Methods for diagnosing malnutrition in patients with esophageal cancer, and the association with nutritional and inflammatory indices: A cross-sectional study

XUEYUAN KONG, PING LIU, GUOTIAN WANG, SHIQING SUN and LING LI

Department of Oncology, Tengzhou Central People's Hospital, Tengzhou, Zaozhuang, Shandong 277500, P.R. China

Received November 20, 2024; Accepted February 14, 2025

DOI: 10.3892/ol.2025.14969

Abstract. Clinically, it is important to diagnose malnutrition for the treatment and prognosis of cancer patients; however, at present, there are no established standards. The present study evaluated the consistency of malnutrition diagnostic tools in association with relevant nutritional and inflammatory markers in patients with advanced esophageal cancer. Specifically, the Patient-Generated Subjective Global Assessment (PG-SGA) and Global Leadership Initiative on Malnutrition (GLIM) tools were assessed. Patients with a new diagnosis of esophageal cancer at Tengzhou Central People's Hospital (Tengzhou, China) between January 2023 and December 2023 were evaluated within 24 h of admission using Nutritional Risk Screening 2002 (NRS2002), GLIM and PG-SGA. Additionally, relevant physical examinations and laboratory data were collected. The malnutrition occurrence rates based on PG-SGA, GLIM and GLIM with NRS2002 screening (NRS2002-GLIM) were 75.01, 51.88 and 41.25%, respectively. The agreement between PG-SGA and GLIM, and between PG-SGA and NRS2002-GLIM diagnoses was weak (κ=0.379, P<0.001; and κ=0.376, P<0.001, respectively). PG-SGA showed a moderate negative correlation with body mass index (BMI) (r_s=-0.460), weak positive correlations with age (r_s=0.234) and IL-6 (r_s=0.249), and very weak negative correlations with albumin (r_s=-0.178) and PNI (r_s=-0.168). While the indicators correlated with GLIM and PG-SGA were consistent, the strength of correlation varied slightly. Logistic regression analysis of PG-SGA and GLIM indicated that age and BMI were independent risk factors for malnutrition. In addition, PG-SGA also showed that the neutrophil count was an independent risk factor for malnutrition. Overall, patients with esophageal cancer exhibit a high incidence of malnutrition, and different diagnostic methods provide varying results. Malnutrition is closely associated with age, inflammatory markers and BMI, suggesting their potential utility in guiding nutritional interventions for patients with esophageal cancer.

Correspondence to: Dr Ling Li, Department of Oncology, Tengzhou Central People's Hospital, 181 Xingtan Road, Tengzhou, Zaozhuang, Shandong 277500, P.R. China
E-mail: lilingtz@126.com

Key words: esophageal cancer, tumor nutrition, Patient-Generated Subjective Global Assessment, Global Leadership Initiative on Malnutrition, inflammation

Introduction

According to the 2020 Global Cancer Epidemiology Database (GLOBOCAN), the incidence of esophageal cancer ranks seventh among all cancer types, and the mortality rate ranks sixth, with China having the highest proportion of patients with esophageal cancer (1). The 2023 National Cancer Report by the China Cancer Center showed that there were 253,000 new patients with esophageal cancer in China in 2016. Patients with esophageal cancer impose a heavy burden on society, and thus, improving treatment outcomes and reducing mortality rates is of great importance. Patients with esophageal cancer often suffer from dysphagia or digestive obstructions, resulting in a higher incidence of malnutrition (2). Malnutrition not only affects treatment plans but may also increase the likelihood of complications and mortality rates, lower a patient's quality of life and subsequently impact clinical outcomes (3,4). Currently, guidelines and standards for nutritional support therapy for tumors have been established both domestically and internationally (5,6). Patients with esophageal cancer should undergo nutritional risk screening, assessment, and related guidance and treatment before, during and after treatment.

The Nutritional Risk Screening 2002 (NRS2002) is a nutritional assessment tool developed by an expert group led by Kondrup under the European Society for Clinical Nutrition and Metabolism in 2002, based on 128 randomized controlled clinical studies (7). It has high evidence-based credibility and effectively identifies the nutritional risk of hospitalized patients, for whom reasonable nutritional support should be provided. The Global Leadership Initiative on Malnutrition (GLIM) is a diagnostic standard for malnutrition jointly developed by the four major global nutrition societies in 2018, aiming to unify the diagnostic standards for malnutrition (6). The Patient-generated Subjective Global Assessment (PG-SGA), adapted by Ottery (8) in 1994, is based on the SGA scale (9) and is a subjective assessment method designed for patients with cancer. The PG-SGA is the preferred method for the nutritional assessment of patients with cancer and is recommended by the Academy of Nutrition and Dietics and the Professional

Committee on Tumor Nutrition and Supportive Care, China Anti-Cancer Association (10). In addition, certain indicators, such as albumin and cholesterol, can serve as references for nutritional assessment. In recent years, certain inflammatory and immune indicators have been significantly associated with the prognosis of various types of cancer (11,12), such as the neutrophil-to-lymphocyte ratio (NLR) for gastroesophageal tumours, platelet-to-lymphocyte ratio (PLR) for small cell lung cancer, nutritional prognostic index (PNI) for hepatocellular carcinoma and systemic immune-inflammation index (SII) for small cell lung cancer. Additionally, malnutrition is related to inflammation and immune status. Thus, studying the association between these indicators, malnutrition and its risks may assist in identifying novel clinical markers that can be used to diagnose or predict malnutrition. Currently, there is a wide array of tools for assessing malnutrition and numerous nutrition-related indicators. However, the variations in their effectiveness and accuracy pose challenges in clinical practice. The aim of the present study was to explore the efficacy of some of these tools and indicators for assessing malnutrition in patients with esophageal cancer.

Patients and methods

Patients and study design. The present study was a single-center cross-sectional study of patients newly diagnosed with esophageal cancer at Tengzhou Central People's Hospital (Tengzhou, China) between January 2023 and December 2023. The inclusion criteria were as follows: i) Esophageal malignancy pathologically diagnosed within 8 weeks before enrollment, staged III-IV according to the Tumor Node Metastasis (TNM) Classification of Malignant Tumours, 8th edition (13) developed by the Union for International Cancer Control and the American Joint Committee on Cancer; ii) age, ≥18 years; iii) expected survival time, ≥3 months; and iv) voluntary participation with signed informed consent. The exclusion criteria were as follows: i) Pregnant or lactating women; ii) patients with severe mental illness and poor compliance; or iii) patients with other diseases that may affect the study results such as the presence of two or more tumors or esophageal fistula.

A total of 160 patients with esophageal cancer were recruited to investigate the incidence of malnutrition, differences in diagnostic methods, and the role and potential application value of nutritional, inflammatory and immune indicators such as NLR, PLR, PNI and SII in nutritional risk assessment.

The present study was approved by the Medical Ethics Committee of Tengzhou Central People's Hospital (approval no. 2023-Ethics Review-02). Prior to patient testing, the patients and representatives were fully informed, and signed informed consent was obtained from the patient or their designated representative.

