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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

Agreements between the Global Leadership Initiative on Malnutrition using left calf circumference as criterion for reduced muscle mass and the Patient-Generated Subjective Global Assessment, and the Global Leadership Initiative on Malnutrition using the appendicular skeletal muscle index for the diagnosis of malnutrition in gastric cancer patients

Concordancias entre la Iniciativa Global de Liderazgo sobre la Desnutrición utilizando la circunferencia de la pantorrilla izquierda como criterio de masa muscular reducida y la Evaluación Global Subjetiva Generada por el Paciente, y la Iniciativa Global de Liderazgo sobre la Desnutrición utilizando el índice de músculo esquelético apendicular para el diagnóstico de desnutrición en pacientes con cáncer gástrico

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Abstract

Objective: this study aimed to explore the agreements between the Global Leadership Initiative on Malnutrition (GLIM) using left calf circumference (CC) as criterion for reduced muscle mass and the Patient-Generated Subjective Global Assessment (PG-SGA), or GLIM using appendicular skeletal muscle index (ASMI) for the diagnosis of malnutrition in gastric cancer patients.

Methods: the Nutritional Risk Screening 2002 (NRS 2002) was used as nutritional risk screening. PG-SGA and GLIM were applied for malnutrition diagnosis. Agreements were evaluated by Kappa, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and area under the curve (AUC).

Results: a total of 405 gastric cancer patients were included. The values of Kappa, sensitivity, specificity, PPV, NPV, accuracy and AUC were 0.463, 67.9 %, 87.3 %, 92.9 %, 52.8 %, 73.6 % and 0.776, and 0.496, 76.7 %, 78.0 %, 89.4 %, 57.9 %,77.0 % and 0.773, respectively, between GLIM using CC with or without NRS 2002 and PG-SGA. All values of agreement were higher than 0.800 or 80.0 % between GLIM using left CC and GLIM using ASMI.

Conclusion: the agreements were both acceptable between GLIM using left CC and PG-SGA, and GLIM using ASMI. Left calf circumference can be one of the credible references indicating a reduced muscle mass in patients with gastric cancer.

Keywords:

Agreement. GLIM. Calf circumference. PG-SGA. Malnutrition. Gastric cancer.

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Resumen

Objetivo: este estudio tenía como objetivo explorar los acuerdos entre la Iniciativa Global de Liderazgo sobre la Desnutrición (GLIM) utilizando la circunferencia de la pantorrilla izquierda (CC) como criterio de masa muscular reducida y la Evaluación Global Subjetiva Generada por el Paciente (PG-SGA), o la GLIM utilizando el índice de músculo esquelético apendicular (ASMI) para el diagnóstico de desnutrición en pacientes con cáncer gástrico.

Métodos: se utilizó el Cribado de Riesgo Nutricional 2002 (NRS 2002) como cribado de riesgo nutricional. PG-SGA y GLIM se utilizaron para el diagnóstico de desnutrición. Los acuerdos se evaluaron mediante Kappa, sensibilidad, especificidad, valor predictivo positivo (VPP), valor predictivo negativo (VPN), exactitud y área bajo la curva (AUC).

Resultados: se incluyó un total de 405 pacientes con cáncer gástrico. Los valores de Kappa, sensibilidad, especificidad, VPP, VPN, exactitud y AUC fueron de 0,463, 67,9 %, 87,3 %, 92,9 %, 52,8 %, 73,6 % y 0,776, y de 0,496, 76,7 %, 78,0 %, 89,4 %, 57,9 %, 77,0 % y 0,773, respectivamente, entre la GLIM utilizando CC con o sin NRS 2002 y PG-SGA. Todos los valores de concordancia fueron superiores a 0,800 u 80,0 % entre la GLIM utilizando la CC izquierda y la GLIM utilizando el ASMI.

Conclusión: los acuerdos fueron aceptables entre la GLIM utilizando la CC izquierda y la PG-SGA, y la GLIM utilizando el ASMI. La circunferencia de la pantorrilla izquierda puede ser una de las referencias creíbles que indiquen reducción de la masa muscular en los pacientes con cáncer gástrico.

Palabras clave:

Acuerdo. GLIM. Circunferencia de la pantorrilla. PG-SGA. Desnutrición. Cáncer gástrico.

INTRODUCTION

Malnutrition is one of the most common health problems that anyone can face. Cancer patients are one of the groups at highest risk for malnutrition, especially patients with gastric cancer (1,2). The prevalence of malnutrition in gastric cancer patients can be higher than 60 % (1). And the diagnosis of malnutrition in gastric cancer patients may have its own specificity. In addition, malnutrition is also negatively associated with adjuvant chemotherapy compliance, survival, mortality, length of stay, hospitalization costs, and postoperative complications in patients with gastric cancer (3-7). Although it is crucial to perform an accurate diagnosis of malnutrition in cancer patients, there is no gold standard for diagnosing malnutrition to date.

