

Prevalence and impact of malnutrition on readmission among hospitalized patients with heart failure in China

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Abstract

Aims Malnutrition is common in patients with heart failure (HF) and is associated with poorer quality of life and increased mortality; however, an effective screening tool for malnutrition and its impact on the readmission of patients with HF is uncertain. Our objectives were to study (i) the nutritional status of Chinese hospitalized patients with HF and its impact on readmission and (ii) the validity of seven malnutrition screening tools.

Methods and results In this study, univariate and multivariate analyses of Cox proportional hazards regression were used to determine important predictors of readmission. The endpoint was readmission due to HF or non-HF. A total of 402 patients were included (66.4% male, median age 62 years [range: 20–92 years], median NT-proBNP 5,229 ng/L). During a median follow-up of 159 days, 150 patients (37%) were readmitted to the hospital. After adjusting for confounders, only malnutrition assessed using the Controlling Nutritional Status (CONUT) nutrition score was independently associated with readmission ($P = 0.0293$). A base model for predicting readmission with a C-statistic of 0.680 and subsequent addition of various nutritional screening tools improved its performance over the base model. Patients with malnutrition had a twofold increased risk of readmission.

Conclusions We found that the prevalence of malnutrition among hospitalized patients with HF in China is very high and that malnutrition significantly increases the risk of readmission in these patients. CONUT is a validated screening tool for malnutrition and may provide valuable prognostic information.

Keywords Heart failure; Malnutrition; Prognosis; Readmission; China

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Introduction

Heart failure (HF) is a multi-faceted and life-threatening syndrome that is currently considered an epidemic, with over 64 million cases of HF worldwide.¹ Heidenreich *et al.*² projected the cost of HF from 2010 to 2030, predicting increases of 200 and 80% in direct and indirect costs, respectively, with a corresponding 25% increase in HF prevalence. Data on the prevalence of HF in the Chinese population are scarce. In the China Hypertension Survey enrolling 22 58 participants, approximately 13.7 million people aged ≥ 35 years in China

had HF, accounting for 1.3% of the country's total population.³ In addition, HF is characterized by high readmission and mortality rates. According to statistics, the readmission rates of patients with HF 30 days and 1 year after discharge are approximately 25 and 70%, respectively,^{4,5} whereas the 30-day and 1-year mortality rates are 10 and 29%, respectively.⁶

Despite medical advances, the prognosis of patients with HF remains very poor.⁷ Rehospitalization is common because of worsening HF or non-cardiovascular events. Readmission is a recognized measure of quality of care and outcomes in HF,

and these patients with progressive decline in cardiac function during readmission often experience severe dyspnoea and fatigue, in addition to a significantly increased risk of death.⁸ This puts medical and economic pressure not only on patients and families but also on society and the country. A study found that readmission after discharge in 25% of patients could be avoided by early risk identification and timely intervention.⁹ Nevertheless, readmission has not been extensively studied in the Chinese population. Therefore, reducing readmission rates, especially in patients with HF, is critical for quality and fiscally focused hospitals to provide accurate health interventions.

Malnutrition is defined as the inadequate intake of nutrients, which ultimately leads to changes in body composition, resulting in reduced body function and worsening clinical outcomes.¹⁰ Recent evidence suggests that malnutrition is an important poor prognostic factor for cardiovascular disease.¹¹ The advantage of malnutrition over other clinical variables is that it is a modifiable risk factor that physicians can act on.¹²

Nutrition is the primary source of energy production for myocardial contractility and to maintaining cardiac efficiency. Malnutrition is common in patients with HF; a meta-analysis showed that the prevalence of malnutrition in these patients ranges from 16 to 90% and is associated with severe disability, morbidity, and mortality.¹³ HF-related malnutrition may be caused by the following mechanisms: low nutritional intake due to intestinal oedema and anorexia,¹⁴ hepatic dysfunction,¹⁵ cytokine-induced hypercatabolism,¹⁶ and insulin resistance.¹⁷ The most severe form of malnutrition is cardiac cachexia—a state of catabolic failure associated with inflammation and neurohormonal activation that is commonly thought to mediate poor outcomes.^{18,19} Nutritional interventions may prevent complications and improve the quality of life of patients.²⁰ Nutritional assessment is the first step in nutritional therapy, and nutritional screening—to determine the presence or absence of malnutrition or nutritional risk in patients with HF using a rapid, accurate approach—is the primary aspect of nutritional management.

Current guidelines recommend assessing the nutritional status of patients with HF²¹; however, there is no gold standard or scientific consensus on the nutritional assessment of these patients. In fact, it is believed that malnutrition is currently under-diagnosed and therefore under-treated. In the absence of a universally accepted definition of malnutrition and a 'gold standard' for its diagnosis, many nutritional screening and assessment tools have been developed. Sze *et al.*²² first performed a comprehensive malnutrition assessment in patients with chronic HF and compared the short-term prognostic significance of nine commonly used malnutrition tools, finding that malnutrition measured using each tool was independently associated with poor prognosis. To the best of our knowledge, there are few studies on the impact of nutritional status on prognosis (especially readmis-

sion) in Chinese hospitalized patients with HF, and no study has yet compared the effectiveness of multiple nutritional screening tools. Given the diverse population and controversial results, we believe it is critical to explore the impact of nutritional status on readmission and to determine effective nutritional screening tools in Chinese hospitalized patients with HF. We believe that these findings will lead to new advances in this field.

