ORIGINAL ARTICLE

Nutrition Alert Form (NAF) as a Screening Tool for Predicting Malnutrition Risk in Outpatients with Cirrhosis: A Cross-Sectional Study

Manon Mitpracha, MD[1], Chanita Unhapipatpong, MD[2], Nint Polruang, PharmD[3], Narachai Julanon, MD[4], Thanachai Panaput, MD[5], Kittithat Taemkaew, MD[6]

[1] Division of Gastroenterology and Hepatology, Department of Medicine, Khon Kaen Hospital, Khon Kaen, Thailand; [2] Division of Clinical Nutrition, Department of Medicine, Khon Kaen Hospital, Khon Kaen, Thailand; [3] Department of Pharmacy, Khon Kaen Hospital, Khon Kaen, Thailand; [4] Division of Dermatology, Department of Medicine, Khon Kaen University, Khon Kaen, Thailand; [5] Division of Nephrology, Department of Medicine, Khon Kaen Hospital, Khon Kaen, Thailand; [6] Clinical Nutrition and Obesity Medicine Unit, Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

Background: Malnutrition is common among cirrhotic patients, leading to increased morbidity and mortality. Validated screening tools are essential for the early identification of malnutrition risk, enabling timely nutritional assessment and intervention.

Objective: To validate the Nutrition Alert Form (NAF) against the Royal Free Hospital-Nutritional Prioritizing Tool (RFH-NPT) in outpatients with cirrhosis, explore the relationship between NAF scores and anthropometric parameters, and evaluate the NAF's diagnostic performance using the Global Leadership Initiative on Malnutrition (GLIM) criteria.

Materials and Methods: The authors conducted a cross-sectional study that included 179 randomly selected cirrhotic outpatients. Various nutrition screening and assessment tools were employed, along with anthropometric measurements and biochemical tests. The NAF encompasses patient-directed questions, body weight, and body mass index (BMI). Alternatively, total lymphocyte count (TLC), or serum albumin (ALB) could replace weight and height when they were unavailable.

Results: Approximately 43% of patients were identified as being at risk for malnutrition by the RFH-NPT, while the NAF-BMI, NAF-TLC, and NAF-ALB identified 41.9%, 46.9%, and 46.3% of patients, respectively. Using GLIM criteria, the prevalence of malnutrition was 18.4%. The NAF-BMI, NAF-ALB, and NAF-TLC showed sensitivities of 93.9%, 96.9%, and 93.9%, with specificities of 69.9%, 65.1%, and 63.7%, respectively. The RFH-NPT exhibited a sensitivity of 90.9% and specificity of 66.4%. A strong correlation (ρ=0.75, $p<0.05$) was observed between the RFH-NPT and NAF-BMI scores. NAF-BMI scores moderately correlated with cirrhosis severity (ρ=0.41, $p<0.05$). Screening completion times did not differ significantly between methods.

Conclusion: Due to its high sensitivity and accuracy, the NAF can serve as a simple and validated tool to screen for risk of malnutrition in cirrhotic patients. It also correlated with the RFH-NPT.

Keywords: Nutrition Alert Form; Cirrhosis; Malnutrition; Royal Free Hospital-Nutritional Prioritizing Tool; Global Leadership Initiative on Malnutrition

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Malnutrition frequently develops among patients with cirrhosis, especially in advanced stages. The prevalence of malnutrition in these patients varies widely, depending on diagnostic methods and clinical settings, ranging from 9.6% to 92%. Cirrhosis and malnutrition are associated with higher complications and mortality, as malnutrition independently contributes to poorer outcomes. These patients also tend to have prolonged hospital stays and increased hospital costs(1). Accelerated starvation, metabolic disturbances, and anabolic resistance can contribute to malnutrition and sarcopenia(2). Early nutritional screening to identify patients at risk is essential but remains challenging. Once these patients are identified, a comprehensive nutritional assessment, a time-consuming process, should be performed, followed by prompt nutritional interventions including dietary counseling, oral nutritional supplementation, branched-chain amino acid supplementation, and

Correspondence to:

Unhapipatpong C.

Division of Clinical Nutrition, Department of Medicine, Khon Kaen Hospital, Khon Kaen 40000, Thailand.

Phone: +66-43-009900; **Fax:** +66-43-236974

Email: chanita@kkumail.com

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other treatment modalities. It is recommended that nutritional assessments be conducted every one to six months during outpatient visits of the patients with cirrhosis and upon admission, as well as periodically throughout their hospital stay[2].

According to guidelines from the European Association for the Study of the Liver (EASL) and the European Society for Clinical Nutrition and Metabolism (ESPEN), the Royal Free Hospital Nutrition Prioritizing Tool (RFH-NPT) is the validated screening tool for patients with cirrhosis. It is more sensitive than other tools such as the Nutrition Risk Screening 2002 (NRS-2002)[2,3]. The RFH-NPT score correlates with clinical complications and disease severity, and a reduction in the score is associated with improved survival in cirrhotic patients. RFH-NPT subjectively assesses patients and has a high negative predictive value (NPV)[4].

