

Combined prognostic value of malnutrition using GLIM criteria and renal insufficiency in elderly heart failure

Mitsutoshi Oguri^{1*}, Hideki Ishii², Kenichiro Yasuda³, Takuya Sumi⁴, Hiroshi Takahashi⁵ and Toyoaki Murohara³

¹Department of Cardiology, Kasugai Municipal Hospital, 1-1-1 Takaki-cho, Kasugai, Aichi 486-8510, Japan; ²Department of Cardiovascular Medicine, Gunma University Graduate School of Medicine, Gunma, Japan; ³Department of Cardiology, Nagoya University Graduate School of Medicine, Nagoya, Japan; ⁴Sumi Clinic and Ichinomiya Municipal Hospital, Ichinomiya, Japan; and ⁵Division of Medical Statistics, Fujita Health University, Toyoake, Japan

Abstract

Aims We aimed to investigate the prognostic impact of malnutrition, defined by the Global Leadership Initiative on Malnutrition (GLIM) criteria, stratified by renal function in hospitalized patients with acute decompensated heart failure (HF).

Methods and results In this retrospective study, 314 patients who were hospitalized for acute decompensated HF from August 2019 to October 2020 were enrolled. We evaluated malnutrition using the GLIM criteria during the time of admission. The primary outcome was 90-day all-cause mortality. The median patient age was 82 years, and 90-day mortality was 14.0%. In total, 76 (24.2%) patients were malnourished according to the GLIM criteria. Malnutrition defined by the GLIM criteria [adjusted hazard ratio (HR) 1.41, 95% confidence interval (CI) 1.02–1.91, $P = 0.036$] and renal insufficiency [adjusted HR 2.59, 95% CI 1.07–6.28, $P = 0.035$ for estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m² vs. ≥ 60 mL/min/1.73 m²] were identified as independent predictors of 90-day mortality after adjustment for age, systolic blood pressure, and serum sodium level. In the combined setting of both variables, patients with malnutrition and eGFR < 30 mL/min/1.73 m² had a markedly higher risk of 90-day mortality compared with those without malnutrition and eGFR ≥ 60 mL/min/1.73 m² (adjusted HR 3.92, 95% CI 1.10–13.9, $P = 0.035$). Adding both eGFR and malnutrition, defined by the GLIM criteria, to the baseline model with established risk factors improved both net reclassification and integrated discrimination greater than that of the baseline model (0.606, $P < 0.001$ and 0.050, $P = 0.002$, respectively), even when compared with the model with malnutrition by the GLIM alone (0.463, $P = 0.002$ and 0.034, $P < 0.001$, respectively).

Conclusions Nutrition screening using the GLIM criteria stratified by renal function could clearly predict 90-day mortality in hospitalized patients with acute decompensated HF.

Keywords Heart failure; Malnutrition; GLIM; Renal function

Received: 24 May 2021; Revised: 30 September 2021; Accepted: 9 October 2021

*Correspondence to: Mitsutoshi Oguri, Department of Cardiology, Kasugai Municipal Hospital, 1-1-1 Takaki-cho, Kasugai, Aichi 486-8510, Japan. Tel: +81-568-57-0057; Fax: +81-568-57-0067. Email: oguricap0909@gmail.com

Introduction

Malnutrition is common in patients with acute decompensated heart failure (HF).^{1,2} Approximately 80% of hospitalized patients with HF have malnutrition.³ The prevalence of malnutrition has been increasing with the aging of the society, especially in elderly patients.⁴ Moreover, malnutrition exacerbates complications, mortality, duration of hospitalization, and healthcare costs.^{5,6} Therefore, there is an increased focus on the assessment of an individual's nutrition status and prevention of malnutrition.

Recently, the Global Leadership Initiative on Malnutrition (GLIM) published a new set of phenotypic criteria that included weight loss, low body mass index, and reduced muscle mass as well as aetiological criteria that included reduced food intake and inflammation.⁷ Hirose *et al.* showed that malnutrition, defined by the GLIM criteria, had an additive prognostic predictive ability to a known definition of malnutrition, the geriatric nutritional risk index, in elderly patients with HF.⁸ This study showed that 42.4% of hospitalized patients were malnourished according to the GLIM criteria. Furthermore, malnutrition, defined by the GLIM criteria,

was a significant and independent factor for increasing mortality. However, the distribution of malnutrition according to renal function and their combined value as a prognostic tool remains to be identified. Thus, we performed this study to examine the combined prognostic utility of malnutrition, defined by the GLIM criteria, and renal function in hospitalized elderly patients with acute decompensated HF.

Methods

In this retrospective study, 314 patients who were hospitalized for acute decompensated HF at Kasugai Municipal Hospital from August 2019 to October 2020 were enrolled. Patients undergoing haemodialysis, those who were hospitalized multiple times for HF during the study period, and those who with HF caused by acute myocardial infarction were excluded. Most patients were followed up at outpatient clinics after hospital discharge.

This study followed the STROBE statement (Supporting Information, *Table S1*). The study protocol complied with the Declaration of Helsinki and was approved by the Committee on Ethics of Kasugai Municipal Hospital. We also offered the opportunity to opt out to all patients (<https://www.hospital.kasugai.aichi.jp/byouin/torikumi/rinsho/rinri/documents/rinri355-3.pdf>). None of the subjects decided to opt out.

