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ORIGINAL ARTICLE
Nutrition

Prognostic Importance of Multiple Nutrition Screening Indexes for 1-Year Mortality in Hospitalized Acute Decompensated Heart Failure Patients

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Background: The purpose of the study was to evaluate the impact of nutritional status on 1-year mortality in hospitalized patients with acute decompensated heart failure (ADHF).

Methods and Results: We enrolled 457 hospitalized ADHF patients. Previously established objective nutritional indexes (controlling nutritional status [CONUT], prognostic nutritional index [PNI], geriatric nutritional risk index [GNRI], and subjective global assessment [SGA]) were evaluated at hospital admission. Malnutrition was defined as CONUT score ≥5, PNI score <38, GNRI score <92, and SGA scores B and C. The frequencies of malnutrition based on CONUT, PNI, GNRI, and SGA were 31.5%, 21.4%, 44.9%, and 27.8%, respectively. All indexes were related to the occurrence of 1-year mortality on univariate Cox regression analysis (P<0.05). We constructed a reference model using age, body mass index, systolic blood pressure, sodium concentration, and renal function on multivariable Cox regression analysis. Adding SGA to the reference model significantly improved both net reclassification improvement (NRI) and integrated discrimination improvement (0.344, P=0.002; 0.012, P=0.049; respectively). Other indexes (CONUT, PNI, and GNRI scores) significantly improved NRI (0.254, P=0.019; 0.273, P=0.013; 0.306, P=0.006; respectively).

Conclusions: Nutritional screening assessed at hospital admission was appropriate for the prediction of 1-year mortality in hospitalized patients with ADHF.

Key Words: Acute heart failure; Nutrition assessment; Prognosis

The prevalence of heart failure increases with age.[1] In Japan, the number of elderly people is increasing rapidly, and the prevalence of acute decompensated heart failure (ADHF) is steadily increasing.[2] Malnutrition is an important factor in the exacerbation of chronic heart failure.[3,4] Regarding the relationship between heart failure and malnutrition, intestinal ischemia affected by low output syndrome causes absorption disorder and decreases peristalsis. Simultaneously, intestinal edema affected by gastrointestinal congestion causes abdominal fullness and loss of appetite, which decreases oral intake despite hypermetabolic conditions due to chronic inflammation in patients with heart failure.[3] Consequently, chronic heart failure results in malnutrition.[5] Taken together, nutrition status has been extensively examined in patients with chronic heart failure. There are several reports on CHF patients, while few studies have evaluated the relationship between clinical prognosis and nutritional status in ADHF. In addition, appropriate nutrition measurement in ADHF has not been well evaluated. Therefore, the purposes of the present study were to evaluate the impact of nutritional status on 1-year mortality and to assess appropriate nutrition measurements in hospitalized patients with ADHF.

Methods

We enrolled 457 consecutive patients with ADHF who were admitted to Kasugai Municipal Hospital, Aichi, Japan, between November 2009 and August 2015. For patients with multiple admissions, the first eligible hospitalization for ADHF was evaluated. We excluded patients with ADHF caused by acute coronary syndrome or malignancy.

Medical records were reviewed to assess clinical characteristics (age, gender, previous medical history, etiology, comorbidities, and laboratory data) and 1-year mortality