The Nutrition Alert Form (NAF) was developed in 2013 and has since been employed across various patient types and clinical settings[5]. Its widespread adoption is attributed to its high accuracy, simplicity as it required no specialized nutrition expertise, and its combination of subjective and objective assessments, including history taking, body weight, and basic laboratory data when body weight is unknown or altered. The Society of Parenteral and Enteral Nutrition of Thailand (SPENT) has endorsed the NAF as a validated assessment tool for assessing nutritional status in hospitalized patients. Its high sensitivity allows the NAF to also serve as a screening tool in outpatient settings[6]. Additionally, anthropometric measurements such as mid-arm muscle circumference (MAMC) and triceps skinfold thickness (TSF) are inexpensive and can be performed at the bedside. These measurements are considered to have prognostic value in predicting mortality rates among cirrhotic patients, when the accuracy of body weight can be affected by fluid retention[7].

Due to the variety of malnutrition assessment tools available, several scientific nutrition societies have reached a consensus on using the Global Leadership Initiative on Malnutrition (GLIM) criteria as the global diagnostic reference for malnutrition. This consensus comes after patients at risk of malnutrition are identified using validated screening tools. In the present study, the authors adopted the GLIM criteria as the reference method for diagnosing malnutrition due to its high diagnostic accuracy compared to the Subjective Global Assessment (SGA)[8].

The primary objective of the present study was to evaluate the correlation between the NAF and the RFH-NPT as screening tools among cirrhotic patients. The secondary objective was to assess the performance of the NAF in identifying patients at risk of malnutrition and to evaluate the agreement among various nutrition screening and assessment methods, including the NAF, RFH-NPT, and anthropometric measurements, against the GLIM criteria.

Materials and Methods

Population selection and study design

The present study was a cross-sectional study in which all participants with cirrhosis were selected through random sampling at the outpatient gastrointestinal and liver clinic at Khon Kaen Hospital, between June 2022 and March 2023. Based on a previous study[5] that reported a prevalence of 40.5% for at-risk malnutrition as evaluated by the NAF, in order to attain a 95% confidence interval (CI): $Z^2_{1-\alpha/2}$=1.96, where α is the type 1 error of 0.05, a sensitivity of 90%[5], and a margin of error of 0.05, the required sample size was estimated to be 176.4 subjects using the formula for a diagnostic test[9].

The authors enrolled 185 cirrhotic patients who met the inclusion criteria, but six were excluded, leaving 179 patients for analysis. The inclusion criteria were age over 18 and diagnosed with cirrhosis based on clinical, biochemical, histological, radiological with ultrasound or computed tomography, or ultrasound-based elastography assessments. Patients were excluded if they had uncontrolled comorbiditi es such as uncontrolled diabetes with HbA1c of 9% or greater, AIDS with active opportunistic infections, end-stage renal disease, congestive heart failure, septicemia, other malignancies, and pregnancy. The study received approval from the Khon Kaen Hospital Institute Review Board in Human Research in Thailand (approval code KEF65008) and was conducted in accordance with the Helsinki Declaration of 1975. All participants provided written informed consent before inclusion in the study.

The authors collected comprehensive demographic and disease data including age, gender, edema, comorbidities, cirrhosis severity, diagnostic tests for cirrhosis, and self-reported historical weight as usual weight. Cirrhosis severity was assessed using the Child-Turcotte-Pugh score (CTP) and the Model for End-Stage Liver Disease score (MELD).

All participants underwent nutrition screening using the NAF and RFH-NPT, and nutrition assessments were confirmed using the GLIM criteria. Anthropometric measurements taken included mid-arm circumference (MAC), TSF, actual body weight, height, and handgrip strength (HGS). MAMC and body mass index (BMI) were calculated the following formulas, MAMC (cm) = MAC − [3.14 × TSF (cm)] and BMI = weight (kg) ÷ height (m^2). These anthropometric indices and nutrition screening tools were evaluated independently by two trained investigators to minimize measurement errors.

Laboratory tests conducted included total protein (g/dL), serum albumin (ALB) (g/dL), blood urea nitrogen (BUN) (mg/dL), creatinine (mg/dL), prothrombin time (seconds), international normalized ratio (INR), total lymphocyte count (TLC) (cells/mm^3), sodium (mmol/L), and total bilirubin (mg/dL). All of those were used in the analysis.

Anthropometric measurements

Anthropometric parameters were measured during the visit. Actual body weight and height were assessed with the patient dressed in light clothing and without shoes. The percentages of involuntary weight loss were calculated using the formula: % weight loss = [(usual weight – actual weight) × 100%] ÷ usual weight. Actual weight was used to calculate BMI, which may be influenced by volume status.

MAC was measured in centimeters using the midpoint between the olecranon process and the acromion of the non-dominant arm. TSF was measured three times at the posterior part of the defined site using a body fat caliper, and the average of these measurements was recorded in millimeters (mm) to minimize practical variability. MAMC was calculated using the specified equation. TSF and MAMC were considered low when values fell below the fifth percentile of the reference value for age and gender[10,11]. HGS was measured three times using handgrip dynamometry while patients were seated with the elbow flexed at 90 degrees, using the non-dominant hand, and the highest value was used for analysis[12].