Definitions

Heart failure was defined according to the American College of Cardiology/American Heart Association guidelines, as the presence of HF signs and symptoms and confirmed left ventricular systolic or diastolic dysfunction.⁹ Anaemia was defined as haemoglobin levels < 13 g/dL for males and < 12 g/dL for females according to the World Health Organization committee.¹⁰ The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.¹¹

Subjective global assessment (SGA) is a nutritional assessment tool that is widely used in various clinical settings.^{12,13} SGA was performed by experienced nurses on Day 2 of admission. The SGA questionnaire included two domains—the patient's medical history, including data on body weight, changes in dietary intake, gastrointestinal symptoms, functional capacity, and degree of stress imposed by the disease, and physical examination, including assessment of the severity of subcutaneous fat loss, muscle wasting, ankle and sacral oedema, and ascites on a 4-point scale (0–3). Patients were subjectively rated as well nourished (A), moderately malnourished (B), or severely malnourished (C).¹⁴

For the GLIM criteria, in the initial step of screening for the risk of malnutrition, SGA was used, with malnutrition indicated by SGA B or C. The second step involved diagnosis of

malnutrition based on the combination of three phenotypic components (non-volitional weight loss, low body mass index, and reduced muscle mass) and two aetiological components (reduced food intake and inflammation). According to the pathophysiology that HF coexists with mild-to-moderate inflammation,¹⁵ all patients met the aetiological criteria. Accordingly, malnutrition was diagnosed based on the presence of at least one of the three phenotypic components necessary for a positive diagnosis. Among the phenotypic components, non-volitional weight loss $> 5\%$ within the past 6 months and body mass index < 18.5 kg/m² for age < 70 years and < 20 kg/m² for age ≥ 70 years were used as cut-offs. For reduced muscle mass, arm circumference ≤ 21 cm was mainly used,¹⁶ which was measured to the nearest 1 mm by trained cardiologists or nurses using a plastic tape from Days 2 to 7. Lower appendicular skeletal muscle mass index (males < 7.0 kg/m², females < 5.7 kg/m²), measured by bioelectrical impedance analysis after adjustment for body fluid, was added if possible.

Data collection

Clinical characteristics (age, gender, body mass index, previous medical history, New York Heart Association functional classification, aetiology of HF, non-cardiac comorbidities, vital signs, and laboratory data), in-hospital treatment, and 90-day all-cause mortality were assessed by chart review. Blood samples for baseline measurements, including measurement of eGFR and serum sodium and plasma B-type natriuretic peptide (BNP) levels, were obtained from patients in the morning on Day 2 of hospital admission. Echocardiographic data during hospitalization were also collected; left ventricular ejection fraction was calculated according to the modified biplane Simpson's rule.

Statistical analysis

SAS software (Version 27; SAS Institute, Inc. Cary, NC, USA) was used for statistical analyses. Categorical variables are expressed as counts and percentages, and continuous variables are expressed as medians and interquartile ranges (IQRs) or means \pm standard deviations. Univariate and multivariate Cox regression analyses were performed to determine the predictors of 90-day mortality. Variables with a *P* value of < 0.05 in univariate analysis were entered into the multivariate model, and *P* values, hazard ratios (HRs), and 95% confidence intervals (CIs) were calculated. Statistical significance was set at *P* < 0.05 . To assess whether the accuracy of mortality prediction would improve after adding eGFR or malnutrition, defined by the GLIM criteria, into a baseline model with established risk factors (i.e. age, gender, systolic blood pressure, and serum sodium level), we calcu-

lated the C-index, net reclassification improvement (NRI), and integrated discrimination improvement (IDI). The C-index, defined as the area under receiver operating characteristic curves between individual predictive probabilities for mortality and the incidence of mortality, was compared between the baseline model and enriched models containing the established risk factors plus eGFR and malnutrition, defined by the GLIM criteria, or each of these variables. NRI indicates how many patients showed improvement in their predicted probability of mortality, and IDI indicates the average improvement in the predicted probability of mortality after adding variables into the baseline model. Differences were considered statistically significant at a *P* value of <0.05.

Results

The characteristics of the enrolled subjects, categorized according to the GLIM criteria (the presence/absence of malnutrition) and eGFR categories (≥ 60 , ≥ 30 to < 60 , and < 30 mL/min/1.73 m²), are shown in *Table 1*. The median patient age was 82 years (IQR 73–86 years), and 54.1% of the patients were men. The 90-day mortality rate was 14.0% (*n* = 44). Kaplan–Meier analysis showed that the 90-day survival rates were 89.1% and 76.3% in patients with and without malnutrition, respectively, according to the GLIM criteria, and 91.6%, 89.2%, and 74.7% in patients with eGFR ≥ 60 , ≥ 30 to < 60 , and < 30 mL/min/1.73 m², respectively (*P* = 0.001 and *P* = 0.004, respectively) (*Figure 1*). In total, 124 (39.4%) patients were malnourished according to the SGA, while 76 (24.2%) patients were malnourished according to the GLIM criteria (Supporting Information, *Table S2*).