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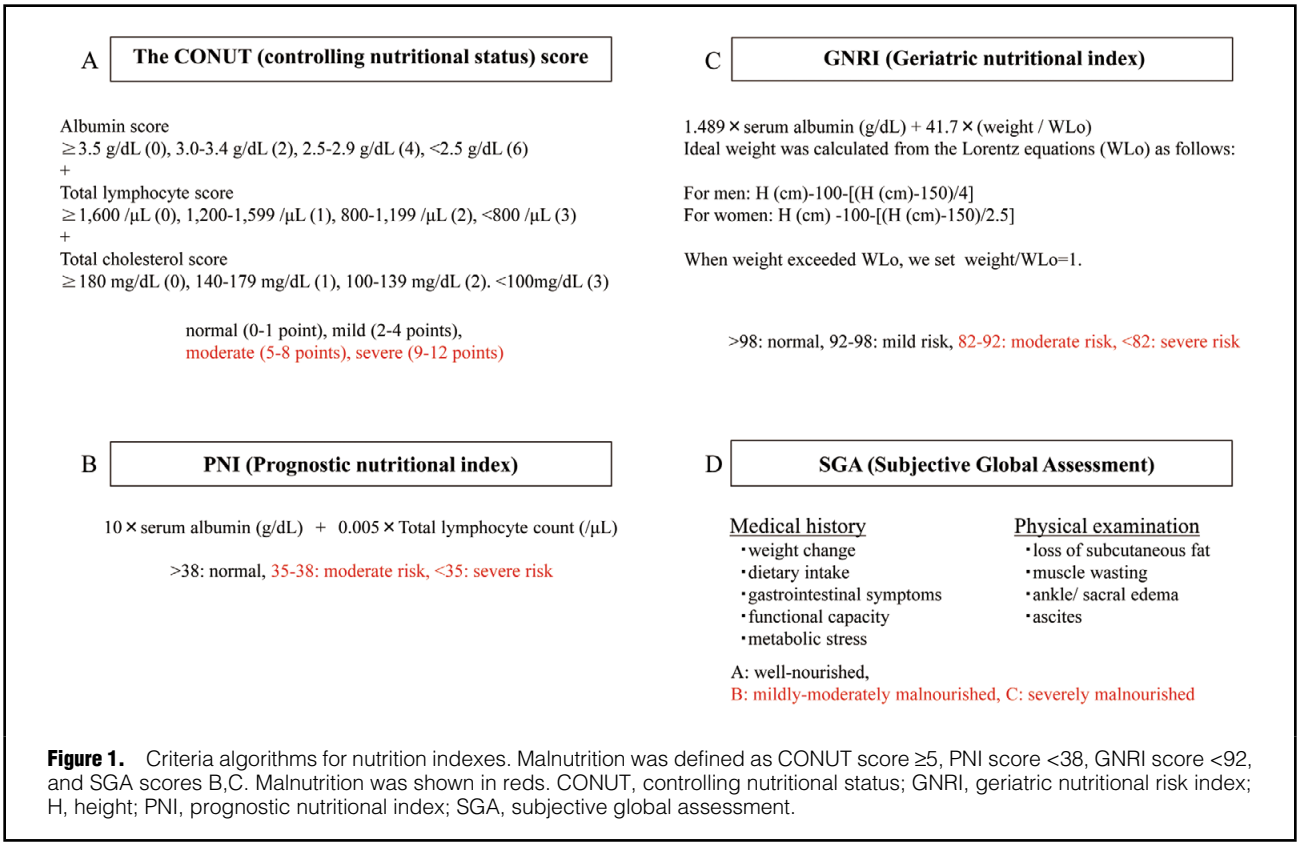

Figure 1. Criteria algorithms for nutrition indexes. Malnutrition was defined as CONUT score ≥5, PNI score <38, GNRI score <92, and SGA scores B,C. Malnutrition was shown in reds. CONUT, controlling nutritional status; GNRI, geriatric nutritional risk index; H, height; PNI, prognostic nutritional index; SGA, subjective global assessment.

rates collected from outpatient visits. All patients were followed up for 1 year and we examined the association between 1-year mortality and nutrition status in patients with ADHF retrospectively. We compared all data according to survival status.

The study protocol complied with the Declaration of Helsinki and was approved by the Committees on the Ethics of Human Research of Kasugai Municipal Hospital. Written informed consent was obtained from each patient.