NRS2002, GLIM and PG-SGA evaluation. Within 24 h of admission, patients were assessed for nutritional risk using NRS2002. The NRS2002 includes three aspects: Disease severity, nutritional status and age. A score of ≥3 (high-risk) indicates a risk of malnutrition and a score of <3 (low risk) indicates no risk of malnutrition. Based on whether NRS2002 screening was performed, all patients underwent GLIM diagnosis, resulting in two outcomes: i) GLIM diagnosis for patients with NRS2002 scores ≥3 (NRS2002-GLIM group) or ii) a direct GLIM diagnosis for all patients (GLIM group). The GLIM criteria encompass two aspects, namely phenotypical and etiological indicators. Phenotypical indicators include involuntary weight loss, low body mass index (BMI) and loss of muscle mass, while etiological indicators include reduced food intake/absorption and inflammation/disease burden. The presence of any one indicator from each category is adequate for a diagnosis of malnutrition, which can be further categorized as moderate or severe malnutrition. Simultaneously, PG-SGA was employed for the nutritional assessment of patients. This assessment method consists of self-assessment and healthcare professional assessment components, with assessment outcomes classified as well-nourished or mildly malnourished (0-3 points), suspected or moderately malnourished (4-8 points) and severely malnourished (≥9 points).

Physical and laboratory examinations. Patient's sex, age, height, weight and fasting blood results before treatment, including neutrophil, lymphocyte and platelet counts, albumin, cholesterol, interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) levels, and peripheral blood cluster of differentiation 3-positive/programmed cell death protein 1-postive ($CD3^+PD\text{-}1^+$), $CD4^+PD\text{-}1^+$ and $CD8^+PD\text{-}1^+$ cell counts.

Calculation of relevant indicators. The following parameters were calculated using the following formulae: NLR=neutrophil count ($x10^9$/l)/lymphocyte count ($x10^9$/l); PLR=platelet count ($x10^9$/l)/lymphocyte count ($x10^9$/l); PNI=serum albumin level (g/l) + 5 x lymphocyte count ($x10^9$/l); SII=platelet count ($x10^9$/l) x neutrophil count ($x10^9$/l)/lymphocyte count ($x10^9$/l); and BMI=weight (kg)/height^2 (m^2).

Statistical analysis. Data analysis was performed using SPSS version 23.0 (IBM Corp.). A Shapiro-Wilk normality test was used to assess for normality. Discrete data are presented as numbers or percentages and compared using a χ^2 test. Normally distributed continuous data are presented as the mean ± SD, and were compared using an independent samples t-test for comparisons between two independent groups or a one-way ANOVA for comparison between ≥3 groups, and the post-hoc test performed after ANOVA was the Bonferroni method. Non-normally distributed data are presented as the median and interquartile range and were compared using a non-parametric test - the Mann-Whitney U-test was used for two samples, the Kruskal-Wallis test was used for three samples, and the Bonferroni method was used to correct for significance level for post-hoc testing. The consistency was assessed using a κ test, with κ values of 0.2-0.4 indicating weak consistency, values of 0.4-0.6 indicating moderate consistency and values of 0.6-0.8 indicating strong consistency. Spearman's correlation analysis was employed for assessing relationships, with correlations ranging from 0-0.2 considered very weak, 0.2-0.4 weak and 0.4-0.7 moderate. Among the 160 samples in the present study, 7 samples had missing data, accounting for <5% of the total. Specifically, albumin level and neutrophil count each had one missing data point, with a missing proportion of 0.623, IL-6 level had five

Table I. Agreement between GLIM and PG-SGA.

	Malnourished							
Screening	PG-SGA	GLIM	Sensitivity, %	Specificity, %	κ	P-value	PPV, %	NPV, %
Without screening	120	83	64.17	85.00	0.379	<0.001	92.77	44.16
NRS2002-GLIM	120	66	55.00	100.00	0.376	<0.001	100.00	42.55

Taking the PG-SGA as the diagnostic criterion, compared the consistency of different diagnostic methods in the diagnosis of malnutrition. The consistency test between PG-SGA and without screening GLIM was conducted using the κ test. The consistency test between PG-SGA and NRS2002-GLIM was conducted using the κ test. PG-SGA, Patient-Generated Subjective Global Assessment; GLIM, Global Leader Initiative on Malnutrition; NRS2002, Nutritional Risk Screening 2002; PPV, positive predictive value; NPV, negative predictive value.

missing data points, with a missing proportion of 3.13%, and PNI had two missing data points, with a missing proportion of 1.25%. To explore the influencing factors of PG-SGA and GLIM, the method of multiple imputation was applied. Mean imputation, median imputation and mode imputation assign a specific value based on known data, while multiple imputation, in this study facilitated by the R4.1.3 language Multivariate Imputation by Chained Equations package with 5 imputations, generated 5 datasets, each yielding distinct results. This method, grounded in Bayesian estimation, posits that the values to be imputed are random, thereby reducing bias. The Akaike Information Criterion values across the five datasets were equivalent (14), one dataset was randomly selected for multivariate logistic regression, a criterion of P<0.100 in univariate analysis was employed as the threshold for inclusion in the logistic regression model, and the results were analyzed using a receiver operating characteristic (ROC) curve. P<0.05 was considered to indicate a statistically significant difference.

Results

Baseline characteristics, prevalence of nutritional risk and malnutrition of the population. Based on the inclusion and exclusion criteria, a total of 160 newly diagnosed patients with stage III-IV esophageal cancer were enrolled, consisting of 117 men (73.13%) and 43 women (26.88%), aged 18-84 years [median age, 69 (interquartile range, 61-74) years]. According to the NRS2002, there were 76 patients (47.50%) in the high-risk group and 84 patients (52.50%) in the low-risk group. Following NRS2002 screening, 66 individuals (41.25%) were considered to exhibit malnutrition. When using GLIM without prior NRS2002 screening, 83 individuals (51.88%) were considered to exhibit malnutrition. Subsequently, utilizing the unscreened GLIM as the standard, these individuals were further categorized into moderate malnutrition (35 individuals, 21.88%) and severe malnutrition (48 individuals, 30.00%). Regarding PG-SGA scores, 40 individuals (25.00%) were classified as well-nourished or mildly malnourished, 53 individuals (33.13%) as suspected or moderately malnourished, and 67 individuals (41.88%) as severely malnourished. These results indicate that the proportion of malnutrition assessed by PG-SGA was the highest, followed by GLIM assessment, with NRS2002-GLIM showing the lowest proportion of malnutrition.

Consistency testing between PG-SGA and GLIM standards. Based on the aforementioned results, malnutrition was defined as a PG-SGA score of ≥4, and its consistency with GLIM was assessed. The κ value between the PG-SGA and the GLIM tools was 0.379, indicating a moderate to weak level of consistency. The sensitivity was 64.17%, the specificity was 85.00%, the positive predictive value was 92.77% and the negative predictive value was 44.16%. Compared with PG-SGA and NRS2002-GLIM, the κ value was 0.376, indicating a generally weak consistency. The sensitivity was 55.00%, the specificity was 100.00%, the positive predictive value was 100.00% and the negative predictive value was 42.55% (Table I). The κ value between the NRS2002-GLIM and the unscreened GLIM was 0.789, indicating a relatively strong level of consistency. The sensitivity was 79.50%, the specificity was 100%, the positive predictive value was 100% and the negative predictive value was 81.91%. Additionally, a McNemar test was performed, revealing statistically significant differences (Table II).

Association between PG-SGA scores and related nutritional and inflammatory indicators. Based on PG-SGA scores, statistically significant differences (P<0.05) were observed for age, neutrophil count, albumin level, IL-6 level and BMI among the three malnutrition groups. No statistically significant differences were found in terms of sex, cholesterol level, lymphocyte count, platelet count, TNF-α level, $CD3^+PD\text{-}1^+$, $CD4^+PD\text{-}1^+$ and $CD8^+PD\text{-}1^+$ cell counts, and PNI, NLR, SII or PLR. Correlation analysis between PG-SGA and nutritional as well as inflammatory markers revealed a moderate negative correlation with BMI (r_s=-0.460), weak positive correlations with age (r_s=0.234) and IL-6 level (r_s=0.249), and very weak negative correlations with albumin level (r_s=-0.178) and PNI (r_s=-0.168) (Table III).