Our objectives were to study (i) the nutritional status of Chinese hospitalized patients with HF and its impact on readmission and (ii) the validity of seven malnutrition screening tools.

Materials and methods

Study population

This was a prospective cohort study that employed a convenience sampling method. It included 433 consecutive patients hospitalized for HF from our hospital between July 2020 and August 2021. Only patients aged 18 years or older were included. HF was diagnosed according to the recommendations of the Chinese guidelines for the diagnosis and treatment of HF.²³ Cardiac function had to be characterized by at least one of the following: a left ventricular ejection fraction (LVEF) of <40%, a plasma B-type natriuretic peptide (BNP) of >35 ng/L, or a plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) of >125 ng/L. Patients who were pregnant or had severe chronic liver or kidney disease, autoimmune or chronic inflammatory disease, or severe cognitive impairment such as Alzheimer's disease and psychiatric disorders were excluded. This study complied with the Declaration of Helsinki and was approved by the Hospital Research Ethics Committee (No. KYLL-202107-031). Informed consent was obtained from all the participants prior to any study-related activities.

Malnutrition evaluation

Based on the description of nutritional screening tools by Sze *et al.*,²² seven commonly used tools—categorized into simple tools and single biochemical assessments—were used in this study.

The simple tools used were as follows:

i Controlling Nutritional Status (CONUT)

CONUT was developed by Ulibarri *et al.*²⁴ in 2005 as an inpatient nutritional screening tool combining serum albumin, cholesterol, and total lymphocyte count, normal nutritional status: score of 0–1; mild, moderate, and severe malnutrition: scores of 2–4, 5–8, and 9–12.

ii Geriatric Nutritional Risk Index (GNRI)

GNRI was proposed by Bouillanne *et al.*²⁵ in 2005 as a nutritional assessment method integrating albumin and body weight. Unlike NRI, the ideal weight according to the Lorentz formula. GNRI was calculated using the following formula: $[1.489 \times \text{albumin (g/L)}] + [41.7 \times \text{current weight[kg]/ideal weight[kg]}]$. According to the Lorenz formulas,²⁵ we set weight: height (cm): $100 - ([\text{height (cm)} - 150]/4)$ for men and height (cm): $100 - ([\text{height (cm)} - 150]/2.5)$ for women, current body weight/ideal body weight = 1 when current body weight exceeded ideal body weight,²⁶ normal nutritional status: GNRI >98, mild, moderate, and severe malnutrition: GNRI 92–98, 82–91, <82.

iii Prognostic Nutritional Index (PNI)

First proposed by Buzby *et al.*²⁷ in 1980, it was initially used to assess the nutritional status of patients and the level of risk present in gastrointestinal surgery. PNI was calculated using the formula $10 \times \text{serum albumin (g/dl)} + 0.005 \times \text{total lymphocyte count (mm}^3)$.²⁷ Normal nutritional status: >38; moderate and severe malnutrition: 35–38, <35. Note that there is no mild category for the PNI. This may affect the accuracy of the results.

iv Nutritional Risk Index (NRI)

The NRI was originally used by Buzby *et al.*²⁷ as a nutritional scoring tool combining albumin and body weight. Specific formula: $[1.519 \times \text{albumin (g/L)}] + [41.7 \times \text{current weight[kg]/ideal weight[kg]}]$. Ideal body weight was calculated using the following formula: $22 \times \text{square of height in meters}$,²⁸ normal nutritional status: NRI ≥ 100 , mild, moderate, and severe malnutrition: NRI 97.5–100, 83.5–97.5, <83.5.

The laboratory tests used were as follows:

Based on a previous study,²² we similarly chose to examine the predictive value of a single laboratory metric for readmission based on the components of the CONUT score.

i Serum cholesterol concentration (mmol/L)

According to the CONUT score cut-off, nutritional status: serum cholesterol concentration >4.65, mild, moderate, and severe malnutrition: serum cholesterol concentration 3.62–4.65, 2.59–3.61, <2.59.²⁴

ii Serum albumin concentration (g/L)

According to the CONUT score cut-off, nutritional status: serum albumin concentration ≥ 35 , mild, moderate, and severe malnutrition: serum albumin concentration 30–34, 25–29, <25.²⁴

iii Serum total lymphocyte count ($\times 10^9/L$)

According to the CONUT score cut-off, nutritional status: serum total lymphocyte count ≥ 1.6 , mild, moderate, and severe malnutrition: serum total lymphocyte count 1.20–1.59, 0.80–1.19, <0.80.²⁴