The univariate Cox regression model revealed that age, body mass index, systolic blood pressure, blood urea nitrogen, serum sodium level, eGFR, plasma BNP level, and malnutrition, defined by the GLIM criteria, were significant predictors of 90-day mortality (Supporting Information, *Table S3*). Among these variables, there was a strong correlation between blood urea nitrogen and eGFR, and body mass index and malnutrition, defined by the GLIM criteria. In addition, plasma BNP level was significantly correlated with malnutrition defined by the SGA B or C, as the first-line screening tool for the GLIM criteria (*P* = 0.026). Therefore, we excluded body mass index, blood urea nitrogen, and plasma BNP level from multivariate Cox regression analysis. A subsequent multivariate Cox regression model identified malnutrition, defined by the GLIM criteria, and eGFR as significant and independent predictors of 90-day mortality after adjusting for age, systolic blood pressure, and serum sodium level (HR 1.41, 95% CI 1.02–1.91, *P* = 0.036 and HR 0.98, 95% CI 0.96–0.99, *P* = 0.008, respectively) (*Table 2*). Next, we investigated predictive values by calculating multivariable-

adjusted HRs for associations between eGFR category and prognostic variables identified by the multivariate Cox regression model (age, systolic blood pressure, serum sodium level, and malnutrition, defined by the GLIM criteria) (*Table 2*). Patients with eGFR < 30 mL/min/1.73 m² had a higher relative risk of 90-day mortality than those with eGFR ≥ 60 mL/min/1.73 m² (adjusted HR 2.59, 95% CI 1.07–6.28, *P* = 0.035) and eGFR ≥ 30 to < 60 mL/min/1.73 m² (adjusted HR 2.39, 95% CI 1.23–4.63, *P* = 0.010). Furthermore, we compared the characteristics and incidence of 90-day mortality stratified by the presence or absence of malnutrition, defined by the GLIM criteria, and eGFR (Supporting Information, *Table S4* and *Figure 2*). The incidence of 90-day mortality was the highest in malnourished patients with eGFR < 30 mL/min/1.73 m² (36.4%). Compared with patients without malnutrition and eGFR ≥ 60 mL/min/1.73 m² (reference group), patients with malnutrition and eGFR < 30 mL/min/1.73 m² had a significantly increased incidence of 90-day mortality after adjusting for age, systolic blood pressure, and serum sodium level (HR 3.92, 95% CI 1.10–13.9, *P* = 0.035) (*Figure 2*). Finally, we calculated the improvement in discrimination and reclassification of malnutrition, defined by the GLIM criteria (*Table 3*). Adding both eGFR and malnutrition, defined by the GLIM criteria, to the baseline model with established risk factors improved NRI beyond that of the baseline model alone (*P* < 0.001) and the model with malnutrition defined by the GLIM criteria alone (*P* = 0.002). In addition, IDI improved significantly after adding both eGFR and malnutrition, defined by the GLIM criteria, beyond that of the baseline model (*P* = 0.002) and the model with malnutrition, defined the GLIM criteria alone (*P* < 0.001). The C-index of malnutrition, defined by the GLIM criteria, and eGFR, in addition to established risk factors, was 0.784 (95% CI 0.713–0.855), which was relatively higher than that of established risk factors and malnutrition, defined by the GLIM criteria [0.770 (95% CI 0.698–0.843)].

Discussion

In this retrospective study, we found that, among hospitalized patients with HF, identifying malnourished patients using the GLIM criteria during early hospitalization may provide useful information for estimating mid-term mortality. Additionally, we found that the mortality of malnourished patients could be predicted based on their renal function.

Recently, several studies have reported the prevalence of malnutrition and the relationship between clinical prognosis and nutritional status in patients with acute decompensated HF using various nutrition screening tools.^{17,18} Given that previous results might be affected by the study population and sample sizes, there is no international consensus on the most adequate screening tool or feasible combinations for