Body mass index (BMI) was calculated using the following formula: BMI=mass (kg)/height^2 (m^2). We defined anemia as serum hemoglobin <13 mg/dL in men and <12 mg/dL in women.[6]

Previously established objective nutritional indexes (controlling nutritional status [CONUT], prognostic nutritional index [PNI], geriatric nutritional risk index [GNRI], and subjective global assessment [SGA]) were evaluated at hospital admission. The control criteria are shown in **Figure 1**. CONUT score was determined using serum albumin level, total cholesterol level, and total lymphocyte count.[7] The formula was as follows: CONUT score=albumin score (≥3.5 g/dL, 0 points; 3.0–3.4 g/dL, 2 points; 2.5–2.9 g/dL, 4 points; <2.5 g/dL, 6 points)+total lymphocyte score (≥1,600/mL, 0 points; 1,200–1,599/mL, 1 point; 800–1,199/mL, 2 points; <800/mL, 3 points)+total cholesterol score (≥180 mg/dL, 0 points; 140–179 mg/dL, 1 point; 100–139 mg/dL, 2 points; <100 mg/dL, 3 points). PNI score was calculated using serum albumin level and total lymphocyte count.[8] The formula was as follows: PNI=10×serum albumin concentration (g/dL)+0.005×total lymphocyte count (/μL). GNRI score was calculated using serum albumin level, and body weight and height.[9] The formula was as follows: GNRI=14.89×serum albumin (g/dL)+41.7×(actual body weight/ideal body weight). Actual body weight/ideal body weight was set to 1 when the patient's body weight exceeded the ideal body weight. The ideal body weight in the present study was calculated using BMI 22 kg/m^2. SGA score was based on history and physical examination: patients were subjectively rated as well nourished (A), moderately malnourished (B), or severely malnourished (C).[10] The examiner asked every patient about any involuntary weight loss and/or changes in dietary intake in the past 6 months and 2 weeks, the presence of any gastrointestinal symptoms for >2 weeks (nausea, vomiting, diarrhea, and anorexia), and his/her performance status. Physical examination assessed the severity of subcutaneous fat loss, muscle wasting, and ankle and sacral edema, as well as ascites on a 4-point scale (0–3).

Malnutrition was defined as CONUT score ≥5, PNI score <38, GNRI score <92, and SGA scores B and C.

Statistical Analysis

The distribution of continuous variables was examined using the Shapiro-Wilk test. Continuous variables are expressed as median (IQR), and categorical variables as n (%). Comparison of continuous variables was performed using the Student's t-test or Mann-Whitney U-test. Categorical variables were analyzed using the chi-squared test or Fisher's exact probability test. All baseline variables with P<0.05 on univariate Cox regression analysis were entered into multivariate Cox regression analysis to determine independent predictors of 1-year mortality.

We then defined the baseline model, which included factors significantly and independently associated with