Data collection

The following information was collected within 24 h of the patient's admission: (i) basic information: age, sex, New York Heart Association (NYHA), body mass index (BMI); (2) disease status: admission heart rate, admission blood pressure, HF aetiology, Charlson Co-morbidity Index (CCI), medication use; (iii) laboratory data: serum albumin, glucose, N-terminal B natriuretic peptidogen (NT-proBNP), serum potassium, haemoglobin, cholesterol, lymphocyte count, etc.; (iv) ancillary tests: electrocardiogram, echocardiogram. BMI was calculated for all patients, defined as the body mass (in kilograms) divided by the square of the body height (in meters). CCI, a weighted index that explains the presence of 17 comorbidities.²⁹

Endpoints and follow-up

The endpoint was readmission due to HF or non-HF. We defined readmission as an unplanned readmission for any reason from the date of discharge, with a length of stay of at least 24 h, with the patient's readmission starting from the date of admission to the hospital to confirm the disease in days.

Patients were routinely treated for HF during hospitalization and discharged with a 6-month telephonic follow-up by a dedicated investigator with the patient or (if deceased) a family member. Follow-up visits of approximately 15–20 min each occurred monthly between August 2020 and November 2021. The date and outcomes of the follow-up (survival, readmission, and death) and the date of readmission were recorded.

We excluded hospital stays that were shorter than 1 day. If the patient had multiple readmissions, only the first readmission was considered. The median follow-up time for all patients was 159 days (IQR, 107–205 days).

Statistical analysis

All the statistical analyses were performed using IBM SPSS/WIN version 26.0 and R 4.1.1. Measures that conformed to normal distribution were expressed as mean \pm standard deviation, and group comparisons were made using independent Student's *t*-test; measures that did not conform to normal distribution were expressed as median [M (P25, P75)], and group comparisons were made using Mann–Whitney *U* test;

Table 1 Baseline characteristics of patients with HF

Factor	HF patients (n = 402)	Readmission (n = 150)	No readmission (n = 252)	P value
Age (years)	61.78 ± 13.73	63.93 ± 12.59	60.41 ± 14.24	0.022
Sex (male)	267(66.4%)	102(68%)	165(65.5%)	0.704
BP systolic (mm Hg)	125.35 ± 21.53	121.28 ± 21.06	127.77 ± 21.46	<0.001
BP diastolic (mm Hg)	74.85 ± 14.00	73.32 ± 14.01	75.75 ± 13.95	0.074
HR (bpm)	80.07 ± 18.11	84.45 ± 19.32	79.25 ± 7.34	0.206
BMI	25.50 ± 4.49	25.16 ± 4.95	25.70 ± 4.18	0.186
NYHA				0.004
II	113(28.1%)	32(21.3%)	81(32.1%)	
III	190(47.3%)	72(48.0%)	118(46.8%)	
IV	99(24.6%)	46(30.7%)	53(21.0%)	
LVEF (%)				0.182
<40%	259(64.4%)	104(69.3%)	155(61.5%)	
40–50%	47(11.7%)	13(8.7%)	34(13.5%)	
>50%	96(23.9%)	33(22.0%)	63(25.0%)	
First HF episode	298(74.1%)	102(68.0%)	196(77.8%)	0.161
Aetiology of HF				0.082
CHD	218(54.2%)	92(61.3%)	126(50.0%)	
DCM	66(16.4%)	22(14.7%)	44(17.5%)	
Other types of cardiomyopathy	118(29.4%)	36(24.0%)	82(32.5%)	
Co-morbidities				
Diabetes mellitus	148(36.8%)	62(41.3%)	86(34.1%)	0.147
Hypertension	217(54.0%)	85(56.7%)	132(52.4%)	0.404
Hyperlipidaemia	22(5.5%)	10(6.7%)	12(4.8%)	0.417
Atrial fibrillation	105(26.1%)	35(23.3%)	70(27.8%)	0.327
CCI	2.34 ± 1.26	2.63 ± 1.39	2.16 ± 1.14	<0.001
Medications				
ACEI	19(4.7%)	5(3.3%)	14(5.6%)	0.352
ARB	27(6.7%)	9(6.0%)	18(7.1%)	0.549
ARNI	230(57.2%)	79(52.7%)	151(59.9%)	0.157
ACEI/ARB/ARNI	273(67.9%)	91(60.7%)	182(72.2%)	0.013
BB	341(84.8%)	123(82.0%)	218(86.5%)	0.220
MRA	315(78.4%)	116(77.3%)	199(79.0%)	0.880
ACEI/ARB/ARNI + BB + MRA	212(52.7%)	71(47.3%)	141(56.0%)	0.023
Digoxin	30(7.5%)	7(4.7%)	23(9.1%)	0.116
Diuretic	337(83.8%)	132(88.0%)	205(81.3%)	0.067
Stains	275(68.4%)	102(68.0%)	173(68.7%)	0.892
Laboratory data				
log[NT-proBNP] (ng/L)	3.33 ± 0.61	3.55 ± 0.58	3.19 ± 0.59	<0.001
RDW	13.71 ± 1.98	14.04 ± 2.34	13.51 ± 1.70	0.002
HGB	134.30 ± 23.50	127.92 ± 23.05	138.10 ± 22.97	<0.001
NA	141.38 ± 3.50	140.81 ± 3.57	141.72 ± 3.42	0.008
K	4.18 ± 0.48	4.19 ± 0.55	4.18 ± 0.44	0.968
MG	0.90 ± 0.21	0.88 ± 0.11	0.91 ± 0.25	0.271
CR	108.54 ± 77.56	126.68 ± 96.45	97.74 ± 61.44	0.001
CYS-C	1.45 ± 0.67	1.66 ± 0.77	1.33 ± 0.58	<0.001
GLU	6.00 ± 2.31	6.38 ± 2.92	5.77 ± 1.83	0.013
Malnutrition tools				
PNI (malnourished)	23(5.7%)	14(9.3%)	9(3.6%)	0.018
GNRI (malnourished)	81(21.1%)	45(30.0%)	36(14.3%)	<0.001
NRI (malnourished)	158(39.3%)	71(47.3%)	87(34.5%)	0.006
CONUT (malnourished)	273(67.9%)	126(84.0%)	147(58.3%)	<0.001
Cholesterol (malnourished)	314(78.1%)	127(84.7%)	187(74.2%)	0.021
Albumin (malnourished)	56(13.9%)	30(20.0%)	26(10.3%)	0.006
Lymphocyte (malnourished)	221(55.0%)	105(70.0%)	116(46.0%)	<0.001

