal muscle mass and European Society for Clinical Nutrition and Metabolism-defined malnutrition in hospitalized older patients. *Ann Nutr Metab* 2017;71:10–5. <https://doi.org/10.1159/000478707>.
- [15] Brito JE, Burgel CF, Lima J, Chites VS, Saragiotto CB, Rabito EI, et al. GLIM criteria for malnutrition diagnosis of hospitalized patients presents satisfactory criterion validity: a prospective cohort study. *Clin Nutr* 2021;40:4366–72. <https://doi.org/10.1016/j.clnu.2021.01.009>.
- [16] Galindo Martín CA, Aportela Vázquez VA, Becerril Hernández F, Aguilar Medina CR, Ayala Carrillo SL, Chavez Flores A, et al. The GLIM criteria for adult malnutrition and its relation with adverse outcomes, a prospective observational study. *Clin Nutr ESPEN* 2020;38:67–73. <https://doi.org/10.1016/j.clnesp.2020.06.015>.
- [17] Ijmker-Hemink V, Heerschoop S, Wanten G, Berg van den M. 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. *J Acad Nutr Diet* 2022;122:595–601. <https://doi.org/10.1016/j.jand.2021.07.011>.
- [18] Balci C, Bolayir B, Eşme M, Arik G, Kuyumcu ME, Yesil Y, et al. Comparison of the efficacy of the global leadership initiative on malnutrition criteria, subjective global assessment, and nutrition risk screening 2002 in diagnosing malnutrition and predicting 5-year mortality in patients hospitalized for acute illnesses. *JPEN - J Parenter Enter Nutr* 2021;45:1172–80. <https://doi.org/10.1002/jpen.2016>.
- [19] Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, et al. Diagnostic criteria for malnutrition – an ESPEN consensus statement. *Clin Nutr* 2015;34:335–40. <https://doi.org/10.1016/j.clnu.2015.03.001>.
- [20] Barone M. Is the use of the BMI alone sufficient to diagnose malnutrition in both male and female adults? *Clin Nutr* 2018;37:1771. <https://doi.org/10.1016/j.clnu.2018.07.003>.
- [21] Ng WL, Collins PF, Hickling DF, Bell JJ. Evaluating the concurrent validity of body mass index (BMI) in the identification of malnutrition in older hospital inpatients. *Clin Nutr* 2019;38:2417–22. <https://doi.org/10.1016/j.clnu.2018.10.025>.
- [22] Chaar DE, Mattar L, Khoury CFE. AND/ASPEN and the GLIM malnutrition diagnostic criteria have a high degree of criterion validity and reliability for the identification of malnutrition in a hospital setting: a single-center prospective study. *JPEN-Parenter Enter* 2022. <https://doi.org/10.1002/jpen.2347>.
- [23] Xu JY, Zhu MW, Zhang H, Li L, Tang PX, Chen W, et al. A cross-sectional study of GLIM-defined malnutrition based on new validated calf circumference cut-off values and different screening tools in hospitalised patients over 70 years old. *J Nutr Health Aging* 2020;24:832–8. <https://doi.org/10.1007/s12603-020-1386-4>.
- [24] Sobestiansky S, Åberg AC, Cederholm T. Sarcopenia and malnutrition in relation to mortality in hospitalised patients in geriatric care – predictive validity of updated diagnoses. *Clin Nutr ESPEN* 2021;45:442–8. <https://doi.org/10.1016/j.clnesp.2021.07.002>.
- [25] Sánchez-Torralvo FJ, Ruiz-García I, Contreras-Bolívar V, Gonzalez-Almendros I, Ruiz-Vico M, Abuin-Fernandez J, et al. CT-determined sarcopenia in GLIM-defined malnutrition and prediction of 6-month mortality in cancer inpatients. *Nutrients* 2021;13:2647. <https://doi.org/10.3390/nu13082647>.
- [26] Liu C, Lu Z, Li Z, Xu J, Cui H, Zhu M. Influence of malnutrition according to the GLIM criteria on the clinical outcomes of hospitalized patients with cancer. *Front Nutr* 2021;8:774636. <https://doi.org/10.3389/fnut.2021.774636>.
- [27] Avesani CM, Sabatino A, Guerra A, Rodrigues J, Carrero JJ. A comparative analysis of nutritional assessment using global leadership initiative on malnutrition versus subjective global assessment and malnutrition inflammation score in maintenance hemodialysis patients. *J Ren Nutr* 2021. <https://doi.org/10.1053/j.jrn.2021.06.008>.
- [28] Oguri M, Ishii H, Yasuda K, Sumi T, Takahashi H, Murohara T. Combined prognostic value of malnutrition using GLIM criteria and renal insufficiency in elderly heart failure. *Escola Hear Fail* 2021. <https://doi.org/10.1002/ehf2.13685>.
- [29] Shahbazi S, Hajimohammadebrahim-Ketabforoush M, Vahdat Shariatpanahi M, Shahbazi E, Vahdat Shariatpanahi Z. The validity of the global leadership initiative on malnutrition criteria for diagnosing malnutrition in critically ill patients with COVID-19: a prospective cohort study. *Clin Nutr ESPEN* 2021;43:377–82. <https://doi.org/10.1016/j.clnesp.2021.03.020>.