Table 1. Subject Characteristics vs. Survival Status

Parameter	Total	Died	Survived	P-value
No. subjects (n)	457	81	376	
Age (years)	79.0 (70.0–86.0)	84.0 (78.5–90.0)	78.0 (69.0–84.0)	<0.001*
Male gender	53.4	48.2	54.5	0.298
BMI (kg/m^2)	22.4 (19.9–25.1)	20.6 (18.8–22.8)	22.7 (20.4–25.6)	<0.001*
Current or former smoking (%)	43.5	38.3	44.7	0.289
SBP (mmHg)	156 (129–188)	137 (120–175)	161 (133–189)	<0.001*
DBP (mmHg)	88 (72–107)	78 (60–94)	91 (74–110)	<0.001*
Heart rate (beats/min)	102 (86–125)	98 (81–114)	105 (87–125)	0.045*
Etiology (%)				
Ischemic heart disease	31.5	32.1	31.4	0.900
Valvular heart disease	12.4	16.1	11.7	0.297
Cardiomyopathy	13.1	13.6	13.0	0.895
Hypertension	21.4	12.4	23.4	0.021*
Arrhythmia	12.0	7.4	13.0	0.137
Serum TC (mg/dL)	157 (132–821)	147 (121–176)	159 (135–184)	0.009*
Serum TG (mg/dL)	74 (55–102)	79 (55–105)	74 (55–99)	0.797
Serum HDL-C (mg/dL)	41 (33–51)	40 (30–46)	42 (34–52)	0.017*
Serum LDL-C (mg/dL)	94 (71–116)	86 (58–112.3)	95 (73–117)	0.017*
FPG (mg/dL)	134 (108–188)	129 (110–190)	135 (108–188)	0.998
Blood HbA_{1c} (NGSP, %)	5.9 (5.4–6.7)	5.7 (5.2–6.7)	5.9 (5.5–6.7)	0.051*
BUN (mg/dL)	24.9 (17.4–35.3)	33.3 (24.1–51.3)	23.4 (16.7–33.0)	<0.001*
Serum sodium (mEq/L)	141 (138–143)	139 (137–142)	141 (139–143)	<0.001*
Serum potassium (mEq/L)	4.3 (3.8–4.7)	4.5 (4.1–5.0)	4.2 (3.8–4.6)	<0.001*
Serum creatinine (mg/dL)	1.1(0.8–1.7)	1.4 (1.0–2.5)	1.1 (0.8–1.6)	<0.001*
eGFR (mL/min/1.73 m^2)	45.3 (25.9–63.5)	30.9 (15.5–54.4)	47.0 (27.6–64.5)	<0.001*
Serum uric acid (mg/dL)	7.2 (5.5–8.8)	7.4 (5.5–9.9)	7.2 (5.5–8.6)	0.221
Serum albumin (mg/dL)	3.6 (3.2–3.9)	3.5 (3.1–3.7)	3.6 (3.2–3.9)	0.009*
Serum CRP (mg/L)	7.5 (2.2–24.7)	7.4 (1.8–47.5)	7.5 (2.2–21.8)	0.397
BNP (pg/mL)	756 (410–1,405)	971 (507–1,623)	701 (389–1,355)	0.038*
WBC ($10^3/\mu$L)	7.9 (6.1–10.6)	7.8 (6.5–10.8)	8.0 (6.1–10.5)	0.766
Total lymphocytes (/μL)	1,332 (868–1,996)	1,071 (630–1,656)	1,416 (910–2,036)	0.001*
Hb (mg/dL)	11.7 (10.1–13.5)	10.4 (9.1–12.0)	11.9 (12.0–13.8)	<0.001*
Anemia	62.9	84.0	58.4	<0.001*
LVEF (%)	50.0 (39.0–62.8)	54.5 (43.0–60.8)	49.8 (38.0–63.0)	0.319
Comorbidity (%)				
Type 2 DM	39.6	40.7	39.4	0.818
Dyslipidemia	23.4	21.0	23.9	0.566
Hypertension	63.2	59.3	64.1	0.415
AF or AFl	26.3	25.9	26.3	0.940

Data given as % or median (IQR). *P<0.05. AF, atrial fibrillation; AFl, atrial flutter; BMI, body mass index; BNP, brain-type natriuretic peptide; BUN, blood urea nitrogen; CRP, C-reactive protein; DBP, diastolic blood pressure; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; Hb, hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left ventricular ejection fraction; NGSP, National Glycohemoglobin Standardization Program; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; WBC, white blood cells.

1-year mortality on multivariate Cox regression analysis. Finally, we calculated the C-index, net reclassification improvement (NRI), and integrated discrimination improvement (IDI). Differences were considered statistically significant at P<0.05. Statistical analysis was performed using IBM SPSS Statistics 18.0 (IBM, Somers, NY, USA), R version 3.2.1 (R Project for Statistical Computing), and JMP version 5.1 (SAS Institute, Cary, NC, USA).

Results

Baseline patient characteristics are listed in **Table 1**. Eighty-one patients died (17.7%) within 1 year. The rate of cardiovascular and non-cardiovascular death was 70.4% and 29.6%, respectively. Seventy-nine patients (17.3%) were re-admitted due to heart failure within 1 year. The average age was 79 years (IQR, 70–86 years), and 53.4% of the patients were male. Patients who died were significantly older (P<0.001), whereas BMI, systolic blood pressure (SBP), diastolic blood pressure, heart rate, and the frequency of hypertensive heart disease were significantly higher in patients who survived (P<0.05). With regard to laboratory data, blood urea nitrogen, serum potassium, serum creatinine, and brain-type natriuretic peptide were