ACEI, angiotensin-converting enzyme Inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor enkephalinase inhibitor; BB, β-blocker; BMI, body mass index; BP, blood pressure; CCI, Charlson Co-morbidity Index; CHD, coronary heart disease; CR, creatinine; CYS-C, serum cystatin C; DCM, dilated cardiomyopathy; GLU, glucose; HGB, haemoglobin; HR, heart rate; K, potassium; LVEF, left ventricular ejection fraction; MG, magnesium; MRA, mineralocorticoid receptor antagonist; NA, sodium; NYHA, New York Heart Association classification; RDW, red blood cell distribution width.

categorical data are expressed as [n(%)]. The chi-square test was used to compare proportions between groups. A Cox proportional hazards regression analysis was performed to identify predictors of readmission and adjust for possible confounding factors. Significant variables with P values <0.05 in the univariate analysis, which were known predictors of readmission in patients with HF, were included in the multifactorial analysis.

Time-to-event data are presented graphically using Kaplan–Meier curves. Log-rank tests were used to compare survival between groups. To further investigate the relationship between the degree of malnutrition and readmission, we used a multifactorial analysis to calculate the hazard ratio (HR) for each malnutrition screening tool as a continuous and dichotomous variable for further prediction analysis.

In addition, to determine which malnutrition screening tools are more effective predictors of readmission, we created a common underlying model including age, log [NT-proBNP], and systolic blood pressure (SBP) and cystatin C (Cys-C) levels; these variables were all found to be significant predictors of readmission in the multifactorial analysis. To reduce the confounding effect of other factors in the underlying model, we standardized the model so that we could make a fair comparison of the prognostic performance of the different malnutrition screening tools. We added each screening tool to the base model and used Harrell's C-statistic to assess model discrimination in the survival analysis. A C-statistic of 0.5 indicated no discrimination, whereas 1 indicated full discrimination. The net reclassification improvement (NRI) was used to determine if there were significant differences between the base model and the models that included different malnutrition screening tools. All P values were two-sided, and values <0.05 were considered significant.

Results

Baseline characteristics

A total of 433 consecutively hospitalized patients with HF were included in the study. No patients were lost to follow-up because we conducted regular telephone follow-up and checked with the hospital database. A final total of 402 patients were included for analysis, and we excluded 31 patients who died without readmission.

Most patients were male and elderly, with a median NT-proBNP of 5229 (48–63 990) ng/L; more than 70% had severe symptoms (NYHA class III/IV) (*Table 1*). Those patients who were readmitted were older, had more severe symptoms (NYHA class III/IV), and were more likely to be malnourished at baseline compared with those who did not have a readmission at 6 months. They also had higher NT-proBNP concentra-

tions, lower admission systolic blood pressure, and more comorbidities (*Table 1*).

Relation between malnutrition and readmission

During the follow-up period, 37% of patients were readmitted. The clinical variables included in the multivariate analysis used to predict readmission are shown in *Table S1*. All malnutrition screening tools, evaluated separately as binary and continuous variables in the multivariate analysis, were found to be significant predictors of readmission in the CONUT malnutrition screening tools (*Table 2*). A basic model (including age, log[NT-proBNP], SBP, and CYSC) predicted readmission with a C-statistic of 0.680 (*Table 3*). When each malnutrition tool was added individually, the model fit was better, and the C-statistics were all improved compared to the base model. The two variables with the greatest and statistically significant improvement in model performance compared with the base model were: in the simple tool, the CONUT score (C-statistic = 0.693); and in the single laboratory test, when lymphocyte count was used as a continuous variable (C-statistic = 0.686).