Nutrition screening tools

The NAF is a simplified malnutrition screening tool designed to identify nutritional risk[5]. Unlike tools that depend on weight and height for evaluation, the NAF is based on patient-directed questions and simple anthropometric assessments. These include changes in weight, quality and quantity of dietary intake, gastrointestinal symptoms, the patient's ability to access food, comorbidities, body weight, and height, presented as NAF-BMI. Additionally, for cirrhotic patients where weight and height measurements are unreliable or cannot be evaluated, NAF-TLC or NAF-ALB can be substituted. The cutoff scores for the NAF are defined as a score of 0 to 5 indicates no risk of malnutrition, a score of 6 to 10 indicates a moderate risk, and a score greater than 11 signifies a severe risk of malnutrition.

RFH-NPT is a validated nutrition screening tool used to identify the risk of malnutrition in patients with cirrhosis[13]. The evaluation of RFH-NPT involves a three-step approach. First, the authors assess whether patients suffered from acute alcoholic hepatitis or were fed by a tube. Next, the authors evaluate the volume status. If there was no alteration in volume status, then consider factors such as BMI, history of weight loss, and the patient's condition, including acute illness or insufficient intake for more than five days. If there was an alteration in volume status, factors such as fluid overload interfering with dietary intake, history of insufficient intake, and current use of diuretics were considered. The final step involved a scoring system that classified patients as having a low risk with 0 points, moderate risk with 1 point, or high risk of malnutrition with 2 to 7 points.

Nutrition assessment tools

The authors used GLIM as the reference method for diagnosing malnutrition, which required both phenotypic and etiologic criteria. In the phenotypic criteria, at least one of the following must be presented, significant weight loss of more than 5% in six months or more than 10% beyond six months, a low BMI with a cut-off points for Asian participants that is less than 18.5 kg/m^2 if under 70 years, or less than 20 if over 70 years, or reduced muscle mass, assessable using standard anthropometric measures such as MAMC or HGS[14]. This approach was chosen because standard body composition methods like bioelectrical impedance analysis (BIA), computed tomography (CT), and magnetic resonance imaging (MRI) were not universally available in hospitals and could incur significant costs. The present study utilized anthropometric indices to evaluate muscle mass, which were both feasible and cost-effective in most hospital settings. MAMC values below the fifth percentile of the reference values, stratified by gender and age, were considered indicative of low muscle mass, a condition significantly associated with mortality in cirrhotic patients[15,16]. According to the 2019 consensus of the Asian Working Group for Sarcopenia, a decrease in muscle strength is defined as having an HGS below 28 kg for males and below 18 kg for females[17]. In the etiologic criteria, a reduction in food intake, defined as consuming less than 50% of energy requirements for more than one week or any reduction for more than two weeks, was considered[14].

Statistical analysis

All analyses were performed using R software, version 4.1.2 (R Core Team, Vienna, Austria)[18]. Categorical variables were presented as numbers or percentages and analyzed using the chi-square test, Fisher's exact test, or the McNemar test. Continuous variables are described as mean values with standard deviations (SD) or as medians with interquartile ranges (IQR), depending on the normality of the data. The Shapiro-Wilk test was used to assess data normality.

A receiver operating characteristic (ROC) curve analysis and area under the curve (AUC) were generated to assess the performance of the RFH-NPT, NAF-BMI, NAF-TLC, and NAF-ALB, using GLIM as the reference standard. AUC of 0.5 indicates no discrimination as the test cannot distinguish between patients with and without the disease or condition. An AUC of 0.7 to 0.8 was deemed acceptable, 0.8 to 0.9 was considered excellent, and above 0.9 is regarded as outstanding. Sensitivity, specificity, positive predictive value (PPV), NPV, and test accuracy were calculated for these nutrition screening tools, with the diagnosis of malnutrition based on GLIM criteria serving as the gold standard, according to the Youden index[19].

The Spearman rank correlation coefficient (ρ) was used to assess the correlation among the NAF, RFH-NPT, and all anthropometric parameters. The absolute value of the Spearman rank correlation coefficients falls within ranges of 0 to 0.29, 0.3 to 0.49, 0.5 to 0.69, 0.7 to 0.89, and 0.9 to 1.00, indicating negligible, low, moderate, high, and very high correlation, respectively[20]. The Cohen's kappa test (k-value) was employed to evaluate the agreement between these variables and GLIM, with ranges of 0 to 0.2, 0.21 to 0.39, 0.4 to 0.59, 0.6 to 0.79, 0.8 to 0.9, and 0.9 to 1.0, indicating none, minimal, weak, moderate, strong, and almost perfect agreement, respectively[21]. Continuous variables were categorized according to their cutoff values for malnutrition. All tests were two-sided, and a p-value of less than 0.05 was considered statistically significant.

Results

Demographics and clinical characteristics

One hundred seventy-nine patients met the inclusion criteria and were enrolled for analysis. The mean age of the participants was 54.3±11.05 years, with 73% being male. The median body weight and BMI were 61 kg (IQR 54 to 71) and 23.0 kg/m² (IQR 20.9 to 25.5), respectively. For anthropometric assessments, the mean MAMC for male and female participants was 23.0±3.9 cm and 21.9±3.9 cm, respectively. The mean HGS was 25.4±8.5 kg and 16.8±6.4 kg in male and female patients, respectively. Table 1 displays the baseline characteristics of the study population classified by CTP category. The most frequent etiologies of cirrhosis were hepatitis C virus (HCV) cirrhosis in 47% of the cases, alcoholic cirrhosis in 27% of cases, and hepatitis B virus (HBV) cirrhosis in 19%. Diagnosis of cirrhosis was determined by ultrasonography in 70% of cases, clinical relevance in 12.8%, and CT scan in 8.9%. Regarding the CTP classification, 113 of 179 (63.2%) were classified as CTP-A, 50 of 179 (27.9%) as CTP-B, and 16 of 179 (8.9%) as CTP-C. One hundred twenty-nine of 179 (72.1%) of the participants had a MELD score less than the cutoff point of 15[22]. Other baseline characteristics of the present study population are presented in Table 1.