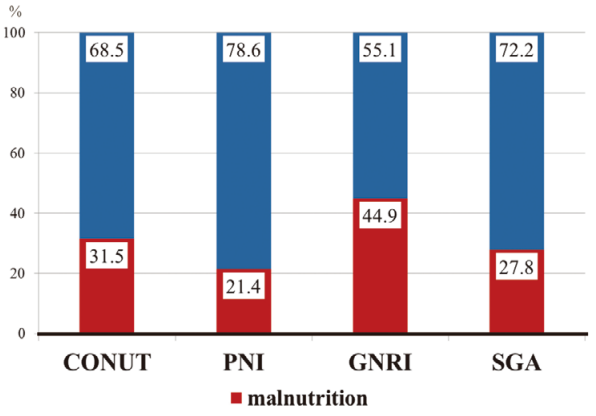

Figure 2. Distribution of malnutrition according to nutrition index. Abbreviations as in Figure 1.

significantly higher in patients who died (P<0.05), whereas serum sodium, estimated glomerular filtration rate (eGFR), serum albumin, serum total cholesterol, and hemoglobin, and total lymphocyte count were significantly lower in patients who died (P<0.05). Left ventricular ejection fraction and the frequency of systolic dysfunction were not different between the 2 groups. The prevalence of atrial fibrillation or atrial flutter was 25.9% in patients who died, 26.3% in patients who survived, and there was no significant difference between the 2 groups. The use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, β-blocker, aldosterone blocker, and diuretics at hospital admission was similar between the 2 groups (**Supplementary Table**). The frequency of malnutrition based on each nutrition index is shown in **Figure 2**. Malnutrition was observed in 31.5% based on CONUT score, 21.4% based on PNI score, 44.9% based on GNRI score, and 27.8% based on SGA score.

We compared malnutrition between the 2 groups (**Figure 3**). In patients who died, malnutrition was observed in 42.0% based on CONUT score, 32.1% based on PNI score, 60.5% based on GNRI score, and 45.7% based on SGA score. In patients who survived, malnutrition was observed in 29.3% based on CONUT score, 19.2% based on PNI score, 41.5% based on GNRI score, and 23.9% based on SGA. In all indexes, malnutrition was significantly more prevalent in patients who died than in those who survived (P<0.05; **Figure 4**).

We examined predictors of 1-year mortality on univariate and multivariate Cox regression analyses (**Table 2**). Variables with P<0.05 on univariate Cox regression analysis were included in the multivariate Cox regression analysis. Age, BMI, SBP, eGFR, and serum sodium were significantly associated with 1-year mortality in this study. Therefore, we defined the baseline model using age, BMI, SBP, eGFR, and serum sodium.

Finally, we calculated the C-index, NRI, and IDI (**Table 3**). Adding each nutrition index to the baseline model improved the prediction of 1-year mortality compared with the baseline model alone (P<0.05). The addition of CONUT, PNI, or GNRI score significantly improved NRI (P<0.05). The addition of SGA significantly improved both NRI and IDI (P<0.05).

Discussion

The principal findings of this study were as follows: (1) malnutrition was a predictor of 1-year mortality even in patients with ADHF (similar to the results obtained in a previous study involving patients with chronic heart failure); and (2) adding each nutrition index improved the prediction of 1-year outcome in hospitalized patients with ADHF.

Low BMI or sarcopenia is related to poor prognosis in patients with heart failure.[11–14] In contrast, some reports suggest that the severity of chronic disease contributes to frailty status.[15] The frailty cycle centered on sarcopenia is attracting attention with regard to chronic diseases that