Kaplan–Meier curves illustrate the relation between malnutrition screening tools and readmission. According to the CONUT score, patients with at least moderate malnutrition had twice the readmission risk of non-malnourished patients (*Figure S1*). The 6-month readmission rate was much higher in patients with the worst nutritional status (9.3–84.7%) than in those with the best nutritional status (3.6–74.2%).

Discussion

To our knowledge, our study is the first comprehensive comparison of several common malnutrition screening tools in Chinese hospitalized patients with HF. The results of this study showed a very high prevalence of malnutrition (5.7–78.1%) in Chinese hospitalized patients with HF; this prevalence varied depending on the screening tool used. The pathophysiological mechanism of malnutrition is unclear. A possible reason is that patients with HF often have decreased cardiac function, increased peripheral circulatory resistance, increased pulmonary circulatory pressure, and inadequate organ perfusion, resulting in gastrointestinal stasis. This, in turn, leads to low nutritional intake and consequent altered systemic basal metabolism increased consumption and high consumption and low uptake, resulting in a high prevalence of malnutrition.^{30,31} Malnutrition exacerbates fluid retention and impaired molecular synthesis in patients with HF, leading to an irreversible cachectic state.³² Therefore, early identification of malnutrition in patients with HF may enable the initiation of potential treatment to prevent the development of cachexia. Healthcare providers need to pay attention to and

Table 2 Multivariable Cox proportional hazards regression analyses of malnutrition tools predicting readmission

	HR (95% CI)	Wald χ^2	P value
Laboratory tests			
Albumin (g/L)	1.315(0.671 ~ 2.577)	0.640	0.424
Albumin (malnourished compared with not malnourished)	1.211(0.779 ~ 1.882)	0.723	0.394
Cholesterol (mmol/L)	1.220(1.013 ~ 1.470)	4.410	0.036
Cholesterol (malnourished compared with not malnourished)	1.311(0.829 ~ 2.074)	1.346	0.246
Lymphocyte ($\times 10^9/L$)	1.257(0.893 ~ 1.770)	1.716	0.189
Lymphocyte (malnourished compared with not malnourished)	1.618(1.103 ~ 2.375)	6.052	0.014
Simple tools			
CONUT	1.893(1.102 ~ 3.250)	5.336	0.021
CONUT (malnourished compared with not malnourished)	2.183(1.372 ~ 3.472)	10.89	0.001
GNRI	1.556(0.963 ~ 2.512)	3.276	0.071
GNRI (malnourished compared with not malnourished)	1.325(0.897 ~ 1.958)	1.989	0.158
PNI	1.183(0.653 ~ 2.144)	0.314	0.579
PNI (malnourished compared with not malnourished)	1.183(0.653 ~ 2.144)	0.314	0.579
NRI	0.994(0.001 ~ 0.668)	0.001	0.976
NRI (malnourished compared with not malnourished)	1.006(0.704 ~ 1.436)	0.001	0.976

Table 3 Addition of malnutrition tools and its impact on predict readmission

Model	C-statistics (95% CI)	NRI	P value
Base model	0.680(0.639–0.721)	-	-
Laboratory tests			
Base + LYM	0.686(0.645–0.727)	0.2142(–0.0671–0.1866)	<0.001
Base + CHO	0.687(0.646–0.729)	0.0094(–0.0450–0.1247)	0.1717
Base + ALB	0.683(0.642–0.724)	–0.0106(–0.0433–0.1291)	-
Simple tools			
Base + PNI	0.682(0.640–0.723)	0.0013(–0.0323–0.0823)	0.2330
Base + GNRI	0.685(0.643–0.728)	–0.0229(–0.0849–0.1112)	-
Base + NRI	0.681(0.640–0.723)	–0.0186(–0.0557–0.1013)	-
Base + CONUT	0.693(0.653–0.734)	0.0744(–0.0411–0.2663)	0.0293

ALB, albumin; CHO, cholesterol; LYM, lymphocyte.

intervene in malnutrition in patients with HF; this plays an important role in preventing deterioration and improving prognosis.

The findings of our study differ from those of most previous studies in that we included readmission as a primary outcome indicator, with the aim of exploring the impact of malnutrition on readmission in hospitalized patients with HF and screening for tools that could better predict readmission. Readmission and death are the two most common adverse prognoses in patients with HF, and death is the most common outcome indicator in the current study; however, readmission has been shown in numerous studies to significantly increase the risk of death.^{33–36} Therefore, we believe that the use of readmission as an outcome indicator complements previous studies by better confirming and building on findings from other HF cohort studies that malnutrition is a significant predictor of poor outcomes, either readmission or death.

