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A modified GLIM criteria-based nomogram for the survival prediction of gastric cancer patients undergoing surgical resection

Xi Luo[1*], Bin Cai[2,3*] and Weiwei Jin[1]

Abstract

Background This study aimed to develop a comprehensive model based on five GLIM variables to predict the individual survival and provide more appropriate patient counseling.

Methods This retrospective cohort study included 301 gastric cancer (GC) patients undergoing radical resection. C-reactive protein (CRP) as an inflammatory marker was included in GLIM criteria and a nomogram for predicting 5-year overall survival (OS) in GC patients was established. The Bootstrap repeated sampling for 1000 times was used for internal validation.

Results Of the total 301 patients, 20 (6.64%) died within 5 years. CRP improved the sensitivity and accuracy of the survival prediction model (AUC = 0.782, 0.694 to 0.869 for the model without CRP; AUC = 0.880, 0.809 to 0.950 for the model adding CRP). Besides, a GLIM-based nomogram was established with an AUC of 0.889. The C-index for predicting OS was 0.878 (95% CI: 0.823 to 0.934), and the calibration curve fitted well. Decision curve analysis (DCA) showed the clinical utility of the nomogram based on GLIM.

Conclusion The addition of CRP improved the sensitivity and accuracy of the survival prediction model. The 5-year survival probability of GC patients undergoing radical resection can be reliably predicted by the nomogram presented in this study.

Keywords GLIM, C-reactive protein, Malnutrition, Gastric cancer, Overall survival, Prediction

Background

As a common digestive tract tumor, gastric cancer (GC) has a high incidence in East Asia, especially in China, Japan, and South Korea [1–3]. According to the latest data in 2020, the incidence and mortality of GC in China ranked third among all malignancies [3]. To date, surgical resection remains the main treatment option for GC [3]. However, the stress of surgery can rapidly deplete the body's nutrient reserves, thereby affecting the body's functional recovery and wound healing. Conditions such as neoadjuvant therapy implemented postoperatively may also contribute to the impairment of nutrient reserves, further affecting the patient's recovery. In

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addition, it is well known that malnutrition is a common problem among patients with cancer [4]. The prevalence of malnutrition in patients with GC is the highest among all malignancies [5] due to factors such as digestive tract obstruction, delayed gastric emptying, impaired digestion and absorption, which directly affect nutrient uptake, digestion, and absorption [4].

Early diagnosis and timely intervention of malnutrition can significantly reduce medical costs, shorten hospital stays, improve treatment outcomes, and prolong patient survival [6–8]. Nevertheless, there have been no internationally recognized standards in the diagnosis of malnutrition. To identify malnutrition, different studies have used different assessment tools. Research in this field is significantly behind other disease areas [9, 10]. Therefore, the European Society for Parenteral and Enteral Nutrition (ESPEN) and the American Society for Parenteral Enteral Nutrition (ASPEN) published the GLIM consensus on the diagnosis definition of malnutrition [11, 12]. Since publication, validation has been reported in patients with head and neck [13], gastrointestinal [14, 15], and pulmonary [16, 17] tumors. However, none of these studies explored the diagnostic and predictive value of inflammatory indicators. More information on the choice of indicators for the evaluation of inflammation in etiological criteria is still pending. Besides, the GLIM criteria for identifying malnutrition require patients to meet at least one etiologic criterion and one phenotypic criterion [11, 12]. The six different diagnostic combinations formed by the two etiologic and three phenotypic criteria of the GLIM consensus may lead to differences in the prediction of clinical outcome and survival. Accurate nutritional diagnosis is the prerequisite for rational nutritional therapy. Thus, a comprehensive model built based on these variables is required for patient counseling and survival prediction.

In this study, the diagnostic value of C-reactive protein (CRP), mentioned several times in the GLIM consensus, was evaluated. Furthermore, a GLIM-based nomogram was established using the five indicators of GLIM.