Numerous methods have been developed and applied to the diagnosis of malnutrition in clinical practice and scientific research, such as the Patient-Generated Subjective Global Assessment (PG-SGA), the Subjective Global Assessment (SGA), the European Society of Clinical Nutrition and Metabolism (ESPEN) Consensus Statement, and so on (8-10). However, there has long been no consensus on the diagnosis of malnutrition. In January 2016, the Global Leadership Initiative on Malnutrition (GLIM) was developed under the cooperation of several core global clinical nutrition societies, including ESPEN, the American Society of Parenteral and Enteral Nutrition (ASPEN), the Federación Latinoamericana de Terapia Nutricional, Nutrición Clínica y Metabolismmo (FELANPE) and the Parenteral and Enteral Nutrition Society of Asia (PENSA) (11).

GLIM is a two-step approach. The first step is malnutrition risk screening to identify the "at risk" status by using any validated screening tool. The second step is the diagnosis and severity grading of malnutrition. The diagnosis of malnutrition requires at least one phenotypic criterion and one etiologic criterion. Phenotypic criteria involve weight loss, low body mass index, and reduced muscle mass. Etiologic criteria include reduced food intake or assimilation, and inflammation (11). Several studies have been performed to validate GLIM in practical applications, and its consistency with other diagnostic tools (12,13). However, the operational standards of this process have not yet been fully validated, especially in gastric cancer patients. Some criteria lack clearly defined cut-off values (14), such as the threshold value of calf circumference (CC). Considering the accessibility of assessment tools or equipment, CC is one of the simplest and most effective methods for reduced muscle mass, especially in low- and middle-income countries and in rural areas where the bioelectrical impedance analysis (BIA) or other assessing equipment may be unavailable. In addition, it is not clear how the use and non-use of the screening tool will affect the outcome of the GLIM process.

Considering that the consistency between GLIM and current clinical practice is still unclear in gastric cancer patients, it is crucial to explore the validation of GLIM using left calf circumference as the criterion for reduced muscle mass for malnutrition diagnosis, and the impact of screening tools on the diagnostic performance of GLIM. The PG-SGA was developed by Ottery, and is a nutritional status assessment method initially designed for cancer patients (10). The PG-SGA has been widely used in different patient populations and is known as the "semi-gold standard" for diagnosing malnutrition. As the reference values of appendicular skeletal muscle mass index (ASMI) were suggested in the GLIM consensus, GLIM using ASMI as the criterion for reduced muscle mass was also chosen as the complementary alternative "semi-gold standard" for assessing the validation of GLIM using left calf circumference as the criterion for reduced muscle mass (11). Therefore, the purpose of this study was to investigate agreements between GLIM using left CC as the criterion for reduced muscle mass and PG-SGA, and between GLIM using left CC and GLIM using ASMI for malnutrition diagnosis in patients with gastric cancer, and establish its validation.

MATERIAL AND METHODS

STUDY DESIGN AND PARTICIPANTS

This cross-sectional study was carried out at the Department of Gastrointestinal Surgery, Department of Hepatobiliary and Pancreatic Surgery, and Department of Medical Oncology, Affiliated Jinhua Hospital, Zhejiang University School of Medicine (Jinhua Municipal Central Hospital) from December 2020 to May 2022.

The inclusion criteria were as follows: a) aged 18 years or above; b) gastric cancer was confirmed by pathology; c) Eastern Cooperative Oncology Group Performance Status (ECOG-PS) lower than four; d) planned to undergo antitumor surgery or have already undergone antitumor surgery; and e) have not receive any treatment for gastric cancer at this admission; and 6) able to give informed consent. The exclusion criteria were: a) uncontrolled diabetes *mellitus*; b) receiving glucocorticoid therapy; c) liver and/or renal failure; and d) other conditions not suitable for inclusion in the study. We calculated the required sample size for our study using the 'kappaSize' package, which is freely available in the R version 4.2.1 software (15,16). The 'CIBinary' function in the kappaSize package uses a confidence interval perspective to estimate the sample size needed to test the value of Kappa. The preliminary studies indicated that the initial value of Kappa was 0.483 with a margin of 0.2 on each side (17,18), suggesting that the expected lower and upper confidence limits for Kappa were 0.283 and 0.683, respectively. We also assumed that the proportion of malnutrition was 0.742 based on the results of a previous study (17). Based on the information from these preliminary studies, the estimated sample size required is at least 129 cases at a 5 percent level of significance (i.e., alpha = 0.05). Therefore, with a 20 % dropout rate, the selected sample size ($n = 405$) is sufficient for the current study.

ETHICAL STATEMENT

This study was conducted in accordance to the Helsinki Declaration, and approved by the Medical Ethics Committee of Jinhua Municipal Central Hospital -(研)2022-伦理审查-210, (研)2021-伦理审查-142, (研)2020-伦理审查-240, (研)2020-伦理审查-298 and (研)2022-伦理审查-87). The informed consent was signed voluntarily by all patients.