All patients included in this study had a clear clinical diagnosis of HF and were discharged after receiving guideline-directed HF treatment for improvement. After 6 months of follow-up, malnutrition was found to be a valid predictor of readmission in these patients with HF. In a causal analysis, we found that malnutrition—as determined by serum cholesterol level, CONUT score as a continuous vari-

able and total lymphocyte count as a categorical variable—was associated with readmission. Lim *et al.*³⁷ found that the incidence of readmission in older adults at risk for malnutrition was increased by threefold to fourfold. Moreover, the results of a prospective cohort study showed that malnutrition was an independent predictor of readmission in older adults, which is consistent with the results of the present study. Therefore, healthcare providers should perform nutritional assessment and monitoring upon admission of patients with HF and, to reduce readmission, promptly intervene if there is a risk of malnutrition.

In an analysis of the impact of malnutrition on prognostic outcomes in patients with HF, we found that malnutrition—assessed only using the CONUT score and total lymphocyte count—improved the performance of the base model and better predicted readmission, although only by a small degree. This may be owing to malnutrition being associated with variables that form part of the underlying model, such as increasing age and worsening HF.³⁸ By comparing the base model and new models, we determined that the CONUT score and total lymphocyte count were statistically significant valid predictors of readmission—with the greatest improvement observed with their addition to the base model. In further continuous and dichotomous analyses of the screening

tools, the CONUT score was the best predictor of readmission regardless of classification; therefore, we considered the CONUT score to be the most valuable. Currently, biochemical parameters,³⁹ such as albumin and prealbumin level and BMI, have long been used individually to evaluate nutritional status. However, the value of single nutritional indicators was not found in this study, and Sze *et al.*²² found that serum albumin had a prognostic value similar to that of more complex malnutrition tools when performing laboratory indicator evaluations. To the best of our knowledge, albumin has also been shown to be a valid single indicator for predicting patient mortality outcomes in various other studies; however, the present study found that albumin was not a valid tool for readmission, possibly because it was conducted with readmission as the primary outcome indicator, which remains to be validated in more high-quality studies.

This study has several limitations. First, it was a single-centre study conducted in China with a limited sample size, which requires further expanded external validation. Second, some of the patients with HF were treated with statins, which can influence the cholesterol levels. A recent study suggests that statin use affects the efficacy of CONUT,⁴⁰ but previous findings are inconsistent. The results of the present study suggest that the effect of statins on CONUT was less, probably because statins were used in similar proportions in all groups in relation to the indications of patients with ischaemic heart disease. Further studies on the effect of statins on CONUT performance are needed in the future. Finally, this study was only conducted over 6 months, which is a relatively short period; hence, we cannot comment on the long-term prognostic significance of malnutrition in patients with HF. However, studies^{11,41} have shown that more than 50% of patients with a first diagnosis of chronic HF in a real-world Chinese setting do not seek healthcare assistance until they become overly symptomatic; therefore, it is more clinically relevant to study the 6-month readmission risk in Chinese patients with HF and more in line with the actual Chinese national situation.

Conclusions

This study found a very high prevalence of malnutrition among hospitalized patients with HF in China. Furthermore,

malnutrition as measured using the CONUT malnutrition tool was a strong predictor of readmission in these patients. CONUT is a valid tool for predicting readmission. Therefore, it is necessary for healthcare professionals to strengthen the detection of poor nutritional status and to enhance education on healthy eating habits and lifestyles provided to patients with HF, while optimizing their treatment, to reduce the adverse health effects of malnutrition.

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Conflict of interest

We declare that we have no conflicts of interest.

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Supporting information

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

Table S1. Multivariable Cox proportional hazards regression analyses predicts readmission.

Figure S1. Kaplan–Meier curves illustrating the relation between malnutrition tools and readmission.

References

1. Savarese G, Becher PM, Lund LH, Seferovic P, Rosano GMC, Coats AJS. Global burden of heart failure: A comprehensive and updated review of epidemiology. *Cardiovasc Res.* 2022; cvac013.
2. Heidenreich PA, Trogdon JG, Khavjou OA, Butler J, Dracup K, Ezekowitz MD, Finkelstein EA, Hong Y, Johnston SC, Khara A, Lloyd-Jones DM, Nelson SA, Nichol G, Orenstein D, Wilson PWF, Woo YJ. Forecasting the future of cardiovascular disease in the United States. *Circulation.* 2011; **123**: 933–944.
3. Hao G, Wang X, Chen Z, Zhang L, Zhang Y, Wei B, Zheng C, Kang Y, Jiang L, Zhu