Methods

Study population

This single-center, observational, and hospital-based retrospective cohort study aimed to evaluate the prevalence of malnutrition in GC patients undergoing surgical resection as the first-line treatment and the correlation of malnutrition diagnosed by the GLIM criteria with overall survival (OS). All participants who met the following inclusion and exclusion criteria were consecutively enrolled between January 2015 and July 2021. Inclusion criteria: (1) aged ≥ 18 years old; (2) hospitalized patients properly diagnosed with GC and undergoing elective surgery; (3) never received surgery, radiotherapy, chemotherapy, and other anti-tumor treatments (including immunotherapy); (4) willing to participate in this study. Exclusion criteria: (1) aged < 18 years old; (2) with admission time no more than 48 h; (3) suffered from severe heart, liver, and brain dysfunction; (4) suffered from active systemic infection; (5) hospitalized patients properly diagnosed with GC and undergoing palliative surgery; (6) refused to participate in this study.

Data was obtained from the Electronic Medical Record (EMR) System and retrospectively analyzed. Within the first 48 h after admission, general information, anthropometric data, laboratory results, existing comorbidities, nutrition-related data, and medical history of all patients were gathered and documented by doctors, nurses, and clinical dietitians. The oncotherapy-related data and follow-up information were also recorded in the EMR system. The eighth edition of the AJCC TNM staging system was used to determine all pathological staging.

The primary outcome of this study was mortality in the 5-year follow-up survival cohort. All participants were monitored from the initial admission to death or until the end of July 2024. The study was approved by the Medical Ethics Committee of Tongde Hospital of Zhejiang Province (No.2022147JY). The need for written informed consent was waived by the Institutional Review Board of Tongde Hospital of Zhejiang Province due to retrospective nature of the study. All methods were performed in accordance with the relevant guidelines and regulations.

Malnutrition diagnosed by GLIM criteria

The GLIM criteria for the diagnosis of malnutrition require that individuals meet at least one etiologic criterion and one phenotypic criterion [11, 12]. The GLIM criteria are summarized in Supplement Table 1. All data were available from medical records and nutritional assessment records. Supplement Table 2 provides a list of the GLIM indicators for diagnosing and assessing the severity of nutritional status [18, 19].

Development of a nomogram model

The five indicators including two etiologic indexes and three phenotypic indexes were applied to establish a prediction model. The relationship between the GLIM criteria and OS was verified using a multivariate Cox regression analysis, then a nomogram based on each GLIM criterion's hazard ratio (HR) was created. The Bootstrap repeated sampling for 1000 times was used for internal validation. Harrell's concordance index (C-index) was calculated by the bootstrap approach with 1000 resamples to evaluate the discrimination of the nomogram. The predictive accuracy for the 5-year OS was examined using the area under receiver operating characteristic curve (AUC). Through a comparison of observed and predicted survival, the nomogram for 5-year OS was

Table 1 Characteristics of GC patients

Characteristics	Normal ($n=164$)	Malnutrition ($n=137$)	*P* value
General information			
Age, years, mean ± SD	61.66 ± 10.61	68.64 ± 10.13	< 0.001
Sex, male, n (%)	118 (71.95)	93 (67.88)	0.443
Education, n (%)			0.929
below high school	110 (67.48)	90 (65.69)	
high school	27 (16.56)	23 (16.79)	
above college school	26 (15.95)	24 (17.52)	
LOS, days, median (IQR)	20 (17, 24)	22 (19, 30)	0.003
Cost, yuan, median (IQR)	60130.26 (53121.29,68477.24)	64973.34 (55584.66, 80400.89)	< 0.001
Alcohol, yes, n (%)	36 (21.95)	25 (18.25)	0.426
Smoking, yes, n (%)	35 (21.47)	31 (22.63)	0.810
Chronic disease, n (%)			0.481
0–1	130 (79.27)	113 (82.48)	
≥2	34 (20.73)	24 (17.52)	
Diabetes mellitus, n (%)	27 (16.46)	17 (12.41)	0.321
Hypertension, n (%)	66 (40.24)	55 (40.15)	0.986
Current disease and treatment			
Pathologist classification, n (%)			0.760
Adenocarcinoma	103 (62.80)	93 (67.88)	
SRCC	6 (3.66)	3 (2.19)	
Mixed (≥ 2)	46 (28.05)	35 (25.55)	
Others	6 (3.66)	3 (2.19)	
Nerve invasion, yes, n (%)	70 (42.68)	70 (51.09)	0.145
Vascular invasion, yes, n (%)	54 (32.93)	54 (39.42)	0.242
Stages, n (%)			0.760
I	23 (14.02)	16 (11.68)	
II	69 (42.07)	56 (40.88)	
III	72 (43.90)	65 (47.45)	
Differentiation grade, n (%)			0.246
Poor	74 (45.12)	75 (54.74)	
Moderate	64 (39.02)	45 (32.85)	
Well	26 (15.85)	17 (12.41)	
Tumor size, n (%)			0.011
< 4 cm	90 (54.88)	55 (40.15)	
≥ 4 cm	74 (45.12)	82 (59.85)	
Operation method, n (%)			0.281
Radical total gastrectomy	56 (34.15)	59 (43.07)	
Distal gastrectomy	99 (60.37)	72 (52.55)	
Proximal gastrectomy	9 (5.49)	6 (4.38)	
Postoperative complications, yes, n (%)	46 (28.05)	73 (53.28)	< 0.001
30 days mortality, n, (%)	0 (0.00)	1 (0.73)	0.273
Unplanned admission, yes, n (%)	1 (0.61)	13 (9.49)	< 0.001
Curative chemotherapy, yes, n (%)	129 (78.66)	108 (79.41)	0.873
Nutrition-related information			
BMI, kg/m2, mean ± SD	22.97 ± 2.39	20.48 ± 3.20	< 0.001
GLIM severity grading, n (%)			< 0.001
Moderate malnutrition	0 (0.00)	60 (43.80)	
Severe malnutrition	0 (0.00)	57 (41.61)	
PNS, yes, n (%)	151 (92.07)	130 (95.59)	0.213
ENS, yes, n (%)	46 (28.22)	77 (56.62)	< 0.001