GENERAL INFORMATION

Gender, age (years), tumor location, histopathological diagnosis, cancer stage, duration science diagnosis (days), cancer therapy phase were obtained through the electronic medical record system. Weight (kilogram [kg]), height (centimeter (cm)), educational level, occupation status, marital status, residence status and financial pressure were obtained by asking patients and caregivers. The financial pressure is a patient's self-evaluation of their own financial burden, which was self-reported via one item "Do you feel any financial pressure?" with four options "Not at all, A little bit, Somewhat, and Very much." Body mass index (BMI), and ECOG-PS score were measured and assessed by the research nurses.

NRS 2002

The Nutritional Risk Screening (NRS 2002) was applied as a screening tool (11). The NRS 2002 was developed by Kondrup et al., involving impaired nutritional status with 0 to 3 points, severity of disease with 0 to 3 points, and age with 0 to 1 point. The total score is 0 to 7 points. Malnutrition risk was defined as a score of 3 or above. This is step 0: Screening (19) (Fig. 1).

GLIM

Malnutrition was diagnosed using the Global Leadership Initiative on Malnutrition (GLIM) criteria that at least one phenotypic criterion and one etiologic criterion should be present (11). Three phenotypic criteria were: a) weight loss > 5 % within the past 6 months, or > 10 % beyond 6 months; b) body mass index (BMI) < 18.5 kg/m^2 if < 70 years, or < 20 kg/m^2 if ≥ 70 years (Asia); and c) reduced muscle mass. Two etiologic criteria were: a) reduced food intake or assimilation; and b) inflammation. A left calf circumference (CC) < 30 cm (male) or < 29.5 cm (female), or an appendicular skeletal muscle mass index (ASMI) < 7 kg/m^2 (male) or < 5.7 kg/m^2 (female) were considered as reduced muscle mass (11,20). The left CC were measured by research nurses using a flexible and non-elastic tape (20). ASMI were measured by technicians using body composition analyzer (InBody 720, Biospace, Korea) based on bioelectrical impedance analysis (BIA). Gastric cancer was identified as reduced food intake or assimilation. This is step 1: Diagnosis (Fig. 1).

Phenotypic metrics for grading severity as moderate (stage 1) malnutrition and severe (stage 2) malnutrition are proposed. Moderate malnutrition required one phenotypic criterion that meets this grade: a) weight loss 5-10 % within the past 6 months, or 10-20 % beyond 6 months; b) BMI < 18.5 kg/m^2 if < 70 years, or < 20 kg/m^2 if ≥ 70 years (Asia); 3) CC < 30 cm (male) or < 29.5 cm (female) (11,20). Severe malnutrition required one phenotypic criterion that meets this grade: 1) weight loss > 10 % within the past 6 months, or > 20 % beyond 6 months; 2) BMI < 17.0 kg/m^2 if < 70 years, or < 17.8 kg/m^2 if ≥ 70 years (Asia); and c) CC < 28 cm (male) or < 27.5 cm (female) (11,20). Regarding GLIM using ASMI, malnutrition severity was graded by weight loss and BMI due to there is no consensus on the grading reference values. This is step 2: Severity (Fig. 1).

PG-SGA

The Patient-Generated Subjective Global Assessment (PG-SGA) has a patient component and a professional component. The patient component includes weight, food intake, symptoms, and activities and function. The professional component involves scoring weight loss, disease and its relation to nutritional requirements, metabolic demand, physical exam, and global assessment categories (10). In this study, a score of four or above was identified as malnutrition (moderate malnutrition), and severe malnutrition was nine points or above.