- Z, Zhang J, Wang Z, Gao R, for the China Hypertension Survey Investigators. Prevalence of heart failure and left ventricular dysfunction in China: The China hypertension survey, 2012–2015. *Eur J Heart Fail.* 2019; **21**: 1329–1337.
4. Dharmarajan K, Hsieh AF, Kulkarni VT, Lin Z, Ross JS, Horwitz LI, Kim N, Suter LG, Lin H, Normand SLT, Krumholz HM. Trajectories of risk after hospitalization for heart failure, acute myocardial infarction, or pneumonia: Retrospective cohort study. *BMJ.* 2015; **350**: h411.
 5. Dharmarajan K, Hsieh AF, Lin Z, Bueno H, Ross JS, Horwitz LI, Barreto-Filho JA, Kim N, Bernheim SM, Suter LG, Drye EE, Krumholz HM. Diagnoses and timing of 30-day readmissions after hospitalization for heart failure, acute myocardial infarction, or pneumonia. *JAMA.* 2013; **309**: 355–363.
 6. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Cheng S, Delling FN, Elkind MSV, Evenson KR, Ferguson JF, Gupta DK, Khan SS, Kissela BM, Knutson KL, Lee CD, Lewis TT, Liu J, Loop MS, Lutsey PL, Ma J, Mackey J, Martin SS, Matchar DB, Mussolino ME, Navaneethan SD, Perak AM, Roth GA, Samad Z, Satou GM, Schroeder EB, Shah SH, Shay CM, Stokes A, VanWagner LB, Wang NY, Tsao CW, on behalf of the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2021 update. *Circulation.* 2021; **143**: e254–e743.
 7. Agra Bermejo RM, González Ferreiro R, Varela Román A, Gómez Otero I, Kreidieh O, Conde Sabaris 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.
 8. Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M, Nodari S, Lam CSP, Sato N, Shah AN, Gheorghiu M. The global health and economic burden of hospitalizations for heart failure: Lessons learned from hospitalized heart failure registries. *J Am Coll Cardiol.* 2014; **63**: 1123–1133.
 9. Brown JR, Alonso A, Mazimba S, Warman EN, Bilchick KC. Improved 30 day heart failure rehospitalization prediction through the addition of device-measured parameters. *ESC Heart Failure.* 2020; **7**: 3762–3771.
 10. Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, Compber C, Correia I, Higashiguchi T, Holst M, Jensen GL, Malone A, Muscaritoli M, Nyulasi I, Pirlich M, Rothenberg E, Schindler K, Schneider SM, de van der Schueren MAE, Sieber C, Valentini L, Yu JC, van Gossom A, Singer P. ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr.* 2017; **36**: 49–64.
 11. Joaquín C, Alonso N, Lupón J, de Antonio M, Domingo M, Moliner P, Zamora E, Codina P, Ramos A, González B, Rivas C, Cachero M, Puig-Domingo M, Bayes-Genis A. Mini nutritional assessment short form is a morbi-mortality predictor in outpatients with heart failure and mid-range left ventricular ejection fraction. *Clin Nutr.* 2020; **39**: 3395–3401.
 12. Freeman AM, Morris PB, Barnard N, Esselstyn CB, Ros E, Agatston A, Devries S, O'Keefe J, Miller M, Ornish D, Williams K, Kris-Etherton P. Trending cardiovascular nutrition controversies. *J Am Coll Cardiol.* 2017; **69**: 1172–1187.
 13. 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.
 14. Krack A, Sharma R, Figulla HR, Anker SD. The importance of the gastrointestinal system in the pathogenesis of heart failure. *Eur Heart J.* 2005; **26**: 2368–2374.
 15. Valentová M, von Haehling S, Doehner W, Murín J, Anker SD, Sandek A. Liver dysfunction and its nutritional implications in heart failure. *Nutrition.* 2013; **29**: 370–378.
 16. Kalantar-Zadeh K, Anker SD, Horwich TB, Fonarow GC. Nutritional and anti-inflammatory interventions in chronic heart failure. *Am J Cardiol.* 2008; **101**: 89E–103E.
 17. von Haehling S, Doehner W, Anker SD. Nutrition, metabolism, and the complex pathophysiology of cachexia in chronic heart failure. *Cardiovasc Res.* 2007; **73**: 298–309.
 18. Pittman JG, Cohen P. The pathogenesis of cardiac cachexia. *N Engl J Med.* 1964; **271**: 453–460.
 19. Anker SD, Ponikowski P, Varney S, Chua TP, Clark AL, Webb-Peploe KM, Harrington D, Kox WJ, Poole-Wilson PA, Coats AJS. Wasting as independent risk factor for mortality in chronic heart failure. *Lancet (British edition).* 1997; **349**: 1050–1053.
 20. 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. *JACC: Heart Fail.* 2018; **6**: 476–486.
 21. van der Meer P, Gaggin HK, Dec GW. ACC/AHA versus ESC guidelines on heart failure: JACC guideline comparison. *J Am Coll Cardiol.* 2019; **73**: 2756–2768.
 22. Sze S, Pellicori P, Zhang J, Weston J, Clark AL. The impact of malnutrition on short-term morbidity and mortality in ambulatory patients with heart failure. *Am J Clin Nutr.* 2021; **113**: 695–705.
 23. Heart Failure Group of the Cardiovascular Disease Branch of the Chinese Medical Association, Heart Failure Specialty Committee of the Chinese Physicians Association, Editorial Board of the Chinese Journal of Cardiovascular Disease. Chinese heart failure diagnosis and treatment guidelines 2018. *Chin J Cardiol.* 2018; 760–789.
 24. Ignacio DUJ, González-Madroño A, de Villar NG, González P, González B, Mancha A, Rodríguez F, Fernández G. CONUT: A tool for controlling nutritional status. First validation in a hospital population. *Nutr Hosp.* 2005; **20**: 38–45.
 25. Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I, Benazeth S, Cynober L, Aussel C. Geriatric nutritional risk index: A new index for evaluating at-risk elderly medical patients. *Am J Clin Nutr.* 2005; **82**: 777–783.
 26. Cereda E, Pedrolli C. The geriatric nutritional risk index. *Curr Opin Clin Nutr Metab Care.* 2009; **12**: 1–7.
 27. Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. *Am J Surg.* 1980; **139**: 160–167.
 28. Raposeiras Roubín S, Abu Assi E, Cespon Fernandez M, Barreiro Pardo C, Lizancos Castro A, Parada JA, Pérez DD, Blanco Prieto S, Rossello X, Ibanez B, Íñiguez Romo A. Prevalence and prognostic significance of malnutrition in patients with acute coronary syndrome. *J Am Coll Cardiol.* 2020; **76**: 828–840.
 29. Ondeck NT, Bovonratwet P, Ibe IK, Bohl DD, McLynn RP, Cui JJ, Baumgaertner MR, Grauer JN. Discriminative ability for adverse outcomes after surgical management of hip fractures: A comparison of the Charlson comorbidity index, Elixhauser comorbidity measure, and modified frailty index. *J Orthop Trauma.* 2018; **32**: 231–237.
 30. Valentova M, von Haehling S, Bauditz J, Doehner W, Ebner N, Bekfani T, Elsner S, Slizuk V, Scherbakov N, Murín J, Anker SD, Sandek A. Intestinal congestion and right ventricular dysfunction: A link with appetite loss, inflammation, and cachexia in chronic heart failure. *Eur Heart J.* 2016; **37**: 1684–1691.
 31. Andreae C, Strömberg A, Årestedt K. Prevalence and associated factors for decreased appetite among patients with stable heart failure. *J Clin Nurs.* 2016; **25**: 1703–1712.
 32. Habaybeh D, de Moraes MB, Slee A, Avgerinou C. Nutritional interventions for heart failure patients who are malnourished or at risk of malnutrition or cachexia: A systematic review and meta-analysis. *Heart Fail Rev.* 2021; **26**: 1103–1118.
 33. Labrosciano C, Horton D, Air T, Tavella R, Beltrame JF, Zeitz CJ, Krumholz HM, Adams RJT, Scott IA, Gallagher M, Hossain S, Hariharaputhiran S, Ranasinghe I. Frequency, trends and in-