GLIM, the global leadership initiative on malnutrition; SD, standard deviation; LOS, length of stay; GC, gastric cancer; SRCC, Signet-ring cell carcinoma; NRS2002, the nutritional risk screening 2002; PNS, parenteral nutritional support; ENS, enteral nutritional support

Table 2 The univariable and multivariable cox regression analysis of each GLIM criteria for OS

GLIM criteria	Model 1	Model 2	Model 3
	HR (95% CI) *P* value	HR (95% CI) *P* value	HR (95% CI) *P* value
Unintentional weight loss			
Normal	1 (Ref)	1 (Ref)	1 (Ref)
Moderate malnutrition	6.957 (1.868, 25.914) 0.004	5.658 (1.509, 21.222) 0.010	9.213 (2.061, 41.175) 0.004
Severe malnutrition	34.352 (11.900, 99.162) < 0.001	25.799 (8.639, 77.041) < 0.001	17.449 (4.739, 64.251) < 0.001
Low BMI			
Normal	1 (Ref)	1 (Ref)	1 (Ref)
Moderate malnutrition	7.211 (2.034, 25.561) 0.002	6.340 (1.620, 24.817) 0.008	4.959 (1.348, 18.241) 0.016
Severe malnutrition	11.980 (3.755, 38.218) < 0.001	7.340 (2.171, 24.815) 0.001	4.463 (1.139, 17.483) 0.032
Reduce muscle			
Normal	1 (Ref)	1 (Ref)	1 (Ref)
Malnutrition	8.262 (3.420, 19.957) < 0.001	5.522 (2.204, 13.833) < 0.001	3.387 (1.133, 10.120) 0.029
Reduce intake			
Normal	1 (Ref)	1 (Ref)	1 (Ref)
Malnutrition	5.868 (1.947, 17.683) 0.002	3.965 (1.287, 12.212) 0.016	3.236 (1.025, 10.213) 0.045
CRP index			
CRP < 3 mg/L	1 (Ref)	1 (Ref)	1 (Ref)
CRP ≥ 3 mg/L	8.536 (2.853, 25.538) < 0.001	8.094 (2.703, 24.230) < 0.001	5.943 (1.822, 19.380) 0.003

HR, hazard ratio; CI, confidence interval; GLIM, the global leadership initiative on malnutrition; OS, overall survival; BMI, body mass index; CRP, C-reactive protein

Model 1: univariable analysis

Model 2: adjust for age

Model 3: adjust for age, chronic disease, tumor size, tumor stage, nerve invasion, vascular invasion, pathologist classification, differentiation grade, chemotherapy, albumin, neutrophil, lymphocyte, monocyte and platelet

calibrated. Finally, decision curve analysis (DCA) was used to evaluate the clinical utility of the GLIM-based nomogram.