Regarding the classification based on the GLIM criteria, statistically significant differences were found for age, albumin level, BMI and PNI among the three nutritional status groups (P<0.05). No statistically significant differences were observed in the other indicators. Correlation analysis between the GLIM classification and nutritional as well as inflammatory markers showed a moderate negative correlation with BMI (r_s=-0.627), weak positive correlations with age (r_s=0.207) and IL-6 level (r_s=0.177), and weak negative correlations with albumin level (r_s=-0.264) and PNI (r_s=0.247). The indicators showing correlations with both PG-SGA and GLIM were consistent,

Table II. Agreement between GLIM with and without NRS2002 screening.

	GLIM without screening							
NRS2002-GLIM	Malnourished	Normal	Sensitivity, %	Specificity, %	κ	P-value	PPV, %	NPV, %
Malnourished	66	0	79.50	100.00	0.789	<0.001	100.00	81.91
Normal	17	77						

The consistency test between GLIM without screening and NRS2002-GLIM was conducted using the κ test. GLIM, Global Leader Initiative on Malnutrition; NRS2002, Nutritional Risk Screening 2002; PPV, positive predictive value; NPV, negative predictive value.

Table III. Association between PG-SGA and related nutritional and inflammatory indicators.

Variable	Mild malnutrition	Moderate malnutrition	Severe malnutrition	F/χ^2	P-value for F/χ^2	r_s	P-value for r_s
Age[a]	62.18±11.99	67.17±8.32	68.58±9.22	5.629	0.004[b]	0.234	0.003[b]
Sex[c]				0.140	0.933	-	-
Male	29 (72.50)	38 (71.70)	50 (74.63)				
Female	11 (27.50)	15 (28.30)	17 (25.37)				
ALB[d]	36.13 (40.25, 43.10)	36.25 (40.50, 3.30)	35.45 (37.75, 0.45)	6.432	0.040[e]	-0.178	0.024[e]
TC[a]	4.29±1.17	4.35±0.96	4.52±0.96	0.734	0.482	0.099	0.224
NEU[d]	3.05 (4.08, 5.14)	2.61 (3.64, 4.68)	3.24 (4.22, 6.32)	8.044	0.018[e]	0.124	0.121
LYM[d]	1.06 (1.41, 1.84)	1.00 (1.34, 1.59)	0.99 (1.30, 1.67)	0.820	0.663	-0.056	0.482
PLT[a]	266.75±97.50	237.96±77.13	253.75±101.46	1.117	0.330	0.004	0.961
IL-6[d]	2.33 (4.66, 8.86)	2.59 (5.94, 11.41)	4.12 (7.78, 15.59)	9.682	0.008[b]	0.249	0.002[b]
TNF-α[d]	0.47 (0.76,2.34)	0.43 (0.81, 1.73)	0.48 (0.99, 1.93)	0.300	0.861	0.038	0.640
$CD3^+PD\text{-}1^{+d}$	4.15 (6.60, 15.55)	2.50 (6.50, 11.85)	3.85 (7.60, 12.00)	1.669	0.434	-0.005	0.946
$CD4^+PD\text{-}1^{+d}$	2.80 (6.90, 11.25)	2.35 (3.70, 7.90)	3.25 (6.00, 10.05)	4.060	0.131	0.004	0.958
$CD8^+PD\text{-}1^{+d}$	1.10 (2.40, 4.20)	0.60 (1.40, 3.35)	0.90 (2.00, 4.15)	3.370	0.185	-0.034	0.672
BMI[a]	24.13±3.39	23.07±3.50	20.41±2.58	20.780	<0.001[f]	-0.460	<0.001[f]
PNI[a]	48.15±9.02	46.70±5.34	44.92±6.86	2.705	0.070	-0. 168	0.035[e]
NLR[d]	2.04 (2.78, 3.89)	2.02 (2.73, 4.47)	2.20 (3.37, 5.74)	4.301	0.116	0.148	0.062
SII[d]	472.52 (728.96, 1,097.04)	409.29 (718.37, 938.05)	482.17 (741.16, 1,600.65)	2.098	0.350	0.04	0.615
PLR[d]	138.75 (175.23, 269.60)	138.82 (183.17, 246.66)	134.86 (196.87, 265.04)	0.178	0.915	0.021	0.790

Statistical analysis was performed on the related nutritional and inflammatory indicators among the three different nutritional states classified by the PG-SGA score. Statistical methods included [a]one-way ANOVA, [c]χ^2 test, [d]Kruskal-Wallis test and Spearman's correlation analysis. [e]P<0.05, [b]P<0.01, [f]P<0.001. Data are presented as the [a]mean ± SD, [c]n (%) or [d]median (interquartile range). ALB, albumin; TC, total cholesterol; NEU, neutrophil; LYM, lymphocyte; PLT, platelet; IL-6, Interleukin-6; TNF-α, tumor necrosis factor-α; CD, cluster of differentiation; PD-1, programmed cell death protein 1; BMI, body mass index; PNI, nutritional prognostic index; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; PLR, platelet-to-lymphocyte ratio.

albeit with slight variations in the strength of the correlations (Table IV).

Logistic regression analysis of PG-SGA and GLIM scores. Using PG-SGA scores divided into three groups as the dependent variable, based on the aforementioned test results, statistically significant variables, including age, albumin level, neutrophil count, IL-6 level and BMI, were included in a logistic regression model. Additionally, PNI was also included in the model due to a P-value of <0.100. Using severe malnutrition as the reference group, the results revealed that age of the mild malnutrition group, and the neutrophil count and BMI of the mild and moderate malnutrition group, were independent risk factors for malnutrition. The probability of severe malnutrition increased with age, higher neutrophil count and lower BMI (Table V).

Using the three different nutritional statuses based on the GLIM criteria as the dependent variable, statistically significant variables were included based on the aforementioned test results. It was found that age and BMI were independent

Table IV. Relationship between GLIM and related nutritional and inflammatory indicators.