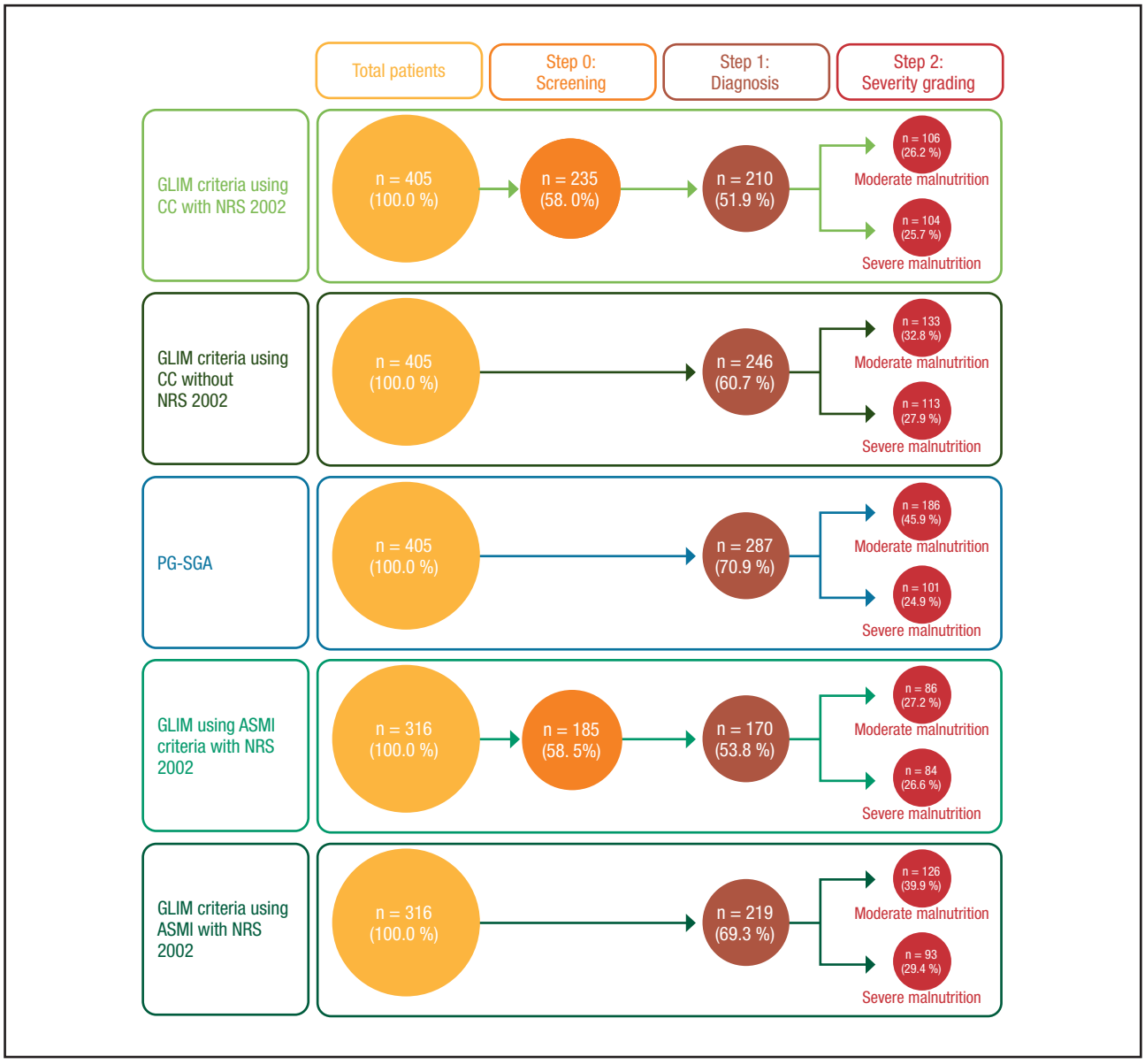

Figure 1.

Comparisons of diagnosis of malnutrition by the GLIM process with and without screening and by the PG-SGA method. The circles represent the number and prevalence of patients being identified at each of the steps. Nutritional risk was screened by NRS 2002 (orange circles): score ≥ 3. The diagnosis of malnutrition was based on GLIM criteria with NRS 2002, GLIM criteria without NRS 2002 and PG-SGA (brown circles). The severity of malnutrition was graded both according to GLIM and PG-SGA (red circles).

STATISTICAL ANALYSES

The Statistical Package for the Social Sciences (SPSS) version 26.0 was used for data analysis. Categorical variables were described as frequencies (percentages). The normality of continuous variables was tested using the Kolmogorov-Smirnov (K-S) test. Normally distributed data were described as mean (standard deviation [SD]), whereas non-normally distributed data were shown as median (25^{th}-75^{th} percentile). The agreements were assessed using Cohen's kappa (k) value (14). A k value of 0.41-0.60 is considered moderate agreement, and > 0.80 is recommended (14,21). Considering PG-SGA or GLIM using ASMI a gold standard, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and area under the curve (AUC) of GLIM using left CC and GLIM using ASMI were calculated using the methods described in a recent guidance (14). All p values were two-tailed with a statistical significance level of $p < 0.05$.

RESULTS

PATIENT CHARACTERISTICS

A total of 418 gastric patients were recruited, of which 13 were excluded due to missing PG-SGA data. Of the included 405 patients with gastric cancer, 291 (71.9 %) were men, the median age was 66.0 (57.0-72.0) years, the median weight was 55.0 (50.0-63.5) kg, 373 (92.1 %) were married, 377 (93.1 %) did not live alone, and the median duration since diagnosis was 41.5 (5.8-322.3) days. Only 19 (4.7 %) participants had university or above degrees, 28 (6.9 %) reported financial pressure very much, and 38 (9.4 %) were diagnosed with cancer stage IV (Table I).