Statistical analysis

The data were analyzed with the statistical package R (The R Foundation; http://www.r-project.org; version 3.6.3). Quantitative data were presented as mean ± standard deviation. Differences between the two groups were analyzed by the Students' t-test. Non-parametric tests (Mann Whitney or Kruskall Wallis) were utilized for variables that did not follow a normal distribution. A chi-square test was used to compare qualitative variables, with Fisher adjustment if necessary. Besides, OS data were analyzed using the Cox regression and Kaplan-Meier curve. To account for potential confounders, a multivariate Cox regression analysis was also carried out utilizing backward selection. Finally, a GLIM-based nomogram that was adjusted for potential confounders was built. The threshold of statistical significance was set at P-value < 0.05.

Results

The baseline characteristics of the patients are summarized in Table 1 (n = 301). The nutritional status of the patients was retrospectively assessed using GLIM criteria. The incidence of malnutrition in GC patients was 45.51%, of which 43.80% were moderate malnutrition and 41.61% were severe malnutrition. As shown in Table 1, GC patients in the malnutrition group presented significantly higher age, cost, and the proportion of postoperative complications, unplanned admission, and enteral nutritional support compared to the normal nourished group; meanwhile, they had a lower BMI. Kaplan-Meier curve was used to analyze the relationship between GLIM and OS. The 5-year survival rate was 98.78% (162/164) in the normally nourished group and 86.86% (119/137) in the malnutrition group. Compared to patients in the normally nourished group, patients in the malnourished group had a poorer OS rate (Fig. 1A). Additionally, the degree of malnutrition status was linked to OS (Fig. 1B). Cox model validation showed that nutritional status was strongly related to an increased risk of mortality according to GLIM criteria. Severe malnutrition continued to be an independent predictive factor even after adjustment for confounding variables (Table 2). Among the five criteria, unintentional weight loss (HR = 9.213, 95% CI: 2.061 to 41.175 for moderate malnutrition and HR = 17.449, 95% CI: 4.739 to 64.251 for severe malnutrition) was found to be the main factor affecting mortality when the weights of each GLIM criterion were calculated (Table 2). Besides, the inclusion of CRP as an inflammatory marker in GLIM criteria improved the sensitivity and accuracy of the survival prediction model (Model 1 without CRP, AUC = 0.782, 95% CI: 0.694 to 0.869, sensitivity: 0.895, specificity: 0.654; Model 2 inclusion of CRP, AUC = 0.880, 95% CI: 0.809 to 0.950, sensitivity: 0.700, specificity: 0.886), as shown in Fig. 2. In addition, we also