Table 1 Characteristics of study subjects

Characteristic	All patients N = 314	GLIM criteria		P value
		Without malnutrition N = 238	Malnutrition N = 76	
Age (years)	82 (73, 86)	80 (71, 86)	85 (79, 90)	<0.001
Gender (male/female, %)	54.1/45.9	60.5/39.5	34.2/65.8	<0.001
Current or former smoker (%)	44.3	50.0	26.3	<0.001
Body mass index (kg/m ²)	22.6 (19.8, 25.4)	23.4 (21.1, 26.6)	19.3 (17.6, 21.7)	<0.001
Dyslipidaemia (%)	24.5	27.3	15.8	0.042
Type 2 diabetes mellitus (%)	36.9	39.1	30.3	0.166
Hypertension (%)	72.6	75.6	63.2	0.034
Atrial fibrillation or atrial flutter (%)	34.7	31.5	44.7	0.035
Previous myocardial infarction (%)	20.4	21.4	17.1	0.415
Previous stroke (%)	7.6	8.0	6.6	0.808
Previous heart failure hospitalization before the study period (%)	32.2	30.3	38.2	0.199
Ischaemic aetiology (%)	28.0	28.5	26.3	0.711
Initial evaluation				
Systolic blood pressure (mmHg)	132 (114, 148)	131 (114, 148)	131 (113, 149)	0.891
Diastolic blood pressure (mmHg)	74 (64, 88)	75 (64, 87)	73 (62, 88)	0.908
Heart rate (b.p.m.)	84 (72, 96)	83 (72, 96)	85 (71, 98)	0.607
NYHA functional classification IV (%)	48.4	45.7	57.6	0.091
Blood urea nitrogen (mg/dL)	23.6 (17.4, 33.6)	23.3 (17.4, 32.7)	23.9 (17.3, 35.0)	0.548
Sodium (mEq/L)	141 (137, 143)	141 (138, 143)	140 (136, 143)	0.242
Potassium (mEq/L)	4.1 (3.7, 4.5)	4.1 (3.7, 4.5)	4.1 (3.7, 4.5)	0.593
eGFR (mL/min/1.73 m ²)	43.8 (29.4, 62.0)	43.3 (29.7, 59.7)	44.1 (26.2, 66.9)	0.898
Albumin (mg/dL)	3.6 (3.3, 3.9)	3.7 (3.4, 4.0)	3.4 (3.1, 3.8)	<0.001
Total cholesterol (mg/dL)	147 (127, 177)	147 (127, 178)	149 (127, 176)	0.853
CRP (mg/dL)	0.49 (0.19, 1.90)	0.47 (0.19, 1.96)	0.56 (0.18, 1.67)	0.777
BNP (pg/mL)	481 (246, 844)	470 (225, 789)	551 (306, 992)	0.072
Anaemia (%)	64.7	63.9	67.1	0.607
Left ventricular ejection fraction (%)	51 (37, 66)	52 (38, 66)	50 (35, 65)	0.713
Hospital length of stay (days)	15 (11, 22)	15 (11, 22)	16 (11, 24)	0.416
90-day mortality (%)	14.0	10.9	23.7	0.008
eGFR (mL/min/1.73 m ²)				
Characteristic	≥60 N = 83	≥30 to <60 N = 148	<30 N = 83	P value
Age (years)	77 (66, 86)	83 (76, 87)	81 (73, 87)	0.003
Gender (male/female, %)	60.2/39.8	52.7/47.3	50.6/49.4	0.410
Current or former smoker (%)	49.2	43.9	41.0	0.640
Body mass index (kg/m ²)	22.3 (19.1, 25.1)	22.6 (20.2, 25.7)	22.5 (19.6, 25.8)	0.444
GLIM (%)	28.9	20.3	26.5	0.288
Dyslipidaemia (%)	18.1	22.3	34.9	0.028
Type 2 diabetes mellitus (%)	25.3	38.5	45.8	0.021
Hypertension (%)	63.9	73.7	79.5	0.072
Atrial fibrillation or atrial flutter (%)	24.1	37.2	41.0	0.051
Previous myocardial infarction (%)	8.4	23.7	26.5	0.006
Previous stroke (%)	8.4	6.1	9.6	0.591
Previous heart failure hospitalization (%)	12.1	32.4	51.8	<0.001
Ischaemic aetiology (%)	20.5	28.1	35.4	0.104
Initial evaluation				
Systolic blood pressure (mmHg)	132 (116, 144)	132 (116, 149)	128 (106, 149)	0.372
Diastolic blood pressure (mmHg)	81 (68, 93)	74 (64, 88)	69 (60, 80)	0.001
Heart rate (b.p.m.)	87 (78, 103)	84 (72, 96)	78 (65, 93)	0.002
NYHA functional classification IV (%)	50.6	47.8	47.4	0.900
Blood urea nitrogen (mg/dL)	16.0 (11.5, 20.9)	22.8 (18.5, 27.9)	44.6 (32.7, 58.0)	<0.001
Sodium (mEq/L)	140 (137, 142)	141 (138, 143)	141 (137, 143)	0.201
Potassium (mEq/L)	3.9 (3.5, 4.2)	4.1 (3.7, 4.4)	4.4 (3.9, 5.0)	<0.001
eGFR (mL/min/1.73 m ²)	73.6 (67.2, 85.7)	43.8 (37.5, 51.3)	19.0 (12.9, 25.2)	<0.001
Albumin (mg/dL)	3.6 (3.2, 4.0)	3.06 (3.3, 3.9)	3.6 (3.3, 3.9)	0.901
Total cholesterol (mg/dL)	154 (134, 184)	146 (126, 177)	140 (122, 169)	0.076
CRP (mg/dL)	0.42 (0.21, 1.53)	0.47 (0.17, 1.70)	0.71 (0.18, 2.65)	0.473
BNP (pg/mL)	434 (154, 581)	479 (247, 844)	575 (323, 1402)	0.003
GLIM (%)	28.9	20.3	26.5	0.288
Anaemia (%)	44.6	64.2	85.5	<0.001
Left ventricular ejection fraction (%)	52 (36, 65)	51 (38, 68)	50 (37, 66)	0.817
Hospital length of stay (days)	13 (10, 19)	15 (11, 21)	18 (11, 29)	0.015
90-day mortality (%)	8.4	10.8	25.3	0.002

BNP, B-type natriuretic peptide; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; GLIM, Global Leadership Initiative on Malnutrition; NYHA, New York Heart Association.

Categorical variables are described as percentages, and continuous variables are given as median and 25th–75th percentile range.

Figure 1 Kaplan–Meier curves for all-cause mortality according to the presence or absence of malnutrition, defined by the GLIM criteria, and eGFR category. eGFR, estimated glomerular filtration rate; GLIM, Global Leadership Initiative on Malnutrition.