Table I. Demographic and clinical characteristics of the participants

Characteristics	All participants (*n* = 405)
Gender, n (%)	
Male	291 (71.9)
Female	114 (28.1)
Age, year, n (%)	
< 70 years	246 (60.7)
≥ 70 years	159 (39.3)
Weight, kg, median (25^{th}-75^{th} percentile)	55.0 (50.0-63.5)
Height, cm, median (25^{th}-75^{th} percentile)	165.0 (158.0-170.0)
BMI, kg/m^2 (5^{th}, 15^{th} percentile)	
< 70 years	16.2, 17.8
≥ 70 years	16.4, 17.3
Left calf circumference, cm (5^{th}, 15^{th} percentile)	
Male	28.5, 29.9
Female	28.4, 29.5
ASMI, kg/m^2 (5^{th}, 15^{th} percentile)[a]	
Male	5.6, 6.2
Female	4.7, 5.0
Education level	
Primary school or below	236 (58.3)
High school	150 (37.0)
University or above	19 (4.7)
Occupation status	
Unemployed	269 (66.4)
Employed	136 (33.6)
Marital status	
Single	32 (7.9)
Married	373 (92.1)

(Continues on next column)

Table I (cont.). Demographic and clinical characteristics of the participants

Characteristics	All participants (*n* = 405)
Solitude	
No	377 (93.1)
Yes	28 (6.9)
Financial pressure	
Not at all	208 (51.4)
A little bit	123 (30.4)
Somewhat	46 (11.4)
Very much	28 (6.9)
ECOG-PS score	
0	144 (35.6)
1	187 (46.2)
2	48 (11.9)
3	26 (6.4)
Excessive alcohol consumption[b]	
No	234 (63.4)
Yes	135 (36.6)
Smoking status[b]	
No	284 (77.0)
Yes	85 (23.0)
Tumor location[c]	
Upper third	128 (32.3)
Middle third	97 (24.5)
Low third	161 (40.7)
Mixed tumor location	10 (2.5)
Histopathological diagnosis[d]	
Adenocarcinoma	314 (79.9)
Non-adenocarcinoma	58 (14.8)
Mixed histopathological diagnosis	21 (5.3)
Cancer stage[e]	
I	69 (17.5)
II	99 (25.1)
III	188 (47.7)
IV	38 (9.6)
Duration since diagnosis, day, median (25^{th}-75^{th} percentile)	41.5 (5.8-322.3)
Cancer therapy phase	
Before operation	118 (29.1)
After operation before chemotherapy	126 (31.1)
After operation undergoing chemotherapy	67 (16.5)
After operation after chemotherapy	94 (23.2)

n = 405. BMI: body mass index; ASMI: appendicular skeletal muscle mass index; ECOG-PS: Eastern Cooperative Oncology Group performance status. [a]n = 316, [b]n = 369, [c]n = 396, [d]n = 393, [e]n = 394.

THE RESULTS OF THE GLIM CRITERIA

The proportion of weight loss > 5 % within the past 6 months or > 10 % beyond 6 months in gastric cancer patients was 26.9 % (Table II). The percentage of BMI < 18.5 kg/m^2 if < 70 years or < 20 kg/m^2 if ≥ 70 years was 19.3 %; 50 (12.3 %) patients with gastric cancer were classified as left calf circumference < 30 cm (male) or < 29.5 cm (female). Of the 405 participants, 316 participants underwent a BIA with another 89 being excluded due to missing BIA data, and the number of subjects with ASMI < 7 kg/m^2 (male) or < 5.7 kg/m^2 (female) was 151 with a proportion of 47.8 %.

MALNUTRITION DIAGNOSED WITH GLIM AND NRS 2002

In the step 0 of screening, 235 (58.0 %) and 185 (58.5 %) gastric cancer patients were considered at risk for malnutrition, respectively (Fig. 1). In the step 1 of diagnosis, 210 (51.9 %) and 170 (53.8 %) participants were diagnosed with malnutrition by GLIM using left CC or ASMI with NRS2002, respectively. The final step 2 was severity grading, and the number of subjects with moderate malnutrition and severe malnutrition were 106 (26.2 %) and 104 (25.7 %) by GLIM using left CC, and 86 (27.2 %) and 84 (26.6 %) by GLIM using ASMI, respectively.

Table II. The results of the GLIM criteria

Criteria	*n*	%
Phenotypic criteria		
Weight loss > 5 % within past 6 months or > 10 % beyond 6 months	109	26.9
Weight loss > 10 % within the past 6 months or > 20 % beyond 6 months	74	18.3
BMI < 18.5 kg/m^2 if < 70 years or < 20 kg/m^2 if ≥ 70 years	78	19.3
BMI < 17.0 kg/m^2 if < 70 years or < 17.8 kg/m^2 if ≥ 70 years	50	12.3
Left calf circumference < 30 cm (male) or < 29.5 cm (female)	50	12.3
Left calf circumference < 28 cm (male) or < 27.5 cm (female)	12	3.0
ASMI < 7 kg/m^2 (male) or < 5.7 kg/m^2 (female)*	151	47.8
Etiologic criteria		
Reduced food intake or assimilation	405	100.0
Inflammation*	65	20.6

n = *405. BMI: body mass index; ASMI: appendicular skeletal muscle mass index.* *n = *316.*