Variables	Normal nutrition	Moderate malnutrition	Severe malnutrition	F/χ^2	P-value for F/χ^2	r_s	P-value for r_s
Age[a]	65 (58.5, 73.5)	69 (60, 71)	71.5 (65.25, 75.00)	7.702	0.021[b]	0.207	0.009[c]
Sex[d]				2.410	0.300	-	-
Male	53 (68.83)	29 (82.86)	35 (72.92)				
Female	24 (31.17)	6 (17.14)	13 (27.08)				
ALB[a]	40.50 (36.65, 43,30)	38.10 (36.20, 41.78)	37.65 (33.78, 40.26)	11.055	0.004[c]	-0.264	<0.001[e]
TC[f]	4.36±1.07	4.57±0.94	4.35±0.99	0.565	0.569	0.004	0.957
NEU[a]	3.94 (3.02, 5.12)	4.09 (2.69, 5.46)	4.06 (2.78, 5.98)	0.322	0.852	0.043	0.597
LYM[a]	1.40 (1.04, 1.67)	1.28 (0.94, 1.82)	1.29 (0.93, 1.54)	1.193	0.551	-0.087	0.278
PLT[f]	248.39±87.20	244.00±95.56	262.86±102.23	0.510	0.602	0.090	0.257
IL-6[a]	5.38 (2.42, 7.80)	7.93 (3.86, 16.01)	7.46 (2.96, 14.30)	2.270	0.321	0.177	0.027[b]
TNF-α[a]	0.81 (0.44, 1.82)	0.83 (0.55, 1.72)	0.92 (0.40, 2.12)	0.028	0.986	-0.013	0.868
$CD3^+PD\text{-}1^+$[a]	6.30 (3.13, 13.00)	8.60 (3.18, 11.80)	8.50 (4.00, 13.70)	2.112	0.348	0.114	0.159
$CD4^+PD\text{-}1^+$[a]	4.5 (2.48, 8.70)	5.50 (3.15, 8.45)	6.50 (3.50, 10.20)	2.056	0.358	0.105	0.194
$CD8^+PD\text{-}1^+$[a]	1.95 (0.80, 3.58)	1.75 (0.48, 4.23)	1.80 (0.90, 3.80)	0.027	0.987	-0.013	0.871
BMI[a]	23.60 (22.05, 26.09)	21.30 (19.80, 22.90)	18.95 (17.93, 20.65)	62.465	<0.001[e]	-0.627	<0.001[e]
PNI[a]	47.55 (43.95, 51.48)	44.90 (41.64, 49.36)	44.05 (41.05, 47.25)	9.662	0.008[c]	0.247	0.002[c]
NLR[a]	2.80 (2.09, 3.95)	3.27 (1.88, 4.99)	3.06 (2.19, 5.22)	1.219	0.544	0.087	0.274
SII[a]	1,032.30 (640.70, 1,256.96)	987.35 (511.94, 1,476.49)	1,055.60 (575.75, 1,550.01)	0.437	0.804	0.044	0.850
PLR[a]	177.89 (135.20, 229.07)	191.55 (122.33, 280.95)	219.76 (151.51, 270.24)	3.302	0.192	0.139	0.081

Statistical analysis was performed on the related nutritional and inflammatory indicators among the three different nutritional states classified by the GLIM. Statistical methods included [f]one-way ANOVA, [d]χ^2 test, [a]Kruskal-Wallis test and Spearman's correlation analysis. [b]P<0.05, [c]P<0.01, [e]P<0.001. Data are presented as the [f]mean ± SD, [d]n (%) or [a]median (interquartile range). ALB, albumin; TC, total cholesterol; NEU, neutrophil; LYM, lymphocyte; PLT, platelet; IL-6, Interleukin-6; TNF-α, tumor necrosis factor-α; CD, cluster of differentiation; PD-1, programmed cell death protein 1; BMI, body mass index; PNI, nutritional prognostic index; NLR, neutrophil-to-lymphocyte ratio; SII, systemic immune-inflammation index; PLR, platelet-to-lymphocyte ratio.

risk factors for malnutrition. The probability of malnutrition increased with age and lower BMI, leading to a higher risk of severe malnutrition (Table V).

ROC curve analysis. Utilizing the PG-SGA regression equation to delineate the ROC curve, the results indicated that age, neutrophil count and BMI had predictive significance for malnutrition. The optimal cutoff value for age was 68.50 years, with an AUC of 0.610, a sensitivity of 64.20% and a specificity of 58.10%. For neutrophil counts, the optimal cutoff value was $9.25x10^9$/l, yielding an AUC of 0.615, a sensitivity of 41.80% and a specificity of 83.90%. The optimal cutoff value for BMI was 22.05 kg/m^2, resulting in an AUC of 0.765, a sensitivity of 77.60% and a specificity of 65.60% (Table VI; Fig. 1).

Using the GLIM regression equation to construct the ROC curve, the results demonstrated that age and BMI had predictive significance for malnutrition. The optimal cutoff value for age was 68.50 years, with an AUC of 0.579, a sensitivity of 62.70% and specificity of 61.00%. For BMI, the optimal cutoff value was 22.30 kg/m^2, yielding an AUC of 0.836, a sensitivity of 80.70% and specificity of 74.00% (Table VI; Fig. 2).

Discussion

Malnutrition can directly affect the efficacy of tumor treatment, increase the incidence of complications, reduce the quality of life and even affect prognosis (3,4). It has been reported that 40% of patients with a tumor die directly from malnutrition (15). In 2020, Cao *et al* (2) assessed 1,482 patients with esophageal cancer from 72 hospitals in China using PG-SGA. The results showed that 17.98% of patients scored 0-3, 35.09% scored 4-8 and 41.39% scored ≥9, consistent with the present findings. Additionally, the incidence of malnutrition diagnosed using GLIM was 41.25%, and it was 51.88% without NRS2002 screening, which is similar to the findings of Clark *et al* (16) in elderly rehabilitation patients. Utilizing different diagnostic tools can result in contrasting outcomes. The results of the present study revealed a significantly higher prevalence of malnutrition diagnosed by PG-SGA compared with diagnoses made by GLIM. Specifically, 43 individuals were diagnosed as malnourished by PG-SGA who were otherwise assessed as nutritionally normal by GLIM. This disparity can be attributed to the common symptoms experienced by patients with late-stage esophageal cancer, such as difficulties in eating, retrosternal pain, a decreased appetite

Table V. Logistic regression analysis of PG-SGA and GLIM.[a]

A, PG-SGA

Group	Variable	β	Standard error	Odds ratio	Wald index	95% confidence interval		P-value
Mild malnutrition group	Intercept	-3.924	2.953	-	1.766	-	-	0.184
	Age	-0.070	0.027	0.932	6.883	0.884	0.982	0.009[b]
	ALB	-0.033	0.080	0.968	0.170	0.828	1.131	0.680
	NEU	-0.292	0.144	0.746	4.134	0.563	0.990	0.042[c]
	IL-6	-0.033	0.022	0.976	2.285	0.928	1.010	0.131
	BMI	0.449	0.093	1.567	23.305	1.306	1.880	<0.001[d]
	PNI	-0.024	0.060	1.024	0.157	0.910	1.152	0.692
Moderate malnutrition group	Intercept	-4.951	2.726	-	3.298	-	-	0.069
	Age	-0.025	0.025	0.975	1.026	0.928	1.024	0.311
	ALB	0.066	0.078	1.068	0.703	0.916	1.244	0.402
	NEU	-0.476	0.132	0.622	13.059	0.480	0.804	<0.001[d]
	IL-6	0.000	0.007	1.000	0.000	0.986	1.014	0.999
	BMI	0.376	0.085	1.456	19.525	1.233	1.720	<0.001[d]
	PNI	-0.048	0.066	0.953	0.519	0.837	1.086	0.471

B, GLIM

Group	Variable	β	Standard error	Odds ratio	Wald index	95% confidence interval		P-value
Normal/moderate-severe	Intercept	-8.804	2.335	-	14.215	-13.38	-4.227	<0.001[d]
Normal-moderate/severe	Intercept	-7.391	2.298	-	10.343	-11.896	-2.2887	0.001[d]
	Age	0.041	0.02	1.042	4.309	0.002	0.08	0.0038[b]
	ALB	0.029	0.061	0.971	0.229	-0.15	0.091	0.632
	BMI	-0.041	0.076	0.611	41.514	-0.641	-0.342	<0.001[d]
	PNI	0.012	0.048	1.012	0.06	-0.082	0.106	0.807