Prevalence of at-risk malnutrition and malnutrition

The prevalence of either moderate or high malnutrition risk was as follows, 77 out of 179 (43%) are based on the standard cutoff values of the RFH-NPT score, 75 out of 179 (41.9%) are based on the NAF-BMI score, 84 out of 179 (46.9%) are based on the NAF-TLC score, and 83 out of 179 (46.3%) are based on the NAF-ALB score. More than 60% of patients with CTP-A had a low risk of malnutrition as assessed by both the RFH-NPT and all NAF tools, while more than 60% of those with CTP-C were identified as having a high risk of malnutrition by RFH-NPT and NAF-ALB. The prevalence of malnutrition diagnosed based on GLIM criteria was 18.4%. Among all the methods, the RFH-NPT and NAF showed significant differences among CTP classes ($p<0.05$), as shown in Table 2.

Correlation analysis of nutrition screening tools, severity of cirrhosis, and anthropometric indices

NAF-BMI score was significant and correlated with that of the RFH-NPT, as a strong correlation, the severity of cirrhosis as measured by CTP and MELD scores, and all anthropometric outcomes. A scatter plot illustrating the correlation between NAF-BMI and RFH-NPT is shown in Figure 1.

Table 1. The baseline characteristics of the study population as stratified by CTP category

Parameter	Overall (n=179)	CTP A (n=113)	CTP B (n=50)	CTP C (n=16)	p-value*
Age (years); mean±SD	54.3±11.05	55±11	52±10	59±12	0.08
Male; n (%)	130 (73)	82 (73)	35 (70)	13 (81)	0.70
Body weight (kg); median (IQR)	61 (54, 71)	62 (55, 71)	60 (51, 70)	57 (50, 62)	0.12
Body mass index (kg/m^2); median (IQR)	23.0 (20.9, 25.5)	23.5 (21.5, 26.2)	22.5 (20.5, 24.9)	21.0 (18.2, 23.2)	0.03
Mean MAMC (cm); mean±SD					
Male	23.0±3.9	24.0±3.3	21.7±4.6	19.8±3.0	<0.001
Female	21.9±3.9	23.2±3.0	19.2±3.5	21.1±8.1	0.004
HGS (kg); mean±SD					
Male	25.4±8.5	26.7±8.2	25.2±8.5	17.3±6.1	<0.001
Female	16.8±6.4	18.1±6.5	14.9±5.9	12.5±5.5	0.15
TLC (cells/uL); median (IQR)	1,826 (1,299, 2,432)	2,038 (1,606, 2,768)	1,538 (1,018, 2,072)	1,491 (1,295, 1,904)	<0.001
Albumin (g/dL); median (IQR)	3.60 (2.95, 4.10)	3.90 (3.60, 4.20)	3.10 (2.70, 3.20)	2.40 (2.20, 2.60)	<0.001
Cause of cirrhosis; n (%)					0.09
Alcoholism	48 (27)	21 (19)	20 (40)	7 (44)	
HBV	34 (19)	24 (21)	7 (14)	3 (19)	
HCV	85 (47)	60 (53)	20 (40)	5 (31)	
MAFLD	3 (2)	3 (3)	0 (0)	0 (0)	
Others	9 (5)	5 (4)	3 (6)	1 (6)	
Diagnostic tools; n (%)					0.02
CT scan	16 (9)	12 (11)	4 (8)	0 (0)	
Clinical	23 (13)	7 (6)	10 (20)	6 (38)	
Laboratory	9 (5)	7 (6)	2 (4)	0 (0)	
Ultrasonography	126 (70)	82 (73)	34 (68)	10 (62)	
Elastography	5 (3)	5 (4)	0 (0)	0 (0)	
Co-morbidity; n (%)	63 (35)	38 (34)	17 (34)	8 (50)	0.40

CT=computed tomography; CTP=Child-Turcotte-Pugh score; HBV=hepatitis B virus; HCV=hepatitis C virus; HGS=handgrip strength; MAMC=mid-arm muscle circumference; MAFLD=metabolic associated fatty liver disease; TLC=total lymphocyte count

* Kruskal-Wallis rank sum test, Fisher's exact test, significance is shown as p<0.05

Table 2. Risk of malnutrition among the study population as stratified by CTP category