Table III. Agreements between GLIM using left CC and PG-SGA

	Classification	GLIM using left CC	PG-SGA (≥ 4)	Kappa (95 % CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	AUC (95 % CI)
GLIM using CC with NRS 2002	Malnutrition	210	287	0.463 (0.383-0.543)	67.9	87.3	92.9	52.8	73.6	0.776 (0.728-0.824)
	Moderate/Severe malnutrition	106/104	186/101	0.324 (0.255-0.393)	-	-	-	-	54.3	-
GLIM using CC without NRS 2002	Malnutrition	246	287	0.496 (0.410-0.582)	76.7	78.0	89.4	57.9	77.0	0.773 (0.721-0.825)
	Moderate/Severe malnutrition	133/113	186/101	0.339 (0.266-0.412)	-	-	-	-	56.0	-

n = 405. GLIM: Global Leadership Initiative on Malnutrition; CC: calf circumference; PG-SGA: Patient-Generated Subjective Global Assessment; NRS 2002: Nutritional Risk Screening 2002; PPV: positive predictive value; NPV: negative predictive value; AUC: area under the curve.

MALNUTRITION DIAGNOSED WITH GLIM WITHOUT NRS 2002

For GLIM without NRS 2002, the step 0 screening was not included in the diagnosis process. In the step 1 of diagnosis, there were 246 (60.7 %) and 219 (69.3 %) patients with gastric cancer diagnosed with malnutrition by GLIM using left CC or GLIM using ASMI, respectively. Finally, 133 (32.8 %) and 126 (39.9 %) patients were classified as moderate malnutrition, and 113 (27.9 %) and 93 (29.4 %) were severe malnutrition in the step 2 severity grading (Fig. 1).

MALNUTRITION DIAGNOSED WITH PG-SGA

In the PG-SGA assessment, 287 (70.9 %) were diagnosed with malnutrition in the step 1 (Fig. 1). In the following step 2, 186 (45.9 %) and 101 (24.9 %) participants were graded as having moderate and severe malnutrition, respectively.

VALIDATION OF GLIM USING LEFT CC

The agreement between GLIM using left CC and PG-SGA is shown in table III. When comparing GLIM using left CC with NRS 2002 and PG-SGA, the Kappa coefficients were 0.463 (95 % CI: 0.383-0.543) in the distribution of malnutrition and non-malnutrition, and 0.324 (95 % CI: 0.255-0.393) in the categorization of severe malnutrition, moderate malnutrition and non-malnutrition. When PG-SGA was set as gold standard, the specificity, PPV, and AUC of GLIM using left CC with NRS 2002 were 87.3 %, 92.9 %, and 0.776 (95 % CI: 0.728-0.824) for malnutrition versus non-malnutrition. In the comparison between GLIM using left CC without NRS 2002 and PG-SGA, the Kappa coefficients were 0.496 (95 % CI: 0.410-0.582) and 0.339 (95 % CI: 0.266-0.412), respectively, in binary variables (malnutrition/non-malnutrition) and tripartite variables (severe malnutrition/moderate malnutrition/non-malnutrition). The specificity, PPV, and AUC of GLIM using left CC without NRS 2002 were 78.0 %, 89.4 %, and 0.773 (95 % CI: 0.721-0.825) in the categorization of malnutrition and non-malnutrition.

As presented in table IV, the Kappa coefficients for malnutrition versus non-malnutrition were 0.470 (95 % CI: 0.378-0.562) and 0.574 (95 % CI: 0.474-0.674) between GLIM using ASMI with or without NRS 2002 and PG-SGA. When PG-SGA was set as the gold standard in the categorization of malnutrition and non-malnutrition, the specificity, PPV, and AUC were 86.5 %, 92.9 %, and 0.781 (95 % CI: 0.726-0.836) for GLIM using ASMI with NRS 2002, as well as 73.0 %, 89.0 %, and 0.795 (95 % CI: 0.735-0.855) for GLIM using ASMI without NRS 2002. Table V indicates the agreement between GLIM using left CC and GLIM using ASMI. The Kappa coefficients were ranging from 0.840-0.975. The values of sensitivity, specificity, PPV, NPV, accuracy, and AUC were all higher than 80.0 % or 0.800.