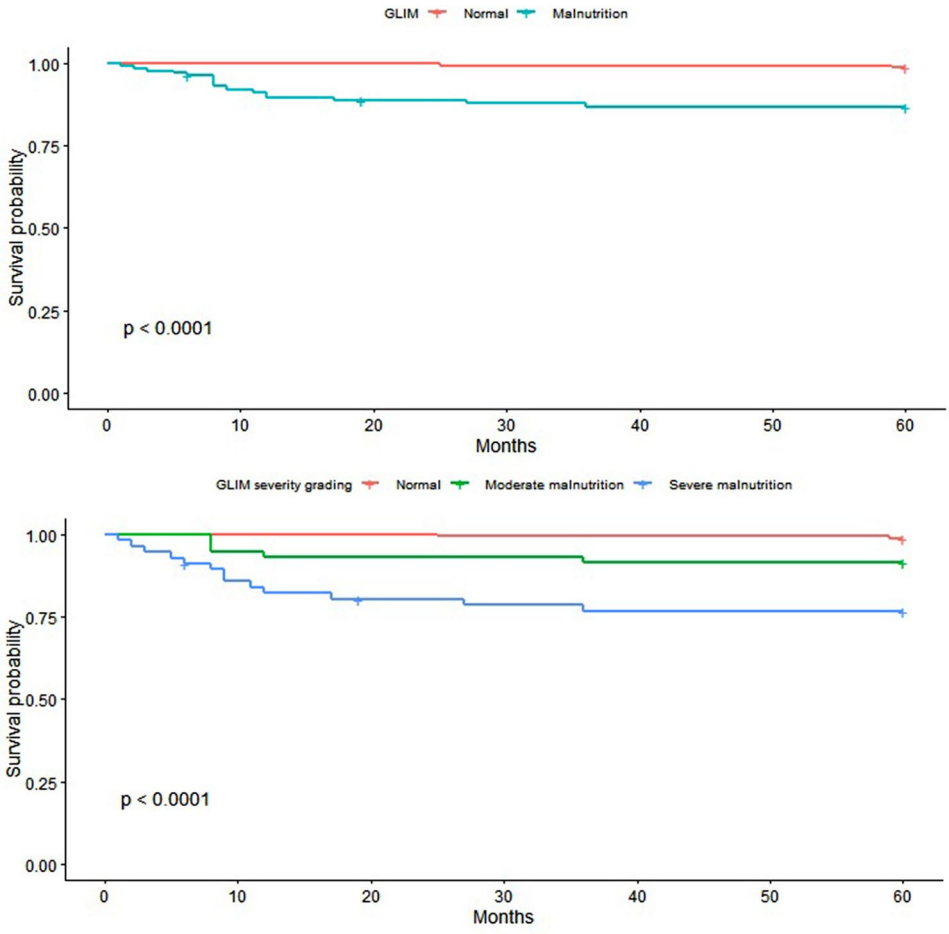

Fig. 1 Kaplan-Meier curves. Kaplan-Meier curve stratified by the GLIM criteria; adjusted by age, chronic disease, tumor size, tumor stage, nerve invasion, vascular invasion, pathologist classification, differentiation grade, albumin, c-reactive protein, neutrophil, lymphocyte, monocyte and platelet

compared the predictive values between CRP and other inflammatory indicators for predicting 5-year mortality [including neutrophil to lymphocyte (NLR), platelet to lymphocyte (PLR), systemic immune inflammation index (SII), and lymphocyte to monocyte (LMR)] (Supplement Fig. 1). The result indicated that CRP (AUC=0.733) had a better predictive value for predicting 5-year mortality than other inflammatory indicators [NLR (AUC=0.630), PLR (AUC=0.628), SII (AUC=0.628), and LMR (AUC=0.621)].

A GLIM-based nomogram was established using the five indicators of GLIM. Each subtype within these variables was assigned a score on the point scale. The nomogram was developed as shown in Fig. 3A. The AUC of model for predicting 5-year mortality was 0.889 (95% CI: 0.830 to 0.948). The C-index for OS prediction was 0.878 (95% CI: 0.823 to 0.934), and the calibration curve fitted well. The internal validation of the nomogram was conducted by performing a 1000 bootstrap analysis. In the internal validation, the C-index for OS prediction was 0.871 (95% CI: 0.804 to 0.938), and the 5-year AUC was 0.884 (95% CI: 0.817 to 0.935). Additionally, DCA showed that the GLIM-based nomogram had clinical application value (Fig. 3D).

Discussion

It is well-recognized that malnutrition has an independently impact on mortality [6, 8], particularly in cancer patients [20]. Completing nutritional assessment before starting cancer treatment is imperative. In this study, we found that the GLIM criteria could effectively evaluate nutritional status. The prevalence of malnutrition demonstrated in this study was 45.51%, which was similar to an earlier published study [20]. Besides, our results suggested that malnutrition diagnosed by GLIM was an independent risk factor for OS.

Among the phenotypic criteria of GLIM consensus, unintentional weight loss was a key phenotypic characteristic that must be taken into account in the evaluation of cancer patients' nutritional status [20]. It has been shown that cancer patients who lose weight will face more and heavier adverse reaction of chemotherapy, often resulting