Screening Tool	Total (n=179)	CTP A (n=113)	CTP B (n=50)	CTP C (n=16)	p-value*
RFH-NPT score; n (%)					<0.001
Low risk (0)	102 (57)	84 (74)	16 (32)	2 (12)	
Moderate risk (1)	26 (15)	12 (11)	11 (22)	3 (19)	
High risk (≥2 to 7)	51 (28)	17 (15)	23 (46)	11 (69)	
NAF-BMI score; n (%)					<0.001
A (0 to 5)	104 (58)	80 (71)	22 (44)	2 (12)	
B (6 to 10)	62 (35)	32 (28)	22 (44)	8 (50)	
C (≥11)	13 (7)	1 (1)	6 (12)	6 (38)	
NAF-TLC score; n (%)					<0.001
A (0 to 5)	95 (53)	76 (67)	17 (34)	2 (12)	
B (6 to 10)	71 (40)	35 (31)	28 (56)	8 (50)	
C (≥11)	13 (7)	2 (2)	5 (10)	6 (38)	
NAF-ALB score; n (%)					<0.001
A (0 to 5)	96 (54)	78 (69)	17 (34)	1 (6)	
B (6 to 10)	62 (35)	35 (31)	22 (44)	5 (31)	
C (≥11)	21 (12)	0 (0)	11 (22)	10 (63)	

ALB=albumin; BMI=body mass index; CTP=Child-Turcotte-Pugh score; NAF=Nutrition Alert Form; RFH-NPT=Royal Free Hospital-Nutritional Prioritizing Tool; TLC=total lymphocyte count

* Fisher's exact test, significance is shown as p<0.05

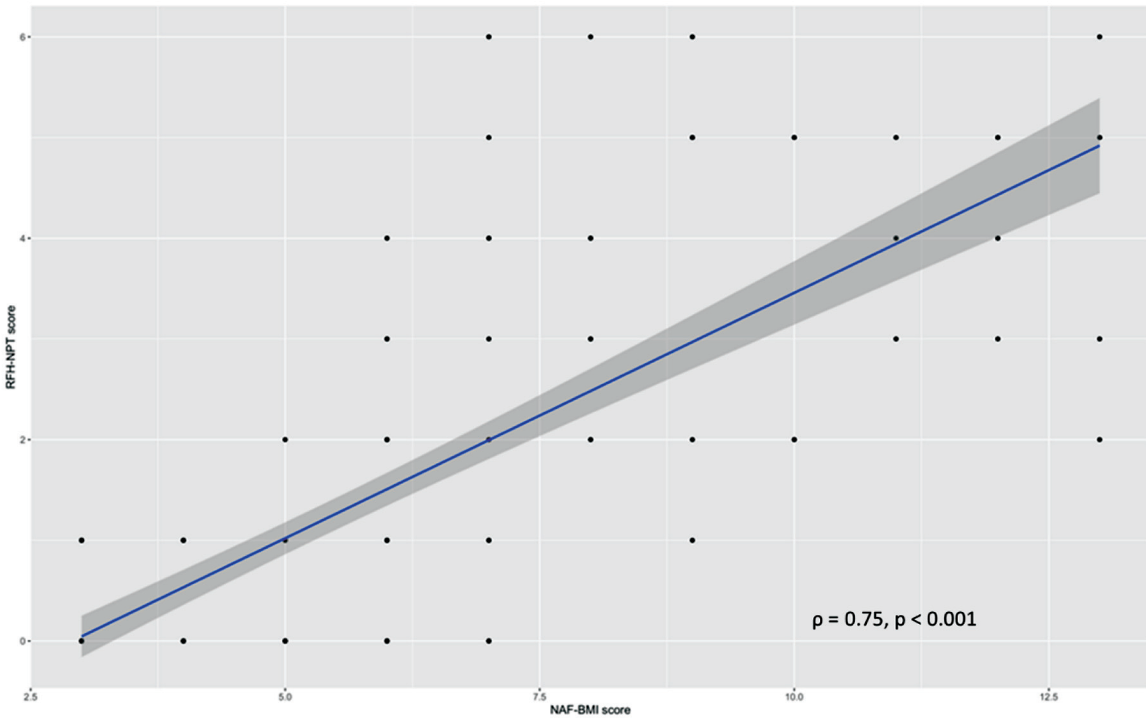

Figure 1. Scatter plot showed the correlation between NAF-BMI and RFH-NPT.

Spearman's rank order correlation (ρ)

The correlation coefficient between NAF-BMI and RFH-NPT was 0.75 ($p<0.05$). Additionally, the correlation coefficients of NAF-BMI with the severity of cirrhosis were CTP, $\rho=0.41$, $p<0.05$; and MELD, $\rho=0.3$, $p<0.05$. The correlation coefficients of NAF-BMI with anthropometric indices were MAMC, $\rho=-0.32$, $p<0.05$, HGS, $\rho=-0.28$, $p<0.05$, TSF, $\rho=-0.16$, $p<0.05$, and BMI, $\rho=-0.25$, $p<0.05$. While the correlation coefficient of NAF-BMI with ALB was –0.35 ($p<0.05$), there was no significant correlation between NAF-BMI and TLC.

The RFH-NPT also exhibited correlations with CTP, $\rho=0.51$, $p<0.05$, and MELD, $\rho=0.38$, $p<0.05$. Furthermore, the RFH-NPT demonstrated statistically significant correlations with both anthropometric measurements and laboratory results in the present study. The relationships between nutrition screening tools and other parameters are summarized in Table 3.