- stitutional variation in 30-day all-cause mortality and unplanned readmissions following hospitalisation for heart failure in Australia and New Zealand. *Eur J Heart Fail.* 2021; **23**: 31–40.
34. Constantinou P, Pelletier-Fleury N, Olié V, Gastaldi-Ménager C, JuillÈre Y, Tuppin P. Patient stratification for risk of readmission due to heart failure by using nationwide administrative data. *J Card Fail.* 2021; **27**: 266–276.
35. Gao S, Yin G, Xia Q, Wu G, Zhu J, Lu N, Yan J, Tan X. Development and validation of a nomogram to predict the 180-day readmission risk for chronic heart failure: A multicenter prospective study. *Front Cardiovasc Med.* 2021; **8**: 731730.
36. Ma C, Zhou W. Predictors of rehospitalization for community-dwelling older adults with chronic heart failure: A structural equation model. *J Adv Nurs.* 2020; **76**: 1334–1344.
37. 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**: 345–350.
38. Zupo R, Castellana F, Guerra V, Donghia R, Bortone I, Griseta C, Lampignano L, Dibello V, Lozupone M, Coelho-Júnior HJ, Solfrizzi V, Giannelli G, de Pergola G, Boeing H, Sardone R, Panza F. Associations between nutritional frailty and 8-year all-cause mortality in older adults: The Salus in Apulia study. *J Intern Med.* 2021; **290**: 1071–1082.
39. Miao J, Quan X, Zhang C, Zhu H, Ye M, Shen L, Guo QH, Zhu GY, Mei QJ, Wu YX, Li SG, Zhou HL. Comparison of two malnutrition risk screening tools with nutritional biochemical parameters, BMI and length of stay in Chinese geriatric inpatients: A multicenter, cross-sectional study. *BMJ Open.* 2019; **9**: e022993.
40. Kinugasa Y, Sota T, Kamitani H, Nakayama N, Nakamura K, Hirai M, Yanagihara K, Kato M, Ono T, Takahashi M, Matsuo H, Matsukawa R, Yoshida I, Kakinoki S, Yonezawa K, Himura Y, Yokota T, Yamamoto K, Tsuchihashi-Makaya M, Kinugawa S. Diagnostic performance of nutritional indicators in patients with heart failure. *ESC Heart Failure.* 2022; **9**: 2096–2106.
41. Tan B, Gu J, Wei H, Chen L, Yan S, Deng N. Electronic medical record-based model to predict the risk of 90-day readmission for patients with heart failure. *BMC Med Inform Decis Mak.* 2019; **19**: 193.