[c]P≤0.05, [b]P≤0.01, [d]P≤0.001. [a]The parallel difference in PG-SGA was found to be <0.05, hence an unordered multivariate logistic regression approach was employed for analysis, using the severe malnutrition group as the reference category. Conversely, the parallel difference in GLIM was >0.05, prompting the use of ordinal logistic regression for analysis. PG-SGA, Patient-Generated Subjective Global Assessment; GLIM, Global Leader Initiative on Malnutrition; ALB, albumin; NEU, neutrophil; IL-6, interleukin-6; BMI, body mass index; PNI, nutritional prognostic index.

and alterations in dietary patterns. These symptoms can lead to inflated self-assessment scores, resulting in elevated overall scores and a subsequent diagnosis of malnutrition when using PG-SGA, potentially influenced by the specific cancer type studied in the present study. Additionally, six individuals were classified as having a normal nutritional status by PG-SGA but were diagnosed as malnourished by GLIM. Among them, three individuals were affected by the fact that PG-SGA tends to rely on weight changes within a month, whereas the diagnostic criteria of GLIM are based on weight changes over a 6-month period. The remaining three individuals were classified based on their low baseline weight and BMI. Furthermore, within the GLIM evaluation, the absence of screening tools led to a 10.63% higher prevalence of malnutrition compared to assessments utilizing the NRS2002 screening tool, resulting in the exclusion of 17 individuals. Subsequent reevaluation of these 17 individuals revealed that this discrepancy stemmed from the NRS2002 tool primarily taking into consideration 3-month changes. For example, seven patients exhibited a significant weight loss of >5% within 6 months, despite minimal recent fluctuations or even a slight upward trend in weight. Additionally, five patients experienced a gradual weight loss of >5% within 6 months but had notably higher baseline weights and BMIs compared to typical obese individuals. Furthermore, five patients showed a weight loss of <5% within 6 months or no significant changes, yet had exceptionally low baseline BMIs. These variations may be influenced by differences in BMI values across various countries, regions and ethnicities. The use of screening tools during the diagnostic process may potentially lead to overlooking certain malnourished patients. Currently, a variety of nutritional assessment methods are commonly employed in clinical settings, each with inherent limitations. Therefore, there is a further need for more accurate and convenient clinical screening and assessment tools.

Table VI. AUC values for PG-SGA and GLIM.

Scoring method	Variable	AUC (95% CI)	Cut-off	Sensitivity	Specificity	P-value
PG-SGA	NEU	0.615 (0.521-0.699)	5.33	0.418	0.839	0.013[a]
	Age	0.610 (0.525-0.706)	68.5	0.642	0.581	0.018[a]
	BMI	0.765 (0.692-0.838)	22.05	0.776	0.656	<0.001[b]
GLIM	Age	0.597 (0.507-0.686)	68.50	0.627	0.610	0.035[a]
	BMI	0.836 (0.774-0.897)	22.30	0.807	0.740	<0.001[b]

[a]P<0.05, [b]P<0.001. PG-SGA, Patient-Generated Subjective Global Assessment; GLIM, Global Leader Initiative on Malnutrition; AUC, area under the curve; BMI, body mass index; NEU, neutrophil; CI, confidence interval.

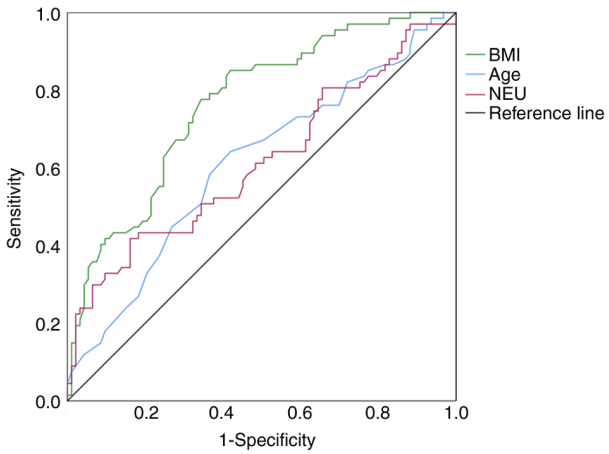

Figure 1. Receiver operating characteristic curve for assessing malnutrition based on the Patient-Generated Subjective Global Assessment. NEU, neutrophil; BMI, body mass index.

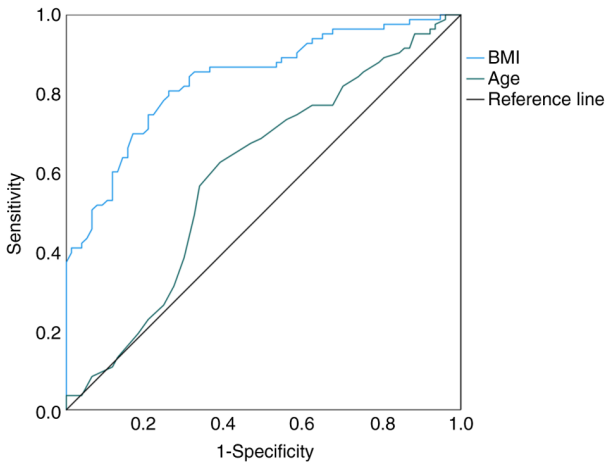

Figure 2. Receiver operating characteristic curve for assessing malnutrition based on the Global Leadership Initiative on Malnutrition scoring criteria. BMI, body mass index.

In September 2018, the Global Nutrition Leadership issued a consensus on malnutrition diagnostic criteria (6). Since then, researchers worldwide have begun clinical validation of its diagnostic value. PG-SGA is still recommended as the gold standard for evaluating the performance of other nutritional screening tools (17). In the present study, a validation analysis between the PG-SGA scale and GLIM was performed, with a κ value of 0.379. Huo *et al* (18) used PG-SGA to assess malnutrition in patients with stage III-IV lung cancer, and found a κ value of 0.38 with GLIM, with a sensitivity of 48.3% and a specificity of 78.4%, similar to the results of the present study. However, Zhou *et al* (19) used GLIM as the standard to test the consistency between PG-SGA and GLIM in patients, and found a κ value of 0.814, with a sensitivity of 81.1% and a specificity of 98.9%, indicating higher consistency. This may be since the study population primarily included patients with biliary and pancreatic cancer. Rosnes *et al* (20) conducted a consistency study between GLIM and PG-SGA in the nutrition clinic of the Cancer Medicine Department at Oslo University Hospital, Norway. The κ value was 0.37, increasing to 0.51 without NRS-2002 screening. Better consistency without screening may be due to PG-SGA being more suitable for patients with cancer, whereas the GLIM standard has broader applicability. PG-SGA and GLIM employ distinct diagnostic criteria, leading to inevitable differences in diagnostic consistency between the two tools. While PG-SGA does not consider BMI, it incorporates more diagnostic dimensions than GLIM. For patients with esophageal cancer, PG-SGA may exhibit higher sensitivity. Currently, it is crucial to recognize that these tools cannot be used interchangeably in clinical practice.