Table 3. Correlation between the NAF, RFH-NPT, severity of cirrhosis and anthropometric parameters

Parameters	NAF-BMI score		RFH-NPT	
	ρ*	p-value	ρ*	p-value
NAF-BMI score			0.75	<0.001
CTP severity	0.41	<0.001	0.51	<0.001
MELD score	0.30	<0.001	0.39	<0.001
MAMC (cm)	–0.32	<0.001	–0.37	<0.001
HGS (kg)	–0.28	<0.001	–0.24	<0.05
TSF (mm)	–0.16	<0.05	–0.22	<0.05
BMI (kg/m^2)	–0.26	<0.001	–0.34	<0.001
Albumin (g/L)	–0.35	<0.001	–0.46	<0.001
TLC (cells/mm^2)	–0.09	0.2	–0.18	<0.05

BMI=body mass index; CTP=Child-Turcotte-Pugh score; HGS=handgrip strength; MAMC=mid-arm muscle circumference; MELD=Model for End-Stage Liver Disease; NAF=Nutrition Alert Form; TLC=total lymphocyte count; RFH-NPT=Royal Free Hospital-Nutritional Prioritizing Tool; TSF=triceps skinfold

* Spearman's rank order correlation (ρ); significance is shown as $p<0.05$

Diagnostic performance of nutrition screening tools and anthropometric measurements

The ROC curves for NAF-BMI, NAF-TLC, NAF-ALB, and RFH-NPT, used to diagnose at-risk malnutrition among cirrhotic patients, are shown in Figure 2. The AUC were RFH-NPT: 0.79 (95% CI 0.72 to 0.85, $p<0.05$), NAF-BMI: 0.82 (95% CI 0.76 to 0.87, $p<0.05$), NAF-ALB: 0.81 (95% CI 0.76 to 0.86, $p<0.05$), and NAF-TLC: 0.79 (95% CI 0.73 to 0.85, $p<0.05$). These results suggested that NAF-BMI and NAF-ALB were excellent tools for malnutrition

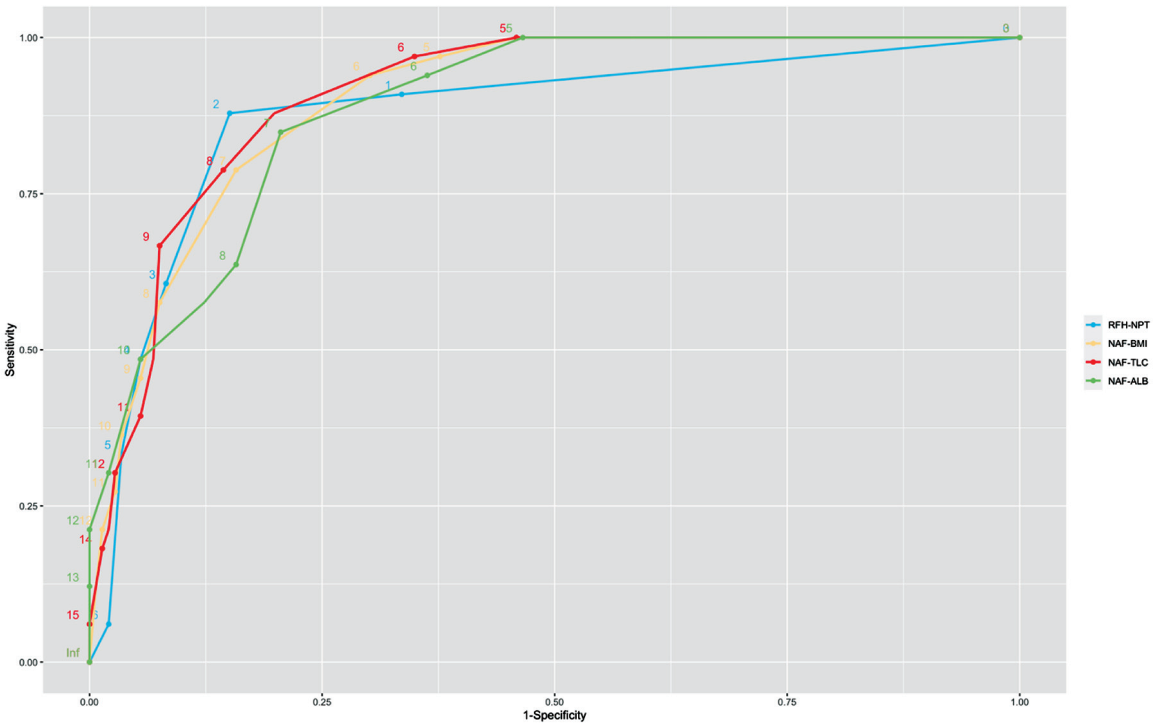

Figure 2. The ROC curves of NAF-BMI, NAF-TLC, NAF-ALB and RFH-NPT.