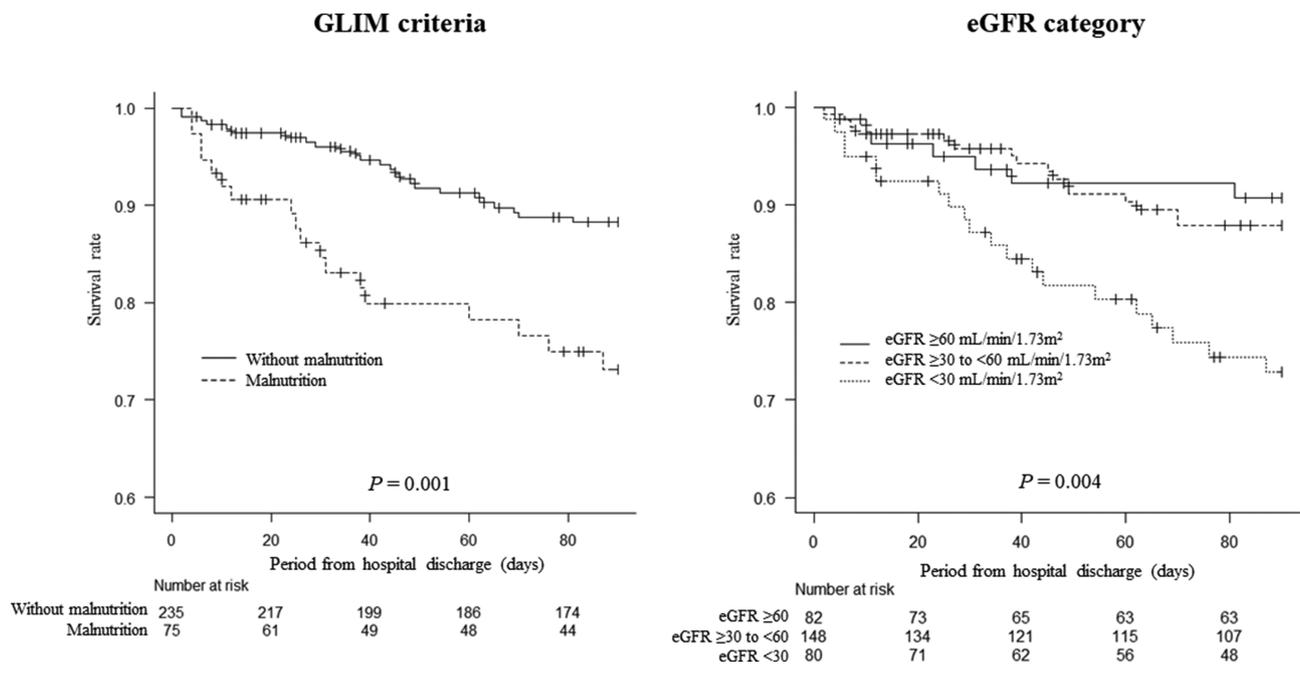


Table 2 Predictors for 90-day mortality by Cox regression analysis

	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Malnutrition by the GLIM criteria	1.59 (1.17–2.14)	0.004	1.41 (1.02–1.91)	0.036 ^a
eGFR (continuous)	0.98 (0.96–0.99)	0.002	0.98 (0.96–0.99)	0.008 ^a
eGFR (vs. ≥ 60 mL/min/1.73 m ²)		0.005 ^b		< 0.001 ^b
≥ 30 to < 60 mL/min/1.73 m ²	1.27 (0.54–3.29)	0.597	1.09 (0.44–2.72)	0.859 ^c
< 30 mL/min/1.73 m ²	3.17 (1.41–8.06)	0.004	2.59 (1.07–6.28)	0.035 ^c

CI, confidence interval; eGFR, estimated glomerular filtration rate; GLIM, Global Leadership Initiative on Malnutrition; HR, hazard ratio.

^aAdjusted for age, systolic blood pressure, and serum sodium level.

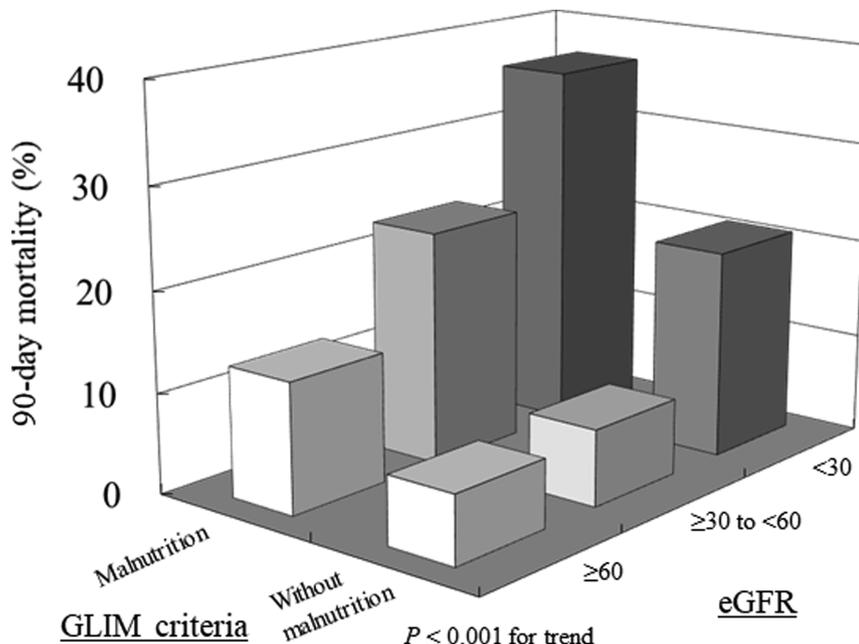
^bP for trend.