The GLIM diagnosis requires at least one phenotypical criterion and one etiological criterion. Phenotypical criteria include involuntary weight loss, low BMI and loss of muscle mass. Involuntary weight loss is the most direct manifestation of malnutrition, with the loss of muscle mass leading to weight reduction and a consequent decrease in BMI. This also explains the moderate predictive ability of BMI for malnutrition. Currently, the World Health Organization defines a BMI of <18.5 kg/m^2 as the threshold for being underweight in the general population (21). However, BMI varies across different countries, regions, ethnicities and age groups. Epidemiological data suggests that the optimal BMI range for older individuals is higher than that for younger individuals. The population under study in the present research was skewed towards older age groups, leading to a higher optimal cutoff value for BMI in the ROC curve. This aligns with the BMI cutoff values used in diagnosing malnutrition in individuals >70 years old in Western populations. Considering the study population was from the coastal regions of northern China, BMI values were expected to be higher compared to southern and more remote areas. Economic development is associated with an increase

in obesity rates, posing new challenges in determining BMI values. Additionally, patients may experience a weight loss of >10% within a certain period while still maintaining a normal BMI. Further research is needed to establish BMI values, particularly in a geographically diverse country such as China, where significant population variations exist. BMI values may need to be interpreted in conjunction with weight loss for accurate diagnosis. The present study suggested that BMI is an independent factor affecting malnutrition, with patients with esophageal cancer and a low BMI having a higher risk of malnutrition and higher PG-SGA scores. The study by Martin *et al* (22) confirmed that weight loss and low BMI predict decreased survival rates and are independent prognostic factors for the survival of patients with cancer. Etiological criteria include reduced food intake/absorption and inflammation/disease burden. Inflammation is a key factor in the risk of malnutrition and plays a significant role in tumor development and progression. Currently, markers such as serum C-reactive protein, albumin or prealbumin are considered potential substitutes (23), but this is not yet conclusive. The present study found that IL-6 level and neutrophil count are risk factors for malnutrition. IL-6 is a pro-inflammatory cytokine with a range of biological functions that serves as a crucial link between inflammation and cancer (22). The persistent presence of inflammation can lead to inhibition of protein synthesis, increased protein breakdown, reduced muscle tissue, and subsequently, malnutrition (24). Puppa *et al* (25) demonstrated that in mice carrying tumors, an increase in plasma IL-6 levels was associated with tumor growth and the development of cachexia. IL-6 can also impact the metabolism of fat and muscle tissues. Rupert *et al* (26) discovered that, in pancreatic cancer cells, IL-6 depletion can halve fat consumption, eliminate muscle wasting, and suggests the presence of a feedback mechanism between fat and muscle tissues, with fat tissue loss preceding muscle fiber atrophy. IL-6 activates metabolic breakdown in skeletal muscle and also inhibits synthesis of metabolic signals (27). IL-6 can induce muscle wasting by activating the STAT3 cellular pathway (28). Haddad *et al* (29) showed that an intramuscular IL-6 infusion can reduce the phosphorylation of S6K1, which is associated with breakdown metabolism, a reduction linked to the loss of protein synthesis capacity. Furthermore, IL-6 not only acts on peripheral organs but also appears to influence the brain, potentially contributing to the development of cachexia (30), although the precise mechanisms remain unclear. Schéle *et al* (31) found that, in mice, IL-6 can affect adiposity and appetite through the hypothalamic arcuate nucleus. Based on the findings of the present study, it is plausible to consider IL-6 as a potential etiological marker. Neutrophils play a significant role in tumor initiation and progression. Penafuerte *et al* (32) observed a significant increase in absolute neutrophil count and neutrophil-derived proteases in patients in pre-cachexia and cachexia states, suggesting their potential involvement in cachexia development. Neutrophil-derived proteases can stimulate the generation of angiotensin II, which through various mechanisms, such as inducing protein degradation and inhibiting protein synthesis, promotes cachexia (33). Deng *et al* (34) found that neutrophils in patients with cachexia with pancreatic cancer can secrete lipopolysaccharide-binding protein-2, which has been associated with anorexia, fat loss, and muscle loss in murine models of pancreatic cancer cachexia (35), suggesting a potential association with malnutrition. Neutrophils appear to induce muscle damage by adhering to myofibers through CD18 and generating iron-dependent hydroxyl radicals (36). In the present study, it was found that the optimal cutoff value for absolute neutrophil count was 9.25×10^9/l. When a patient's absolute neutrophil count exceeds this value, the probability of malnutrition increases. However, neutrophils are susceptible to the influence of cancer treatments such as radiation and chemotherapy, leading to significant variability in values and hindering the monitoring of malnutrition progression.

The NLR is an indicator used to assess inflammatory responses. The present study did not find an association between NLR and malnutrition. In an analysis of patients with esophageal cancer before radiotherapy, the study by Liang *et al* (37) also did not find significant associations between the NLR, the PLR and sarcopenia. However, Penafuerte *et al* (32) observed a significant increase in the NLR in pre-cachectic and cachectic patients compared with non-cachectic individuals, with no difference in absolute lymphocyte count but a notable increase in absolute neutrophil count. This discrepancy may be related to the disease status, as for newly diagnosed patients and those severely malnourished in the present study, the neutrophil counts were higher compared with those with mild to moderate malnutrition. In the present study, patients' absolute neutrophil counts were within the normal range, while the patients in the study by Penafuerte *et al* (32) had a more advanced stage of malnutrition, suggesting that neutrophil levels may increase as malnutrition worsens. In patients with gastric cancer undergoing surgical treatment, Ruan *et al* (38) found that NLR was a predictive indicator of nutritional risk but was not an independent influencing factor for malnutrition. The SII is calculated from platelet, lymphocyte and neutrophil counts, while the PLR is derived from the ratio of platelets to lymphocytes. Both serve as indicators reflecting the immune and inflammatory status within the body. Elevated levels of SII and PLR typically signify a poor prognosis in malignant tumors. Lipshitz *et al* (39) found that, in an analysis of patients with advanced cancer cachexia, neutrophil, lymphocyte and platelet counts remained within normal ranges, and that lymphocyte and platelet counts, NLR, SII and PLR showed no significant correlation with cachexia, in agreement with the results of the present study. The number of neutrophils is influenced by various confounding factors, such as age, disease severity and treatment regimens (40). The patients in the experimental group of the present study were at different stages of chemotherapy, which could have had an impact. Lipshitz *et al* (41) also discovered a significant correlation between the cachexia assessment tool scores and NLR, SII and PLR, suggesting that different reference standards and assessment perspectives may yield varying results. Conversely, in a study on patients with gastric cancer post-surgery, Lin *et al* (42) found a significant association between NLR and PLR with cachexia, possibly linked to surgical alterations in the body's inflammatory and immune status.

In 2019, Song *et al* (23) conducted a demographic study on 24,354 patients with common malignant tumors and found a positive correlation between age and PG-SGA. The

present study also found that age was a significant factor influencing malnutrition, with older age correlating with higher malnutrition scores. The ROC curve suggested that the optimal cutoff age for this population was 68.5 years, with a significant increase in the probability of malnutrition beyond this age. When developing the NRS2002 scale, a logistic regression analysis of baseline characteristics from 114 studies containing information on age indicated that a score weighted age of ≥70 years was the highest weight (6). This suggests a significant increase in the risk of malnutrition in individuals aged ≥70 years, leading to its inclusion as a standalone scoring criterion in the NRS2002 scale. Consensus standards for malnutrition, such as GLIM and the European Society of Clinical Nutrition and Metabolism 2015 diagnostic criteria (5) for malnutrition, use the age of 70 as a delineating point for BMI categorization. Given the potential differences in populations and diseases, and the relatively small sample size, these results may show slight variations. With advancing age, a reduction in the synthesis of various hormones such as testosterone, estrogens and growth hormone may contribute to decreased metabolic function in patients with malnutrition (43). In addition, the present results indicated that patients with esophageal cancer with hypoalbuminemia were more prone to malnutrition. Serum albumin concentration is a reliable indicator of nutritional status and systemic inflammation. Low serum albumin levels in patients with diverse cancer types are associated with poor survival outcomes (6). A study by Wu *et al* (44) showed that pre-treatment hypoalbuminemia is an independent risk factor for the prognosis of patients with esophageal cancer undergoing radical surgery and can be used as an indicator to evaluate treatment and prognosis.