Table 4. Diagnostic performance of different nutrition screening tools using GLIM as reference

	AUC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	K-value* (95% CI)	p-value
RFH-NPT score	0.79	90.9	66.4	37.9	97	70.9	0.37 (0.25 to 0.49)	<0.05
NAF-BMI score	0.82	93.9	69.9	41.3	98.1	74.3	0.43 (0.31 to 0.55)	<0.05
NAF-ALB score	0.81	96.9	65.1	38.5	98.9	70.9	0.39 (0.28 to 0.5)	<0.05
NAF-TLC score	0.79	93.9	63.7	36.9	97.9	69.3	0.36 (0.25 to 0.47)	<0.05
HGS	0.71	96.9	45.2	28.5	98.5	54.73	0.18 (0.14 to 0.22)	<0.05
MAMC	0.58	60.6	54.8	23.2	86.1	55.9	0.05 (–0.01 to 0.11)	0.06
TSF	0.59	39.4	79.5	30.2	85.3	72.1	0.046 (0.01 to 0.09)	0.01

ALB=albumin; AUC=area under the curve; PPV=positive predictive value; NPV=negative predictive value; BMI=body mass index; HGS=handgrip strength; MAMC=mid-arm muscle circumference; NAF=Nutrition Alert Form; TLC=total lymphocyte count; RFH-NPT=Royal Free Hospital-Nutritional Prioritizing Tool; TSF=triceps skinfold

* Kappa-values (K-value) are the agreement between the different nutrition tools compared with GLIM.

screening, while the RFH-NPT and NAF-TLC were considered acceptable screening tools. The diagnostic performance of the nutrition screening tools, along with anthropometric indices and laboratory tests, are presented in Table 4. Using GLIM as a reference, and according to the standard cutoff values of each tool, the sensitivities were 93.9% for both NAF-BMI and NAF-TLC, and 96.9% for NAF-ALB. Specificities were 69.9% for NAF-BMI, 65.1% for NAF-ALB, and 63.7% for NAF-TLC, compared to RFH-NPT, which had a sensitivity of 90.9% and specificity of 66.4%. The PPVs were 41.3% for NAF-BMI, 38.5% for NAF-ALB, and 36.9% for NAF-TLC, while the NPVs were 98.1% for NAF-BMI, 98.9% for NAF-ALB, and 97.9% for NAF-TLC.

Regarding the agreement between different methods and GLIM, the results demonstrated weak agreement for the NAF-BMI score (k=0.43, p<0.05), and minimal agreement for NAF-ALB score (k=0.39, p<0.05) and RFH-NPT score (k=0.37, p<0.05). Despite HSG showing 96.97% sensitivity and 98.51% NPV, there was no significant agreement between HSG and GLIM (k=0.18, p<0.05). The average time taken to administer the NAF and RFH-NPT was 2.1±0.77 minutes and 1.8±0.47 minutes, respectively.

Discussion

In the present study, the authors observed a strong correlation between the NAF and RFH-NPT, which is the recommended screening tool according to current guidelines[2,3]. The NAF demonstrated high sensitivity and specificity in diagnosing malnutrition at risk. The time required to complete assessment using these tools was comparable, taking less than three minutes. The present study is the first to evaluate the performance of the NAF, highlighting its reliability and simplicity. Importantly, in cirrhotic patients, where volume status may be altered, the authors were able to successfully substitute TLC or ALB for body weight in NAF scoring while maintaining reliability. Overall, the NAF, calculated from BMI, TLC, and ALB, proved beneficial for classifying malnutrition risk among cirrhotic patients.

Malnutrition among cirrhotic patients is influenced by multiple factors, including complications from decompensated cirrhosis, dietary restrictions, medication side effects, and metabolic derangements that affect digestion, absorption, and metabolism. It is well-established that malnutrition is prevalent among cirrhotic patients and is associated with poorer outcomes, particularly increased morbidity and mortality[1]. Although improving nutritional status has been shown to result in shorter hospital stays, it does not necessarily lead to differences in mortality and complications, due to the natural progression of liver disease[22,23]. The present study also demonstrated a significant association between risk of malnutrition and the severity of cirrhosis, consistent with the previous research[24]. A validated screening tool can help prioritize at-risk patients, facilitating comprehensive nutrition assessments and urgent nutritional support.

Given the variety of malnutrition assessment tools available, international nutrition societies have reached a consensus on the use of the GLIM criteria to confirm malnutrition following the identification of at-risk patients[8]. In the present study, the authors employed the GLIM criteria as the reference method for diagnosing malnutrition, given the high diagnostic accuracy of the GLIM compared to the SGA, which can be influenced by the disease itself and has been identified as an independent predictor of mortality in patients with chronic liver diseases[25]. HGS has been shown to be a suitable substitute for the skeletal muscle index as part of the GLIM criteria[26]. The reported prevalence of malnutrition varies depending on the diagnostic tools used and the clinical setting. In the present study, the prevalence of malnutrition, as diagnosed by GLIM criteria using anthropometric measurements, was 18.4% among cirrhotic outpatients. In contrast, a 2023 study by Yang et al. reported a malnutrition prevalence of 36.4% among hospitalized cirrhotic patients based on GLIM criteria, while other studies have reported rates ranging from 40% to 76.8% in outpatient liver clinics of tertiary care hospitals using the SGA[27]. However, the prevalence in the present study setting may be underestimated due to the non-hospitalized setting, predominance of Child-Pugh Class A participants, and the low sensitivity of anthropometric assessments in detecting malnutrition, as evidenced by the findings.