^cAdjusted for age, systolic blood pressure, serum sodium level, and malnutrition defined by the GLIM criteria.

predicting mortality thus far. Two studies have assessed nutritional status using the GLIM criteria after it was proposed and have shown its predictive efficacy in patients with cardiovascular diseases, including HF.^{8,19} They evaluated the Malnutrition Universal Screening Tool or the geriatric nutritional risk index as a first-stage screening tool for the risk of malnutrition at hospital discharge. We have previously assessed nutrition measurements for the prediction of 1-year mortality in hospitalized patients with acute decompensated HF.²⁰ The addition of SGA to the established factors significantly improved both NRI and IDI. Other indices (controlling nutritional status, prognostic nutritional index, or geriatric nutritional risk index) improved NRI alone. Given that SGA might have the greatest advantage in the prediction of 1-year mortality, we adapted SGA as the first-line screening

tool for the GLIM criteria. Allard *et al.* performed a comparative study between the GLIM criteria and SGA in hospitalized adult patients²¹ and reported that the prevalence of malnutrition was 45.2% and 19.8% using SGA and the GLIM criteria, respectively. In addition, they reported a worrisome result that the GLIM criteria had high specificity but low sensitivity in diagnosing malnutrition. In our study, the prevalence of malnutrition was 39.4% and 24.2% using SGA and the GLIM criteria, respectively. Although the difference in the assessment of these two tools was smaller than that in the study by Allard *et al.*, some potentially malnourished patients identified using SGA may not be identified using the GLIM criteria. Nevertheless, applying SGA as a first-stage screening tool will be useful in the early detection of malnourished patients at hospital admission.

Figure 2 Ninety-day mortality stratified according to the presence or absence of malnutrition, defined by the GLIM criteria, and eGFR category. Values indicate the adjusted hazard ratio (95% confidence interval). The *P* for trend was <0.001. eGFR, estimated glomerular filtration rate; GLIM, Global Leadership Initiative on Malnutrition.



eGFR category	GLIM criteria	
	Without malnutrition	Malnutrition
≥60 mL/min/1.73m ²	1.00 (reference)	1.53 (0.34–6.92)
≥30 to <60 mL/min/1.73m ²	0.88 (0.27–2.88)	2.58 (0.73–9.09)
<30 mL/min/1.73m ²	2.74 (0.87–8.69)	3.92 (1.10–13.9)

Table 3 Discrimination of each predictive model for 90-day mortality using the C-index, net reclassification improvement, and integrated discrimination improvement

	C-index (95% CI)	<i>P</i> value	NRI	<i>P</i> value	IDI	<i>P</i> value
Established risk factors	0.752 (0.679 to 0.826)	Reference		Reference		Reference
+ eGFR	0.775 (0.701 to 0.848)	0.332	0.448	0.003	0.031	0.007
+ malnutrition by the GLIM	0.770 (0.698 to 0.843)	0.258	0.305	0.032	0.016	0.048
+ malnutrition by the GLIM and eGFR	0.784 (0.713 to 0.855)	0.212	0.606	<0.001	0.050	0.002
The model with GLIM and eGFR vs. the model with GLIM alone	0.014 (–0.026 to 0.053) ^a	0.505	0.463	0.002	0.034	<0.001

CI, confidence interval; eGFR, estimated glomerular filtration rate; GLIM, Global Leadership Initiative on Malnutrition; IDI, integrated discrimination improvement; NRI, net reclassification improvement.

Established risk factors included age, gender, systolic blood pressure, and serum sodium level.

^aEstimated difference of C-index between the two models.

In a randomized controlled trial, the benefit of individualized nutritional intervention was not observed in malnourished patients with cardiovascular diseases.²² A recent randomized trial by Rozentryt *et al.* identified significant weight gain and improvement in quality of life in cachectic patients with chronic HF.²³ Even the first admission for acute

decompensated HF was related to an increased risk of mortality due to aging, coexistent cardiovascular diseases, comorbidities, or malignant diseases. Clinical evidence of nutritional support is desirable from this background, but a precise strategy for elderly patients with HF is unclear. Therefore, it is possible that enthusiastic early detection of malnutrition

using the GLIM criteria, in addition to conventional risk factors, can contribute modestly. Further evaluations are needed to clarify the impact of nutritional support based on nutrition screening using the GLIM criteria in clinical practice.

Impaired renal function is commonly seen in patients with HF and is associated with poor prognosis.^{24–29} The relationship between cardiac and renal function is being increasingly focused on, including worsening renal function and acute kidney injury during hospitalization. Therefore, the current guidelines strongly recommend initial assessment of renal function with the use of eGFR in patients with acute HF.^{9,29} In our analyses, eGFR at hospital admission was an independent predictor of 90-day mortality. Its predictive value was significantly stratified by three eGFR categories, which was consistent with prior observations. We further identified an additive predictive effect of eGFR on malnutrition, defined by the GLIM criteria. Given that there was no association between eGFR categories and the prevalence of malnutrition in this study, our results might be caused by the additive effect of impaired renal function on malnutrition.

According to the data from National Institute of Population and Social Security Research in Japan, the proportion of the population aged ≥ 65 years is estimated to increase from 26.6% in 2015 to 31.9% in 2030.³⁰ The age of patients in the present study was higher than that in prior HF studies, which might reflect the trend of an aging society in Japan.

The present study has some limitations. (i) The results presented here are only from a single hospital and the sample size was relatively small. (ii) We performed the first-line nutritional risk screening using SGA based on our prior observations. Replication of our study or evaluation with other nutritional tools is needed. (iii) We used data on eGFR at hospital admission and did not consider changes in eGFR during hospitalization and proteinuria. Although the presence of proteinuria is a strong predictor of mortality, we had no data in most of our patients. (iv) Measurement bias in arm circumference is potentially present because different cardiologists or nurses took the measurements.