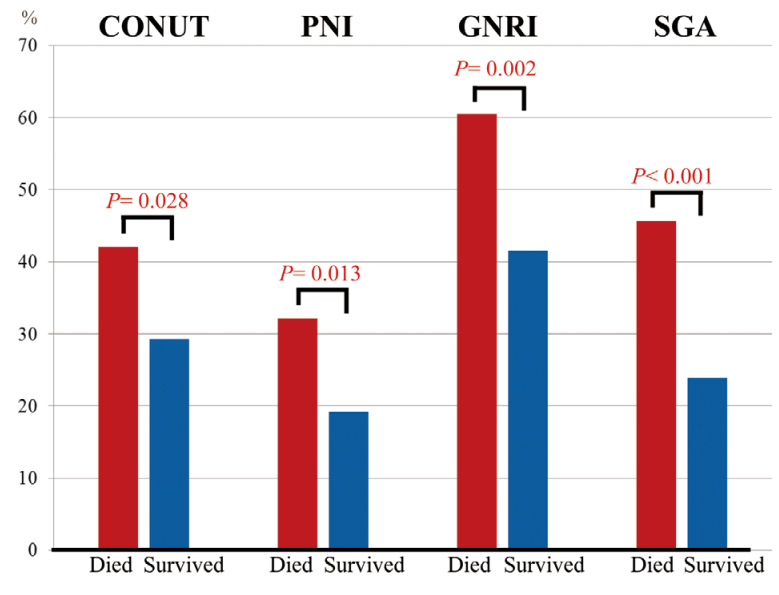

Figure 3. Prevalence of malnutrition according to nutrition index and survival status. Abbreviations as in Figure 1.