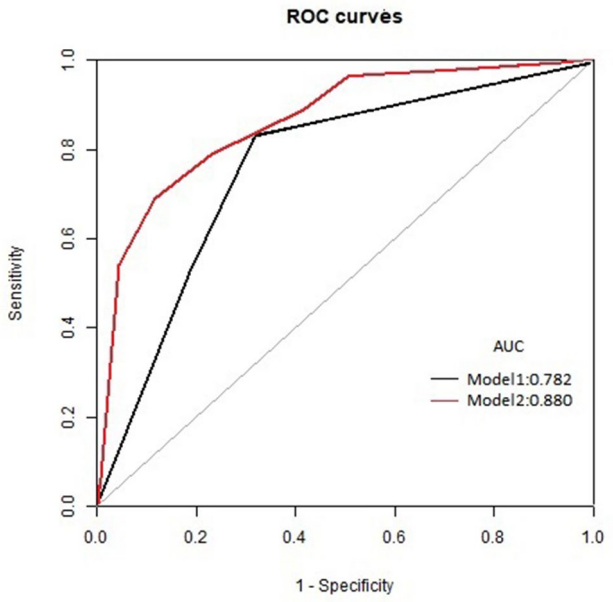

Fig. 2 ROC curves for predicting the overall survival at 5 years. ROC: receiver operator characteristic. AUC: area under curve; BMI, body mass index; CRP: C-reactive protein. Model 1 including unintentional weight loss, low BMI, reduced muscle mass and reduced intake. Model 2 add CRP index. Model 1, AUC = 0.782, 95% CI: 0.694 to 0.869, sensitivity: 0.895, specificity: 0.654. Model 2, AUC 0.880, 95% CI: 0.809 to 0.950, sensitivity: 0.700, specificity: 0.886

in shorter OS and poorer quality of life [21]. In actuality, weight loss was the first obvious or observable indication in cancer patients. A study has shown that approximately 40% of cancer patients reported weight loss of more than 10% at the time of their first diagnosis [20]. In our cohort, 38.87% of the study population satisfied the standards of unintentional weight loss. In addition, during a five-year follow-up, unintentional weight loss was the main factor contributing to mortality in the study population. The results obtained confirmed previous observations that unintentional weight loss was a reliable and independent predictor of OS in cancer patients. Muscle mass loss was also a direct manifestation of malnutrition. Previous studies have shown that approximately 20–70% of cancer patients suffer from muscle mass loss [4, 5, 20], which is related to metabolic abnormalities in patients with cancer. Catabolic proinflammatory cytokines induced by tumor cells could induce catabolism of fat and muscle while inhibiting anabolism [22], which can reduce the tolerance and effectiveness of antitumor therapy and further affect clinical outcomes. Anthropometric and physical examinations, such as CC and mid-arm muscle circumference, were routinely performed during nutritional screening and assessment. Thus, CC was used as an indicator of muscle mass loss in this study. According to the newly published consensus on the diagnosis and treatment of sarcopenia in Asia, the cut-off values of CC were set to <33 cm in men and <32 cm in women [18, 19]. Additionally, an earlier study confirmed that BMI was an independent predictor of OS in cancer patients [21]. However, a low BMI has a restricted ability to assess nutritional status [21]. In the current study, a low BMI also showed a relatively weak effect on survival among the five criteria of GLIM consensus. Besides, only 15.33% of the patients in this study were under the BMI threshold. Cancer patients were frequently found to be overweight or obese, with some even having fluid retention that can mask weight reduction and cause an unnaturally high BMI.

Numerous studies have revealed the potential value of inflammatory factors (such as CRP, lymphocyte, and neutrophil, etc.) in assessing tumor prognosis [23]. However, none of the previous studies discussed the diagnostic and predictive value of inflammatory indicators incorporated into the GLIM-based model. Hence, more information about inflammatory indicators is needed. As a widely recognized representative of the systemic inflammatory response, CRP is also associated with the progression and prognosis of cancer [23]. An elevated CRP value indicates that the body is in a severe state of inflammation and stress, while the metabolic status of the body changes, and the resting energy expenditure increases, which could aggravate the malnutrition of cancer patients [23]. Numerous previous studies also found that patients with high CRP value were generally associated with lower levels of albumin, albumin, total protein, hemoglobin, and lymphocyte [23]. Therefore, despite all included patients automatically satisfied the standard of etiology, CRP was still applied as an inflammatory marker in our prognostic model. The modified Glasgow Prognostic Score (mGPS) has been widely used in the assessment of systemic inflammation in the body, and it is relatively simple, objective, and easy to be implemented in clinical practice [24]. Thus, the cut-off values of the inflammatory markers applied in our model were referenced to the mGPS. Our result revealed that CRP ≥ 3 mg/L had an impact on survival (HR = 5.943, 95% CI: 1.822 to 19.380). Furthermore, we found that CRP improved the sensitivity and accuracy of the survival prediction model. In comparison with an earlier published study, our model had a higher sensitivity and specificity [19]. Another aspect of the GLIM etiologic criteria may be the evaluation and quantification of various symptoms representing obstacles to dietary intake. In newly diagnosed cancer patients, anorexia occurs in roughly 50% of cases [25], which may be associated with the release of specific active factors, such as tumor necrosis factor-alpha, interleukin-1, interleukin-6, and 5-hydroxytryptamine, induced by tumor cells [25]. Symptoms such as anorexia and early satiety may also result from disruption of neuroendocrine pathways between neuropeptides and