In conclusion, this study provides prognostic information that nutrition screening using the GLIM criteria stratified by renal function could predict 90-day mortality in hospitalized patients with acute decompensated HF.

Acknowledgements

We gratefully acknowledge the work of past and present members of our department for helpful discussions and comments on the manuscript. We especially wish to thank S. Ito for collecting medical data.

Conflict of interest

None declared.

Funding

None.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. STROBE Statement.

Table S2. Prevalence of malnutrition according to each nutrition screening tool and components.

Table S3. Predictors of 90-day mortality by univariate Cox regression analysis.

Table S4. Characteristics stratified by the presence or absence of malnutrition, defined by the GLIM criteria, and eGFR category.

References

1. Sze S, Pellicori P, Zhang J, Weston J, Clark AL. Agreement and classification performance of malnutrition tools in patients with chronic heart failure. *Curr Dev Nutr* 2020; 4: nzaa071.
2. Lin H, Zhang H, Lin Z, Li X, Kong X, Sun G. Review of nutritional screening and assessment tools and clinical outcomes in heart failure. *Heart Fail Rev* 2016; 21: 549–565.
3. Agra Bermejo RM, González Ferreiro R, Varela Román A, Gómez Otero I, Kreidieh O, Conde Sabarís P, Rodríguez-Mañero M, Moure González M, Seoane Blanco A, Virgós Lamela A, García Castelo A, González Juanatey JR. Nutritional status is related to heart failure severity and hospital readmissions in acute heart failure. *Int J Cardiol* 2017; 230: 108–114.
4. Martín-Sánchez FJ, Cuesta Triana F, Rossello X, Pardo García R, Llopis García G, Caimari F, Vidán MT, Ruiz Artacho P, González Del Castillo J, Llorens P, Herrero P, Jacob J, Gil V, Fernández Pérez C, Gil P, Bueno H, Miró Ó, Matía Martín P, Rodríguez Adrada E, Santos MC, Salgado L, Brizzi BN, Docavo ML, Del Mar S-CM, Xipell C, Sánchez C, Aguiló S, Gaytan JM, Jerez A, Pérez-Durá MJ, Berrocal Gil P, López-Grima ML, Valero A, Aguirre A, Pedragosa MA, Piñera P, Lázaro-Aragues P, Sánchez Nicolás JA, Rizzi MA, Herrera Mateo S, Alquezar A, Roset A, Ferrer C, Llopis F, Álvarez Pérez JM, López Díez MP,