Table IV. Agreements between GLIM using ASMI and PG-SGA

	Classification	GLIM using ASMI	PG-SGA (≥ 4)	Kappa (95 % CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	AUC (95 % CI)
GLIM using ASMI with NRS 2002	Malnutrition	170	227	0.470 (0.378-0.562)	69.6	86.5	92.9	52.7	74.4	0.781 (0.726-0.836)
	Moderate/Severe malnutrition	111/104	186/101	0.354 (0.276-0.432)	-	-	-	-	55.6	-
GLIM using ASMI without NRS 2002	Malnutrition	219	227	0.574 (0.474-0.674)	85.9	73.0	89.0	67.0	82.3	0.795 (0.735-0.855)
	Moderate/Severe malnutrition	157/112	186/101	0.419 (0.337-0.501)	-	-	-	-	60.0	-

n = 316. *GLIM: Global Leadership Initiative on Malnutrition; ASMI: appendicular skeletal muscle mass index; PG-SGA: Patient-Generated Subjective Global Assessment; NRS 2002: Nutritional Risk Screening 2002; PPV: positive predictive value; NPV: negative predictive value; AUC: area under the curve.*

Table V. Agreements between GLIM using left CC and GLIM using ASMI

Classification		GLIM using left CC	GLIM using ASMI	Kappa (95 % CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	AUC (95 % CI)
GLIM with NRS 2002	Malnutrition	165	170	0.968 (0.941-0.995)	97.1	100.0	100.0	96.7	98.4	0.985 (0.970-1.000)
	Moderate/Severe malnutrition	81/84	86/84	0.975 (0.953-0.997)	-	-	-	-	98.8	-
GLIM without NRS 2002	Malnutrition	196	219	0.840 (0.777-0.903)	89.5	100.0	100.0	80.8	92.7	0.947 (0.923-0.972)
	Moderate/Severe malnutrition	103/93	126/93	0.891 (0.848-0.934)	-	-	-	-	94.1	-

n = 316. GLIM: Global Leadership Initiative on Malnutrition; CC: calf circumference; ASMI: appendicular skeletal muscle mass index; NRS 2002: Nutritional Risk Screening 2002; PPV: positive predictive value; NPV: negative predictive value; AUC: area under the curve.

DISCUSSION

The prevalence of patients with nutritional risk was 58.0 % in this study. Yang et al. study found 61.4 % of patients with gastric cancer were at nutritional risk by NRS 2002 (22). Mao et al. reported 53.8 % of gastric cancer patients were on malnutrition risk when screened with NRS 2002 (23). The results of this study were similar to those of previous studies on nutritional risk rates. According to GLIM using left CC with NRS 2002, the prevalence of malnutrition in this study was 51.9 % with 26.2 % moderate malnutrition and 25.7 % severe malnutrition. The findings in Li et al. study indicated the incidence of malnutrition was 53.0 %, of which 26.0 % and 27.0 % were identified as moderate and severe malnutrition (2). Matsui et al. reported 54.0 % of patients with advanced gastric cancer classified as malnutrition, and the prevalence of moderate malnutrition and severe malnutrition were 29.5 % and 24.5 %, respectively (24). Regarding GLIM using left CC without NRS 2002, 60.7 % (32.8 % moderate and 27.9 % severe) of gastric cancer patients were diagnosed as malnutrition. When screening tools were not used, the prevalence of malnutrition diagnosed by GLIM was higher than when screening tools were used. Similar results have been reported in the study of Rosnes et al. and Henriksen et al (12,25). In this study, the prevalence of malnutrition in patients with gastric cancer was as high as 70.9 % when malnutrition was assessed using PG-SGA. The malnutrition prevalence was 80.4 % and 71.6 % based on PG-SGA in similar studies (26,27). In fact, the prevalence of malnutrition may be overestimated when using PG-SGA for diagnosis (12). Moreover, the prevalence of malnutrition is often higher in patients with gastric cancer than in patients with other types of tumors (1,28).

In the phenotypic criteria, the positivity proportions of left calf circumference were much lower than the positivity proportions of weight loss, BMI, and ASMI. Most studies of GLIM in patients with gastric cancer have used skeletal muscle index as evidence of reduced muscle mass (4,29,30). There are fewer studies that use calf circumference as evidence of reduced muscle mass in gastric cancer patients. However, calf circumference assessment may be the best alternative when other assessment methods for reduced muscle mass are not available, especially in many low- and middle-income countries and rural areas. Li et al. applied calf circumference as the criterion for reduced muscle mass in GLIM diagnosis and used malnutrition to predict overall survival in gastric cancer patients (2). The fifth percentile (p5) and 15th percentile (p15) of the calf circumference were calculated as moderate malnutrition and severe malnutrition, but no specific thresholds were reported (2). In the mixed cancer patients, the cut-off values of calf circumference were reported, male 30 cm or female 29.5 cm for moderate malnutrition and male 28 cm or female 27.5 cm for severe malnutrition (20). Similar cut-off values of calf circumference were commonly applied in GLIM malnutrition diagnosis among patients with other types of tumors, distinguishing between patients' sexes or not (31-33). Our findings can

provide further good real-world value to this field with limited evidence, especially in Chinese patients with gastric cancer. In fact, measuring calf circumference is one of the most convenient and cost-effective ways to rate a patient's muscle mass.