Guidelines from EASL and ESPEN recommend screening for malnutrition in patients with liver disease, particularly cirrhosis, using validated tools. Among these, RFH-NPT is recognized as one of the most sensitive screening tools, surpassing NRS-2002[2]. While SPENT endorses the NAF for malnutrition classification and it has been validated across various conditions, including cancer, non-dialytic chronic kidney disease, and among the elderly, its correlation with RFH-NPT and validation in cirrhotic patients remains unexplored[28-30]. To the authors' knowledge, this is the first study to establish a strong correlation between the NAF and the endorsed validated screening tools, and to underscore the NAF's efficacy in identifying malnutrition risk in cirrhotic patients. All NAF forms demonstrated high sensitivity and NPV, comparable to those of the RFH-NPT. Notably, the NAF can be completed quickly without requiring specialized expertise. However, the present study findings indicated a minimal/weak concordance among all NAF forms and GLIM criteria. The authors noted that 43% and 41.9% of patients were classified as at risk of malnutrition according to the RFH-NPT and NAF-BMI, respectively. This contrasts with findings from a study by Wu et al. in 2020, which reported a 63% risk prevalence using the RFH-NPT[31]. The performance metrics of the RFH-NPT in the present study mirrored the sensitivity and specificity rates reported in the current literature.

In the present study, the NAF demonstrated a weak negative correlation with anthropometric assessments, including HGS and MAMC. While anthropometric assessments provide advantages as bedside tools for objective evaluation in patients with cirrhosis, offering reproducible methods to predict complications and mortality, the study suggests that MAMC and HGS may serve as prognostic factors for cirrhosis rather than assessing nutritional status[12]. The present study also identified a low sensitivity in detecting malnutrition, which may be attributable to the fact that MAMC may not change until the disease progresses significantly. This lack of sensitivity could potentially lead to an overestimation of nutritional status due to excess volume. Consequently, the study recommends using the SGA to evaluate nutritional status instead. Although the present study reported high sensitivity for HGS, it also noted a low accuracy rate in detecting malnutrition, consistent with previous studies that indicated a substantial number of false positive results[32]. A previous study demonstrated reliable results in assessing the nutritional status of patients with cirrhosis using skinfold thickness[33]. However, in the present study, TSF measurements showed low sensitivity. TSF is known to correlate with total body fat, particularly in women, but maintaining precision and accuracy in TSF measurements can be challenging without proper training. Additionally, TSF is not sensitive for monitoring short-term changes in fat storage, as supported by the previous research that showed reductions in TSF at advanced stages of cirrhosis[34,35]. Anthropometric assessments have certain limitations. First, detecting increases in HGS and MAMC following improvements in nutritional status takes time, which may not be practical for responding to changes in clinical conditions[36,37]. Consequently, the NAF is preferred during the follow-up period due to its multimodal assessment capabilities, which allow for the tracking of scores that correlate with improvements or deteriorations in nutritional status[5]. Additionally, the NAF is a contactless screening tool, making it more suitable than anthropometric evaluations, especially for screening patients at risk of malnutrition and monitoring nutritional status amid the COVID-19 pandemic. Furthermore, the present study results indicated no agreement between the GLIM criteria and anthropometric assessments, consistent with the low agreement rates reported in previous studies[38,39].

One of the strengths of the present study is the use of the GLIM as a nutrition assessment tool, which is reproducible and mitigates the potential variation associated with the SGA, which can vary depending on the examiner. In the present study, the GLIM relied on straightforward anthropometric assessments, including BMI, HGS, and MAMC, which are compatible across hospitals of various levels. The NAF was validated against the standard screening tool and proved effective in identifying patients at risk during the follow-up period.

However, the present study has limitations. Although the RFH-NPT has been independently associated with the deterioration of liver function and survival in patients with cirrhosis, the present study was cross-sectional, and the NAF score may only reflect the course of cirrhosis[13]. A longitudinal study is necessary to establish the temporal relationship between nutritional status and NAF score. Additionally, the association between the NAF and mortality rates should be further assessed. Future research should aim to confirm the benefits of improving nutritional status in the early stages of cirrhosis after identifying those at risk through the NAF, and determine whether such interventions can reduce mortality rates.

Conclusion

The NAF is an effective screening tool for identifying malnutrition risk in patients with cirrhosis, owing to its high sensitivity and accuracy. Its user-friendly design makes it suitable for use in outpatient clinics and during patient follow-ups to monitor score improvements. The NAF offers a straightforward and validated method to assess malnutrition risk, which is associated with the severity of cirrhosis.

What is already known on this topic?

Early identification of malnutrition risk using reliable tools should be an integral part of primary care for patients with cirrhosis, as malnutrition contributes to poorer outcomes, increased complications, and higher mortality rates. The SPENT recommends the use of the NAF to classify malnutrition. Although it has been validated in various conditions, it has not yet been validated specifically in patients with cirrhosis.

What does this study add?

The NAF has proven to be a reliable tool for screening malnutrition in patients with cirrhosis, correlating with internationally recommended tools (RFH-NPT) and validated alongside malnutrition assessment tools (GLIM). As a time-saving and contactless screening tool, the NAF is particularly suitable in the context of the COVID-19 pandemic.

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Authors' contributions

MM, CU, and NJ conceived and designed the study and reviewed the manuscript. CU and NP collected the data. CU and NJ analyzed the data and interpreted the results. MM and CU drafted the manuscript. TP and KT provided critique. All authors read and approved the final manuscript.

Conflicts of interest

The authors hereby declare no personal or professional conflicts of interest regarding any aspect of this study. This manuscript is original and has neither been published elsewhere nor submitted for publication simultaneously.

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