- Richard F, Fernández-Cañadas JM, Carratalá JM, Javaloyes P, Andueza JA, Sevillano Fernández JA, Romero R, Merlo Loranca M, Álvarez Rodríguez V, Lorca MT, Calderón L, Soy Ferrer E, Manuel Garrido J, Martín ME, Representing the members of the OAK Register Investigators. Effect of risk of malnutrition on 30-day mortality among older patients with acute heart failure in emergency departments. *Eur J Intern Med* 2019; **65**: 69–77.
5. Sze S, Pellicori P, Kazmi S, Rigby A, Cleland JGF, Wong K, Clark AL. Prevalence and prognostic significance of malnutrition using 3 scoring systems among outpatients with heart failure: A comparison with body mass index. *JACC Heart Fail* 2018; **6**: 476–486.
 6. Inciong JFB, Chaudhary A, Hsu HS, Joshi R, Seo JM, Trung LV, Ungpinitpong W, Usman N. Hospital malnutrition in northeast and Southeast Asia: a systematic literature review. *Clin Nutr ESPEN* 2020; **39**: f30–f45.
 7. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, Baptista G, Barazzoni R, Blaauw R, Coats A, Crivelli A, Evans DC, Gramlich L, Fuchs-Tarlovsky V, Keller H, Llido L, Malone A, Mogensen KM, Morley JE, Muscaritoli M, Nyulasi I, Pirlich M, Pisprasert V, de van der Schueren MAE, Siltharm S, Singer P, Tappenden K, Velasco N, Waitzberg D, Yamwong P, Yu J, Van Gossom A, Compher C, GLIM Core Leadership Committee, GLIM Working Group. GLIM criteria for the diagnosis of malnutrition: a consensus report from the global clinical nutrition community. *Clin Nutr* 2019; **38**: 1–9.
 8. Hirose S, Matsue Y, Kamiya K, Kagiya N, Hiki M, Dotare T, Sunayama T, Konishi M, Saito H, Saito K, Ogasahara Y, Maekawa E, Kitai T, Iwata K, Jujo K, Wada H, Kasai T, Momomura SI, Minamino T. Prevalence and prognostic implications of malnutrition as defined by GLIM criteria in elderly patients with heart failure. *Clin Nutr*. 2021; **40**: 4334–4340.
 9. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Colvin MM, Drazner MH, Filippatos GS, Fonarow GC, Givertz MM, Hollenberg SM, Lindenfeld J, Masouli FA, McBride PE, Peterson PN, Stevenson LW, Westlake C. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines and the Heart Failure Society of America. *Circulation* 2017; **136**: e137–e161.
 10. WHO Scientific Group on Nutritional Anemias and World Health Organization. Nutritional anaemias. Report of the WHO Scientific Group. *WHO Tech Rep Ser* 1968; **405**: 5–37.
 11. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J. CKD-EPI (Chronic kidney disease epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; **150**: 604–612.
 12. Detsky AS, McLaughlin JR, Baker JP, Johnston N, Whittaker S, Mendelson RA, Jeejeebhoy KN. What is subjective global assessment of nutritional status? *J Parenter Enteral Nutr* 1987; **11**: 8–13.
 13. da Silva FJ, de Mello PD, de Mello ED. Subjective global assessment of nutritional status: a systematic review of the literature. *Clin Nutr* 2015; **34**: 785–792.
 14. Detsky AS, Smallley PS, Chang J. The rational clinical examination. Is this patient malnourished? *JAMA* 1994; **271**: 54–58.
 15. Murphy SP, Kakkar R, McCarthy CP, Januzzi JL Jr. Inflammation in heart failure: JACC state-of-the-art review. *J Am Coll Cardiol* 2020; **75**: 1324–1340.
 16. Kamiya K, Masuda T, Matsue Y, Inomata T, Hamazaki N, Matsuzawa R, Tanaka S, Nozaki K, Maekawa E, Noda C, Yamaoka-Tojo M, Matsunaga A, Izumi T, Ako J. Complementary role of arm circumference to body mass index in risk stratification in heart failure. *JACC Heart Fail* 2016; **4**: 265–273.
 17. Shirakabe A, Hata N, Kobayashi N, Okazaki H, Matsushita M, Shibata Y, Nishigoori S, Uchiyama S, Asai K, Shimizu W. The prognostic impact of malnutrition in patients with severely decompensated acute heart failure, as assessed using the prognostic nutritional index (PNI) and controlling nutritional status (CONUT) score. *Heart Vessels* 2018; **33**: 134–144.
 18. Formiga F, Chivite D, Corbella X. Utility of the controlling nutritional status (CONUT) score in patients admitted due to acute heart failure. *Int J Cardiol* 2017; **235**: 203.
 19. Kootaka Y, Kamiya K, Hamazaki N, Nozaki K, Ichikawa T, Nakamura T, Yamashita M, Maekawa E, Reed JL, Yamaoka-Tojo M, Matsunaga A, Ako J. The GLIM criteria for defining malnutrition can predict physical function and prognosis in patients with cardiovascular disease. *Clin Nutr* 2021; **40**: 146–152.
 20. Takikawa T, Sumi T, Takahara K, Kawamura Y, Ohguchi S, Oguri M, Ishii H, Murohara T. Prognostic importance of multiple nutrition screening indexes for 1-year mortality in hospitalized acute decompensated heart failure patients. *Circ Rep* 2019; **1**: 87–93.
 21. Allard JP, Keller H, Gramlich L, Jeejeebhoy KN, Laporte M, Duerksen DR. GLIM criteria has fair sensitivity and specificity for diagnosing malnutrition when using SGA as comparator. *Clin Nutr* 2020; **39**: 2771–2777.
 22. Schuetz P, Fehr R, Baechli V, Geiser M, Deiss M, Gomes F, Kutz A, Tribolet P, Bregenzler T, Braun N, Hoess C, Pavlicek V, Schmid S, Bilz S, Sigrist S, Brändle M, Benz C, Henzen C, Mattmann S, Thomann R, Brand C, Rutishauser J, Aujesky D, Rodondi N, Donzé J, Stanga Z, Mueller B. Individualised nutritional support in medical inpatients at nutritional risk: A randomised clinical trial. *Lancet* 2019; **393**: 2312–2321.
 23. Rozentryt P, von Haehling S, Lainscak M, Nowak JU, Kalantar-Zadeh K, Polonski L, Anker SD. The effects of a high-caloric protein-rich oral nutritional supplement in patients with chronic heart failure and cachexia on quality of life, body composition, and inflammation markers: A randomized, double-blind pilot study. *J Cachexia Sarcopenia Muscle* 2010; **1**: 35–42.
 24. Conrad N, Judge A, Tran J, Mohseni H, Hedgecott D, Crespillo AP, Allison M, Hemingway H, Cleland JG, McMurray JJV, Rahimi K. Temporal trends and patterns in heart failure incidence: A population-based study of 4 million individuals. *Lancet* 2018; **391**: 572–580.
 25. Metra M, Cotter G, Gheorghide M, Dei Cas L, Voors AA. The role of the kidney in heart failure. *Eur Heart J* 2012; **33**: 2135–2142.
 26. Cheng YL, Sung SH, Cheng HM, Huang JT, Guo CY, Hsu PF, Yu WC, Chen CH. Prognostic comparison of the estimations of renal function in patients with acute heart failure. *Circ J* 2019; **83**: 767–774.
 27. Löfman I, Szummer K, Dahlström U, Jernberg T, Lund LH. Associations with and prognostic impact of chronic kidney disease in heart failure with preserved, mid-range, and reduced ejection fraction. *Eur J Heart Fail* 2017; **19**: 1606–1614.
 28. Löffler AI, Cappola TP, Fang J, Hetzel SJ, Kadlec A, Astor B, Sweitzer NK. Effect of renal function on prognosis in chronic heart failure. *Am J Cardiol* 2015; **115**: 62–68.
 29. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GMC, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P, ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2016; **37**: 2129–2200.
 30. National Institute of Population and Social Security Research. Estimated future population. Population statistics of Japan 2017. <http://www.ipss.go.jp/p-info/e/psj2017/PSJ2017.asp> (14 August, 2021).