Moderate concordances were found between GLIM using left CC and PG-SGA, as well as between GLIM using ASMI and PG-SGA. The moderate concordances were also reported between GLIM and PG-SGA for the diagnosis of malnutrition both in patients with gastric cancer and other cancer patients (4,17,18,34-36). With PG-SGA as the gold standard, the sensitivity, specificity, PPV, NPV, AUC and accuracy of GLIM using left CC and GLIM using ASMI were all acceptable. Most studies showed the values of sensitivity and specificity were 48 %-98 % between GLIM with or without NRS 2002 and PG-SGA (12,18,34-38). The PPV and NPV were 47 %-98 % (4,18,35,36). The results of AUC were also moderate and similar to previous studies, from 0.632 to 0.800 (18,34,35,37). The results of this study were similar to those of previous studies. Though few studies have reported accuracy between GLIM and PG-SGA in cancer patients, similar results were found in other populations between GLIM and Subjective Global Assessment (SGA) (39). However, several studies showed the values of Kappa coefficient, PPV and NPV were lower between GLIM with/without NRS 2002 and PG-SGA in cancer patients (12,37,38). In these studies, the assessment results of PG-SGA were divided into well-nourished (A), moderately malnourished or suspected malnourished (B) or severely malnourished (C), which were different from this study (12,37,38). In future similar studies, it is important to pay attention to the threshold of PG-SGA for diagnosing malnutrition, as this may lead to inconsistent findings. In the categorization of severe malnutrition, moderate malnutrition and non-malnutrition, the agreements were all lower than malnutrition versus non-malnutrition between GLIM and PG-SGA. With GLIM using ASMI as the gold standard, higher concordances were demonstrated between GLIM using left CC and GLIM using ASMI with or without NRS 2002, indicating that the two have consistent diagnostic efficacy for malnutrition. Few studies have used GLIM using ASMI as a gold standard to validate GLIM using left CC. Wang et al. evaluated the validity of GLIM using CC or GLIM using ASMI with the Malnutrition Universal Screening Tool (MUST) in diagnosing malnutrition/non-malnutrition compared with PG-SGA among ambulatory cancer patients (36). The values of Kappa coefficient, sensitivity, specificity, PPV and NPV were 0.565, 55.3 %, 97.9 %, 94.9 % and 75.3 % for GLIM using CC, and 0.586, 57.4 %, 97.9 %, 95.1 % and 76.2 % for GLIM using ASMI (36). The agreements were highly consistent between GLIM using CC and GLIM using ASMI when PG-SGA was used as the gold standard. Our findings in this study further confirmed the results in the above study. However, the positivity proportion of left CC was much lower than that of ASMI in this study, which may be related to the different calf circumference thresholds used. The muscle mass reduction (MMR) is defined as CC < 34 cm in men or CC < 33 cm for women in their study (36). It is recommended that future studies explore and analyze the diagnostic process between the two in more detail.

The strengths of this study are as follows: a) the GLIM using left CC was validated according to the recommendations of van der Schueren et al. (14); b) the study population was a single type of gastric cancer patient; c) the sample size was already large for gastric cancer patients. The possible limitations were: a) this is a single-center study, and the findings may not be generalized to all patients with gastric cancer; b) only patients with ECOG-PS scores less than 4 were included in the study, but patients with an ECOG-PS score of 4 may no longer be suitable for effective nutritional interventions or treatments due to their medical condition; and c) considering the differences in body composition across races, the results of this study may only be applicable to Chinese patients.

CONCLUSIONS

The prevalence of nutritional risk and malnutrition were higher in patients with gastric cancer. The prevalence of malnutrition diagnosed through PG-SGA was higher than with GLIM using left CC without NRS 2002, and the prevalence of malnutrition diagnosed by GLIM using left CC without NRS 2002 was higher than that of GLIM using left CC with NRS 2002. The agreements were acceptable both between GLIM using left CC and PG-SGA, and between GLIM using left CC and GLIM using ASMI. The left calf circumference can be one of the credible references that indicating the reduced muscle mass in patients with gastric cancer. The agreements regarding malnutrition versus non-malnutrition were better than those for tripartite variables (severe malnutrition/moderate malnutrition/non-malnutrition).

AUTHOR´S CONTRIBUTIONS

Liang Fu: conceptualization, formal analysis, funding acquisition, methodology, software, writing original draft. Xiaoqian Xu, Haixia Shi, Qiaohui Guan, Lijun Zhang and Yanting Hu: conceptualization, data curation, formal analysis, investigation. Yaoqi Zhang, Jianxiang Jin and Sha Zhu: conceptualization, data curation, methodology, project administration, resources. Bo Zhuang: conceptualization, resources. Lushan Zheng and Xianghong Ye: conceptualization, supervision, validation, visualization, writing original draft, writing review & editing. All authors contributed to and approved the final version of the manuscript.

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