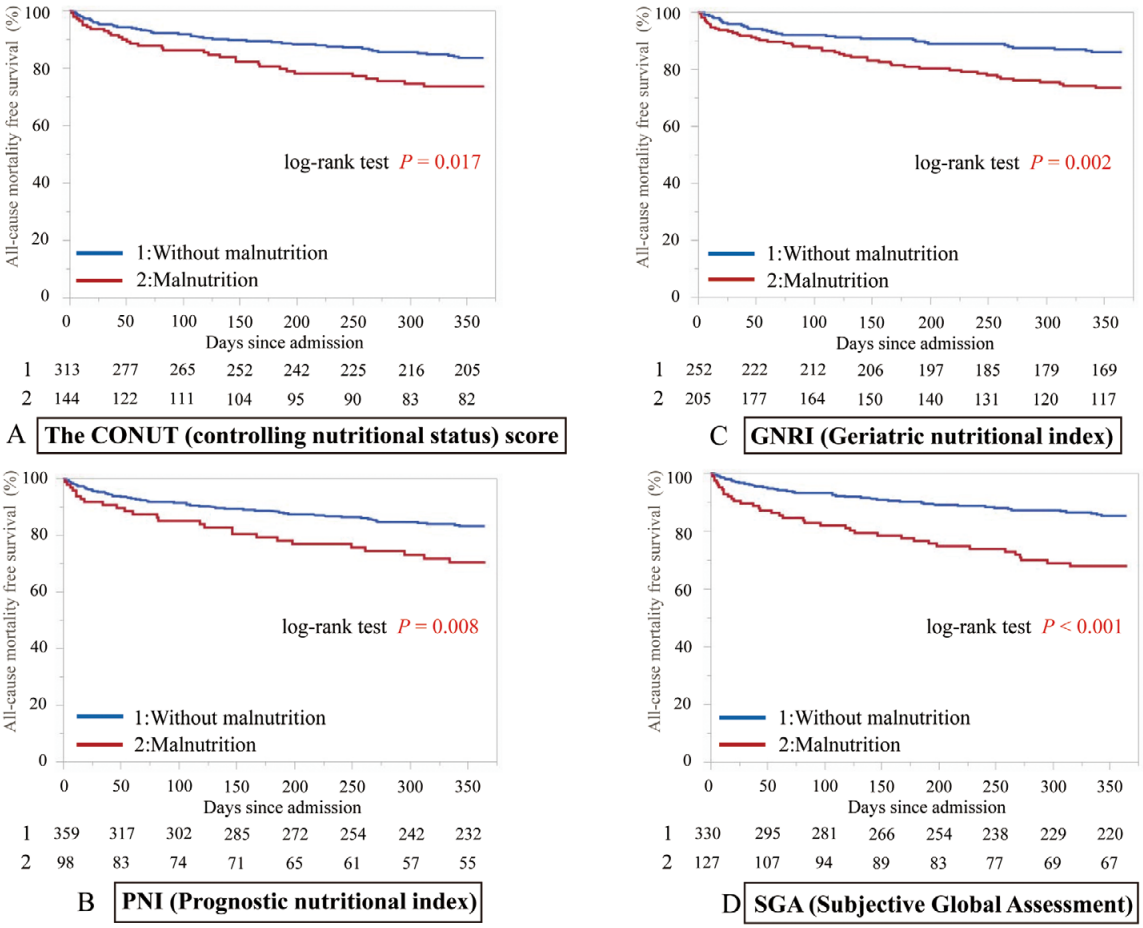

Figure 4. Kaplan-Meier curves for all-cause mortality-free survival up to 1 year according to malnutrition status using (**A**) CONUT score; (**B**) PNI score; (**C**) GNRI score; and (**D**) SGA. Abbreviations as in Figure 1.

may affect elderly individuals. Regarding the relationship between heart failure and nutrition, malnutrition was observed in 25% of hospitalized patients with chronic heart failure.[16] Although the present study also noted variation, the percentage of malnutrition was >20% for each nutrition index.

In the present study patients with malnutrition had a poorer prognosis than the subjects with adequate nutritional status. In short, malnutrition increased the risks of readmission and mortality due to heart failure.[17,18]

Heart failure is a progressive disease that worsens with repeated exacerbation and readmission, regardless of treatment. In this study, nutrition and heart failure were involved even in the acute phase of heart failure.

Plasma albumin concentration is controlled by several factors, including rate of albumin synthesis, catabolic rate, albumin distribution, and exogenous albumin loss.[19–21] Hypoalbuminemia is an independent prognostic predictor in patients with chronic heart failure.[16] Lymphocyte count reflects inflammation and the stress response.[22] Lower lymphocyte count independently predicts clinical events in patients with chronic heart failure.[23] Total cholesterol level reflects lipid metabolism and has also been reported as an independent predictor of clinical events in patients with chronic heart failure.[24] CONUT score is a nutritional screening tool used in various fields.[7] It is a screening tool used to comprehensively evaluate protein metabolism, immunity, and lipid metabolism. PNI is a nutritional screening tool that has been proposed in the field of surgery to evaluate nutritional status and immunity.[8] GNRI is often used for nutritional screening in elderly people.[9] It is also used for nutritional screening in patients undergoing hemodialysis.[25] These nutrition indexes include albumin level, total cholesterol level, and lymphocyte count proportions to some degree. Objective nutrition indexes may also provide additional prognostic information in patients with chronic heart failure.[26] Therefore, we thought that screening using these indexes at the time of admission would be useful to predict 1-year mortality in this study.

SGA is a nutrition screening tool that consists of 5 interviews and 5 physical examinations including both subjective and objective assessments. SGA has been used in patients of almost all ages and can also evaluate the risk of delayed healing or infection.[10] In addition, SGA is a subjective comprehensive evaluation that has a significant correlation with albumin level, total cholesterol level, and total lymphocyte count.[27] SGA is also related to sarcopenia.[28,29] In addition, sarcopenia has also been reported as