The PNI, originally proposed by Japanese scholars in 1984 and subsequently refined by Onodera *et al* (45), is calculated based on serum albumin and lymphocyte counts. PNI is used for assessing the immune and nutritional status of patients with cancer. Wang *et al* (43) explored various screening methods and found that the performance of PNI screening in diagnosing and classifying malnutrition according to the GLIM was suboptimal. The κ value between PNI screening and unfiltered GLIM diagnosis was only 0.045, indirectly indicating a weak correlation between PNI and malnutrition. Cholesterol is primarily used as an indicator in the controlling nutritional status (CONUT) score (46) for assessing patients' nutritional status. Yoshida *et al* (47) confirmed that the CONUT score was associated with postoperative complications in patients with esophageal cancer, with a higher probability of complications in those with moderate to severe malnutrition compared to those with no or mild malnutrition. However, cholesterol is rarely used as a standalone indicator for assessing the nutritional status of patients with tumors. In the present study, there was no correlation between cholesterol levels and malnutrition in patients with esophageal cancer.

The present study has some limitations. First, it was a single-center study with a relatively small sample size, potentially limiting the generalizability of the findings to other demographics. Future efforts should focus on expanding the clinical sample size, conducting multicenter prospective clinical studies to further validate the research outcomes and investigating regional variations. Second, the present study primarily observed the nutritional status and risk of patients upon admission but did not monitor the dynamic changes and associations between nutritional risk and related indicators. Future high-quality prospective clinical studies are required to explore the correlation between nutritional status, related indicators and clinical outcomes.

In summary, patients with esophageal cancer exhibit a higher prevalence of malnutrition, which is closely associated with age, albumin levels and inflammatory markers. These related indicators may play a beneficial role in guiding future nutritional support for the clinical management of patients with esophageal cancer. The diagnosis of malnutrition relies on various diagnostic approaches. Further clinical validation is necessary to establish the specific application of the GLIM score in practice. Future prospective cohort studies with larger sample sizes are needed to monitor the dynamic changes of malnutrition and related indicators in patients using different measurement tools, to assess the effectiveness of these tools and to investigate the variations in indicators across different nutritional states of patients.

Acknowledgements

Not applicable.

Funding

This study was supported by Shandong Provincial Natural Science Foundation Project (grant no. ZR2020LZL019) and The Affiliated Hospital of Xuzhou Medical University Science and Technology Development Fund Outstanding Talent Program (grant no. XYFM202216).