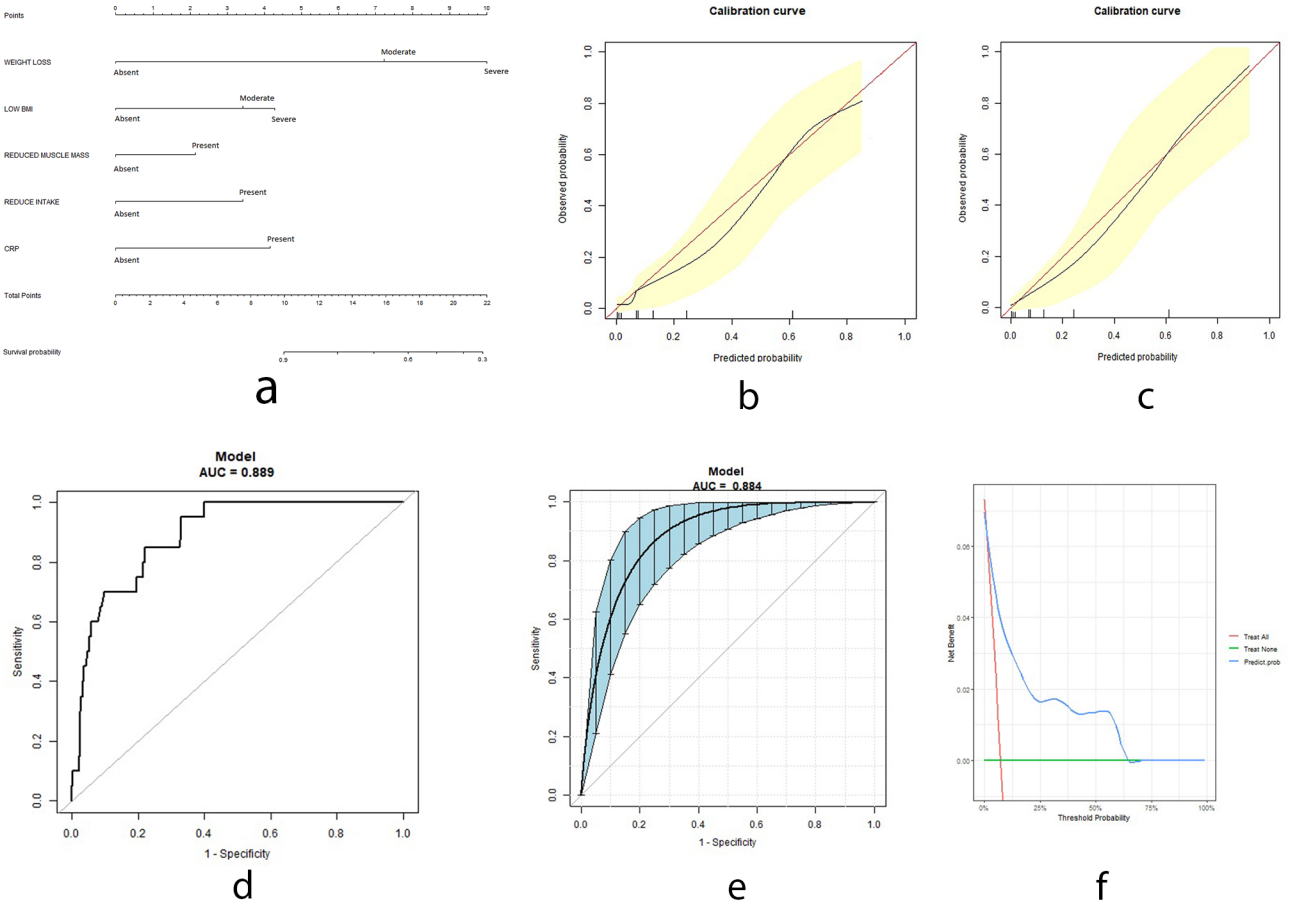

Fig. 3 The nomogram used to quantize the GLIM. ROC: receiver operator characteristic; AUC: area under curve. (**A**) The nomogram used to quantize the GLIM. First, locate each GLIM criteria site on the axis, then draw a line straight upward to the Points axis to determine how many points the patient receives for the variable. Add the points for each of these predicators together and locate the sum on the total points axis to get the scored GLIM (**B**) Calibration curves for the nomogram in the cohort (B1) and by bootstrapping (B = 1000 repetitions) (B2). The x-axis represents the nomogram-predicted probability and y-axis represents the actual probability of the 5 years overall survival. Perfect prediction would correspond to 45°red line (**C**) ROC curve analysis for predicting the overall survival in the cohort (C1) and by bootstrapping (C2). Developing cohort: Harrell's C index: 0.878, 95%CI: 0.823 to 0.934. AUC = 0.889, 95% CI: 0.830 to 0.948, sensitivity: 0.888, specificity: 0.616. Bootstrapping (B = 1000 repetitions): Harrell's C index: 0.871, 95%CI: 0.804 to 0.938. AUC = 0.884, 95% CI: 0.817 to 0.935, sensitivity: 0.821, specificity: 0.688 (**D**) Decision curve analysis on the GLIM based system (blue line). The red line denotes the assumption that all patients have outcome event (death) during follow-up. Green line represents the assumption that no patients have outcome event (death) during follow-up

other neurotransmitters in the central nervous system [21, 25]. In addition, gastrointestinal obstruction caused by gastrointestinal cancers can result in abdominal distention and poor appetite. In this study, 40.53% of subjects had dietary intake symptoms, and malnourished patients showed more symptoms of dietary intake than non-malnourished patients. Reduced appetite can cause inadequate nutrient intake, which in turn can lead to malnutrition and cachexia. Cachexia has been proven to be prevalent in cancer patients, especially in upper gastrointestinal and pancreatic cancers [25].