Table 2. Indicators of 1-Year Mortality

Parameter	Univariate analysis		Multivariate analysis	
	P-value	HR (95% CI)	P-value	HR (95% CI)
Age (years)	<0.001*	1.06 (1.04–1.09)	0.001*	1.04 (1.02–1.07)
Male gender (%)	0.249	0.88 (0.71–1.09)		
BMI (kg/m^2)	<0.001*	0.86 (0.80–0.91)	<0.001*	0.89 (0.83–0.96)
SBP (mmHg)	<0.001*	0.99 (0.98–1.00)	0.005*	0.99 (0.99–1.00)
DBP (mmHg)	<0.001*	0.98 (0.97–0.99)		
Heart rate (beats/min)	0.063	0.99 (0.98–1.00)		
Serum TC (mg/dL)	0.002*	0.99 (0.98–1.00)		
Serum TG (mg/dL)	0.617	1.00 (0.99–1.00)		
Serum HDL-C (mg/dL)	0.005*	0.97 (0.95–0.99)		
Serum LDL-C (mg/dL)	0.004*	0.99 (0.98–1.00)		
FPG (mg/dL)	0.866	1.00 (1.00–1.00)		
Blood HbA_{1c} (NGSP, %)	0.062	0.78 (0.57–1.01)		
BUN (mg/dL)	<0.001*	1.04 (1.03–1.05)		
Serum sodium (mEq/L)	0.025*	0.95 (0.92–0.99)	0.044*	0.96 (0.92–1.00)
Serum potassium (mEq/L)	<0.001*	1.62 (1.23–2.10)		
Serum creatinine (mg/dL)	<0.001*	1.23 (1.11–1.35)		
eGFR (mL/min/1.73 m^2)	<0.001*	0.98 (0.97–0.99)	0.007*	0.99 (0.97–1.00)
Serum uric acid (mg/dL)	0.091	1.08 (0.99–1.18)		
Serum albumin (mg/dL)	0.005*	0.55 (0.37–0.83)		
Serum CRP (mg/L)	0.092	1.05 (0.99–1.10)		
BNP (pg/mL)	0.036*	1.00 (1.00–1.00)		
WBC ($10^3/\mu$L)	0.216	1.00 (1.00–1.00)		
Total lymphocytes (/μL)	0.024*	1.00 (1.00–1.00)		
Hb (mg/dL)	<0.001*	0.79 (0.72–0.87)		
Anemia (%)	<0.001*	1.85 (1.40–2.55)	0.079	1.30 (0.97–1.82)
LVEF (%)	0.217	1.01 (0.99–1.03)		

*P<0.05. Abbreviations as in Table 1.

Table 3. Predictive Model Discrimination for 1-Year Mortality

Parameter	C-index (95% CI)	P-value	NRI	P-value	IDI	P-value
Baseline model	0.769 (0.716–0.823)	Ref.		Ref.		Ref.
Baseline+CONUT score	0.771 (0.717–0.825)	0.743	0.254	0.019*	0.003	0.192
Baseline+PNI	0.772 (0.718–0.826)	0.604	0.273	0.013*	0.005	0.130
Baseline+GNRI	0.770 (0.716–0.824)	0.874	0.306	0.006*	0.002	0.358
Baseline+SGA	0.779 (0.726–0.832)	0.259	0.344	0.012*	0.002	0.049*

*P<0.05. Baseline model included age, BMI, SBP, eGFR, and serum sodium. CONUT, controlling nutritional status; GNRI, geriatric nutritional index; IDI, integrated discrimination improvement; NRI, net reclassification improvement; PNI, prognostic nutrition index; SGA, subjective global assessment. Other abbreviations as in Table 1.

an independent predictor in patients with chronic heart failure.[30] SGA has also been suggested to be a useful nutritional screening tool for chronic heart failure.[31] SGA is an indicator that considers both malnutrition and sarcopenia. This simple score enables all medical staff to evaluate comprehensive nutritional status easily.[8] Moreover, this assessment does not change with timing, indicating sufficient reproducibility. Therefore, SGA might have the greatest advantage because it can be evaluated using only subjective assessments.

In chronic heart failure, nutrition occupies an important position. Stratifying nutrition status at hospital admission in patients with ADHF can lead to an early response by a nutrition support team (NST) and a multifaceted approach, such as cardiac rehabilitation from the acute phase of hospitalization. Taken together, this could reduce the poor prognosis of ADHF.

Study Limitations

This study had several limitations. First, it involved only a small number of enrolled patients and was conducted at a single center. Second, nutritional screening also differs depending on the etiology of heart failure. It was difficult, however, to analyze the data for each etiology of death because of the small number of enrolled patients. As a result, larger sample sizes and multicenter studies are needed. Finally, we evaluated these nutrition indexes only at hospital admission. Additional screening should be done during the hospital stay or at discharge.

Conclusions

Nutrition screening at hospital admission might improve the prediction of 1-year mortality in hospitalized patients with ADHF. Nutrition screening at hospital admission could be useful for the stratification of ADHF patients.

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Disclosures

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Supplementary Files

Please find supplementary file(s);
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