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

XK, PL, GW, SS, and LL collected and analyzed the data. XK wrote the first draft. LL reviewed and edited the manuscript. XK and PL confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was performed in accordance with the Declaration of Helsinki and was approved by the Medical Ethics Committee of Tengzhou Central People's Hospital (approval no. 2023-Ethics Review-02). All subjects included in the study provided written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and Bray F: Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71: 209-249, 2021.
2. Cao J, Xu H, Li W, Guo Z, Lin Y, Shi Y, Hu W, Ba Y, Li S, Li Z, *et al*: Nutritional assessment and risk factors associated to malnutrition in patients with esophageal cancer. Curr Probl Cancer 45: 100638, 2021.
3. Yamano T, Yoshimura M, Kobayashi M, Beppu N, Hamanaka M, Babaya A, Tsukamoto K, Noda M, Matsubara N and Tomita N: Malnutrition in rectal cancer patients receiving preoperative chemoradiotherapy is common and associated with treatment tolerability and anastomotic leakage. Int J Colorectal Dis 31: 877-884, 2016.
4. Illa P, Tomiskova M and Skrickova J: Nutritional risk screening predicts tumor response in lung cancer patients. J Am Coll Nutr 34: 425-429, 2015.
5. Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, Muscaritoli M, Nyulasi I, Ockenga J, Schneider SM, *et al*: Diagnostic criteria for malnutrition - An ESPEN consensus statement. Clin Nutr 34: 335-340, 2015.
6. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, Baptista G, Barazzoni R, Blaauw R, Coats AJS, *et al*: GLIM criteria for the diagnosis of malnutrition-A consensus report from the global clinical nutrition community. J Cachexia Sarcopenia Muscle 10: 207-217, 2019.
7. Kondrup J, Rasmussen HH, Hamberg O and Stanga Z; Ad Hoc ESPEN Working Group: Nutritional risk screening (NRS 2002): A new method based on an analysis of controlled clinical trials. Clin Nutr 22: 321-336, 2003.
8. Ottery FD: Rethinking nutritional support of the cancer patient: The new field of nutritional oncology. Semin Oncol 21: 770-778, 1994.
9. Detsky AS, McLaughlin JR, Baker JP, Johnston N, Whittaker S, Mendelson RA and Jeejeebhoy KN: What is subjective global assessment of nutritional status? JPEN J Parenter Enteral Nutr 11: 8-13, 1987.
10. Jager-Wittenaar H and Ottery FD: Assessing nutritional status in cancer: Role of the patient-generated subjective global assessment. Curr Opin Clin Nutr Metab Care 20: 322-329, 2017.
11. Pirozzolo G, Gisbertz SS, Castoro C, van Berge Henegouwen MI and Scarpa M: Neutrophil-to-lymphocyte ratio as prognostic marker in esophageal cancer: A systematic review and meta-analysis. J Thorac Dis 11: 3136-3145, 2019.
12. Hong X, Cui B, Wang M, Yang Z, Wang L and Xu Q: Systemic immune-inflammation index, based on platelet counts and neutrophil-lymphocyte ratio, is useful for predicting prognosis in small cell lung cancer. Tohoku J Exp Med 236: 297-304, 2015.
13. Brierley JD, Gospodarowicz MK and Wittekind C: TNM Classification of Malignant Tumours. 8th Edition. Wiley-Blackwell, Chichester, 2017.
14. Noghrehchi F, Stoklosa J, Penev S and Warton DI: Selecting the model for multiple imputation of missing data: Just use an IC! Stat Med 40: 2467-2497, 2021.
15. Isenring E, Cross G, Kellett E, Koczwara B and Daniels L: Nutritional status and information needs of medical oncology patients receiving treatment at an Australian public hospital. Nutr Cancer 62: 220-228, 2010.
16. Clark AB, Reijnierse EM, Lim WK and Maier AB: Prevalence of malnutrition comparing the GLIM criteria, ESPEN definition and MST malnutrition risk in geriatric rehabilitation patients: RESORT. Clin Nutr 39: 3504-3511, 2020.
17. Wu M, Lian XJ, Jia JM, Cao WT, Yan N, Xin YM, Liu ZR, Li HY, Fan ZF and Sun P: The role of the Patient-Generated Subjective Global Assessment (PG-SGA) and biochemical markers in predicting anemia patients with cancer. Support Care Cancer 27: 1443-1448, 2019.
18. Huo Z, Chong F, Yin L, Li N, Liu J, Zhang M, Guo J, Fan Y, Zhang L, Lin X, *et al*: Comparison of the performance of the GLIM criteria, PG-SGA and mPG-SGA in diagnosing malnutrition and predicting survival among lung cancer patients: A multicenter study. Clin Nutr 42: 1048-1058, 2023.
19. Zhou L, Fu J, Ding Z, Jin K, Wu R and Ye LX: Comparison of GLIM, SGA, PG-SGA, and PNI in diagnosing malnutrition among hepatobiliary-pancreatic surgery patients. Front Nutr 10: 1116243, 2023.
20. Rosnes KS, Henriksen C, Hoidalen A and Paur I: Agreement between the GLIM criteria and PG-SGA in a mixed patient population at a nutrition outpatient clinic. Clin Nutr 40: 5030-5037, 2021.
21. Physical status: The use and interpretation of anthropometry. Report of a WHO expert committee. World Health Organ Tech Rep Ser 854: 1-452, 1995.
22. Martin L, Senesse P, Gioulbasanis I, Antoun S, Bozzetti F, Deans C, Strasser F, Thoresen L, Jagoe RT, Chasen M, *et al*: Diagnostic criteria for the classification of cancer-associated weight loss. J Clin Oncol 33: 90-99, 2015.
23. Song C, Cao J, Zhang F, Wang C, Guo Z, Lin Y, Shi Y, Hu W, Ba Y, Xu H, *et al*: Nutritional risk assessment by scored patient-generated subjective global assessment associated with demographic characteristics in 23,904 common malignant tumors patients. Nutr Cancer 71: 50-60, 2019.
24. Howard EE, Pasiakos SM, Blesso CN, Fussell MA and Rodriguez NR: Divergent roles of inflammation in skeletal muscle recovery from injury. Front Physiol 11: 87, 2020.
25. Puppa MJ, White JP, Sato S, Cairns M, Baynes JW and Carson JA: Gut barrier dysfunction in the ApcMin/+ mouse model of colon cancer cachexia. Biochim Biophys Acta 1812: 1601-1606, 2011.
26. Rupert JE, Narasimhan A, Jengelley DHA, Jiang Y, Liu J, Au E, Silverman LM, Sandusky G, Bonetto A, Cao S, *et al*: Tumor-derived IL-6 and trans-signaling among tumor, fat, and muscle mediate pancreatic cancer cachexia. J Exp Med 218: e20190450, 2021.
27. Pototschnig I, Feiler U, Diwoky C, Vesely PW, Rauchenwald T, Paar M, Bakiri L, Pajed L, Hofer P, Kashofer K, *et al*: Interleukin-6 initiates muscle- and adipose tissue wasting in a novel C57BL/6 model of cancer-associated cachexia. J Cachexia Sarcopenia Muscle 14: 93-107, 2023.
28. Bonetto A, Aydogdu T, Jin X, Zhang Z, Zhan R, Puzis L, Koniaris LG and Zimmers TA: JAK/STAT3 pathway inhibition blocks skeletal muscle wasting downstream of IL-6 and in experimental cancer cachexia. Am J Physiol Endocrinol Metab 303: E410-E421, 2012.
29. Haddad F, Zaldivar F, Cooper DM and Adams GR: IL-6-induced skeletal muscle atrophy. J Appl Physiol (1985) 98: 911-917, 2005.
30. Sun Q, van de Lisdonk D, Ferrer M, Gegenhuber B, Wu M, Park Y, Tuveson DA, Tollkuhn J, Janowitz T and Li B: Area postrema neurons mediate interleukin-6 function in cancer cachexia. Nat Commun 15: 4682, 2024.
31. Schéle E, Benrick A, Grahnemo L, Egecioglu E, Anesten F, Pálsdóttir V and Jansson JO: Inter-relation between interleukin (IL)-1, IL-6 and body fat regulating circuits of the hypothalamic arcuate nucleus. J Neuroendocrinol 25: 580-589, 2013.
32. Penafuerte CA, Gagnon B, Sirois J, Murphy J, MacDonald N and Tremblay ML: Identification of neutrophil-derived proteases and angiotensin II as biomarkers of cancer cachexia. Br J Cancer 114: 680-687, 2016.
33. Trobec K, von Haehling S, Anker SD and Lainscak M: Growth hormone, insulin-like growth factor 1, and insulin signaling-a pharmacological target in body wasting and cachexia. J Cachexia Sarcopenia Muscle 2: 191-200, 2011.
34. Deng M, Aberle MR, van Bijnen AAJHM, van der Kroft G, Lenaerts K, Neumann UP, Wiltberger G, Schaap FG, Olde Damink SWM and Rensen SS: Lipocalin-2 and neutrophil activation in pancreatic cancer cachexia. Front Immunol 14: 1159411, 2023.
35. Olson B, Zhu X, Norgard MA, Levasseur PR, Butler JT, Buenafe A, Burfeind KG, Michaelis KA, Pelz KR, Mendez H, *et al*: Lipocalin 2 mediates appetite suppression during pancreatic cancer cachexia. Nat Commun 12: 2057, 2021.
36. McLoughlin TJ, Tsivitse SK, Edwards JA, Aiken BA and Pizza FX: Deferoxamine reduces and nitric oxide synthase inhibition increases neutrophil-mediated myotube injury. Cell Tissue Res 313: 313-319, 2003.
37. Liang H, Peng H and Chen L: Prognostic value of sarcopenia and systemic inflammation markers in patients undergoing definitive radiotherapy for esophageal cancer. Cancer Manag Res 13: 181-192, 2021.
38. Ruan HC, Wu XH, Huang DL, Fu XB, Zhang C, Zhou K, Zhu GY, Liu D, Cai JT and Tan MH: The Role of the PNI and NLR in nutritional risk screening and assessment of gastric cancer patients. J Nutr Oncol 7: 192-198, 2022.
39. Lipshitz M, Visser J, Anderson R, Nel DG, Smit T, Steel HC and Rapoport B: Emerging markers of cancer cachexia and their relationship to sarcopenia. J Cancer Res Clin Oncol 149: 17511-17527, 2023.

40. Giese MA, Hind LE and Huttenlocher A: Neutrophil plasticity in the tumor microenvironment. Blood 133: 2159-2167, 2019.
41. Lipshitz M, Visser J, Anderson R, Nel DG, Smit T, Steel HC and Rapoport BL: Relationships of emerging biomarkers of cancer cachexia with quality of life, appetite, and cachexia. Support Care Cancer 32: 349, 2024.
42. Lin J, Zhang W, Huang Y, Chen W, Wu R, Chen X, Lou N and Wang P: Sarcopenia is associated with the neutrophil/lymphocyte and platelet/lymphocyte ratios in operable gastric cancer patients: A prospective study. Cancer Manag Res 10: 4935-4944, 2018.
43. Wang P, Chen X, Liu Q, Liu X and Li Y: Good performance of the Global Leadership Initiative on Malnutrition criteria for diagnosing and classifying malnutrition in people with esophageal cancer undergoing esophagectomy. Nutrition 91-92: 111420, 2021.
44. Wu N, Chen G, Hu H, Pang L and Chen Z: Low pretherapeutic serum albumin as a risk factor for poor outcome in esophageal squamous cell carcinomas. Nutr Cancer 67: 481-485, 2015.
45. Onodera T, Goseki N and Kosaki G: Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. Nihon Geka Gakkai Zasshi 85: 1001-1005, 1984 (In Japanese).
46. Ignacio de Ulíbarri J, González-Madroo A, de Villar NG, González P, González B, Mancha A, Rodríguez F and Fernández G: CONUT: A tool for controlling nutritional status. First validation in a hospital population. Nutr Hosp 20: 38-45, 2005.
47. Yoshida N, Harada K, Baba Y, Kosumi K, Iwatsuki M, Kinoshita K, Nakamura K, Sakamoto Y, Miyamoto Y, Karashima R, *et al*: Preoperative controlling nutritional status (CONUT) is useful to estimate the prognosis after esophagectomy for esophageal cancer. Langenbecks Arch Surg 402: 333-341, 2017.