The primary limitation of this research is the limited sample size. The assessment of muscle mass loss was assessed via anthropometric data in this study, and there was no body composition analysis data available. The established prediction model should be validated by an external cohort, but there is a lack of external validation data. In addition, considering the potential impact of certain complications on a patient's survival, we have excluded some patients (n=6) who had severe heart, liver, brain dysfunction, or active systemic infection in this analysis, which might result in a biased sample. However, we performed a sensitivity analysis about the before the exclusion of patients with complications (n=307). As shown in Supplement Fig. 2, the GLIM-based nomogram still has good predictive performance (AUC=0.835, 95%CI: 0.735 to 0.934; internal validation: AUC=0.832, 95%CI: 0.743 to 0.913). Therefore, our team has initiated an observational, multi-center, and hospital-based prospective cohort study on GLIM.

Conclusions

In summary, the inclusion of CRP as an inflammatory marker in GLIM criteria could improve the sensitivity and accuracy of the survival prediction model. Our study also confirmed that GLIM-diagnosed malnutrition was an independent risk factor for predicting mortality and a major negative factor for clinical prognosis in GC patients undergoing surgical resection. The quantitative scoring system for GC was helpful for accurate nutrition diagnosis and can be applied in individualized clinical nutritional therapy in the perioperative period.

Abbreviations

GC	Gastric cancer
ESPEN	European Society for Parenteral and Enteral Nutrition
ASPEN	American Society for Parenteral Enteral Nutrition
CRP	C-reactive protein
OS	Overall survival
EMR	Electronic Medical Record
HR	Hazard ratio
AUC	Area under receiver operating characteristic curve
DCA	Decision curve analysis

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-024-03395-5.

Supplementary Material 1

Acknowledgements

Not applicable.

Author contributions

Xi Luo and Bin Cai designed the study. Xi Luo wrote the manuscript. Bin Cai and Weiwei Jin collected, analyzed, and interpreted the data. Xi Luo and Bin Cai critically reviewed, edited, and approved the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the Medical Ethics Committee of Tongde Hospital of Zhejiang Province (No.2022147JY). The need for written informed consent was waived by the Institutional Review Board of Tongde Hospital of Zhejiang Province due to retrospective nature of the study. All methods were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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