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ARÁN

Nutrición Hospitalaria

Trabajo Original

Valoración nutricional

A nomogram combining prognostic nutritional index and platelet lymphocyte ratio predicts postoperative pulmonary infection following D2 radical gastrectomy for gastric cancer

Un nomograma que combina el índice nutricional pronóstico y el cociente plaquetario linfocitario predice la infección pulmonar postoperatoria tras la gastrectomía radical D2 por cáncer gástrico

Xinghao Ma[1], Xiumin Lu[2], Xiaoyang Jiang[1], Jiajia Wang[1], Tingting Wang[1], Li Zhang[1]

[1]Department of Clinical Nutrition; [2]Department of Gastrointestinal Surgery. Lu'an Hospital. Anhui Medical University. Lu'an, Anhui Province. People's Republic of China

Abstract

Introduction: the prognostic nutritional index (PNI) and platelet-lymphocyte ratio (PLR) have been found to correlate with outcomes following radical gastrectomy for gastric cancer (GC).

Objectives: to construct a nomogram combining PNI and PLR for individually forecasting the risk of postoperative pulmonary infection (POI) following D2 radical gastrectomy for GC.

Methods: retrospectively, clinical data was gathered from 404 patients treated with D2 radical gastrectomy for GC. The study used multivariate logistic regression analysis to screen independent risk factors for POI after surgery. Subsequently, a nomogram was developed based on the above factors to forecast the POI probability accurately.

Results: the multivariate logistic regression analysis identified age, PNI, PLR, CA199 level, ASA score, and ICU treatment as independent risk variables for POI following D2 radical gastrectomy ($p < 0.001$ or 0.05). The nomogram's area under the receiver operating characteristic curve (AUC) for predicting the risk of POI was 0.736 (95 % confidence interval (CI) = 0.678-0.794). The nomogram was internally validated using the bootstrap approach, involving repeated sampling 1000 times. The result yielded a concordance index (c-index) of 0.707 (95 % CI = 0.705-0.709). The calibration curves demonstrated an excellent concordance between the predicted values of the nomogram and the observed values. The nomogram's clinical value was shown to be high using decision analysis curves.

Conclusions: a nomogram combining PNI and PLR is a dependable tool for forecasting the probability of POI following D2 radical gastrectomy for GC.

Keywords:

Gastric cancer. Prognostic nutritional index. Platelet lymphocyte ratio. Pulmonary infection. Nomogram.

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Data availability: the corresponding author will provide the datasets derived from the current study upon reasonable request.

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Correspondence:

Xinghao Ma. Department of Clinical Nutrition. Lu'an Hospital. Anhui Medical University. Lu'an 237005, Anhui Province. People's Republic of China
e-mail: 271307026@qq.com

Resumen

Introducción: se ha observado que el índice nutricional pronóstico (INP) y el cociente plaquetas/linfocitos (PLR) se correlacionan con los resultados tras la gastrectomía radical por cáncer gástrico (CG).

Objetivos: diseñar un nomograma que combine el INP y la RPL para predecir individualmente el riesgo de infección pulmonar postoperatoria (POI) tras una gastrectomía radical D2 por CG.

Métodos: de forma retrospectiva, se recopilaron datos clínicos de 404 pacientes tratados con gastrectomía radical D2 por CG. El estudio utilizó un análisis de regresión logística multivariante para detectar factores de riesgo independientes de IOP tras la cirugía. Posteriormente, se desarrolló un nomograma basado en los factores mencionados para pronosticar con precisión la probabilidad de POI.

Resultados: el análisis de regresión logística multivariante identificó la edad, el INP, el PLR, el nivel de CA199, la puntuación ASA y el tratamiento en la UCI como variables de riesgo independientes para el POI tras la gastrectomía radical D2 ($p < 0,001$ o 0,05). El área bajo la curva ROC (característica operativa del receptor) AUC del nomograma para predecir el riesgo de POI fue de 0,736 (intervalo de confianza [IC] del 95 % = 0,678-0,794). El nomograma se validó internamente mediante el método *bootstrap,* que consiste en repetir el muestreo 1000 veces. El resultado fue un índice de concordancia (índice c) de 0,707 (IC del 95 % = 0,705-0,709). Las curvas de calibración demostraron una excelente concordancia entre los valores predichos del nomograma y los valores observados. El valor clínico del nomograma se demostró elevado mediante curvas de análisis de decisión.

Conclusiones: un nomograma que combina INP y PLR es una herramienta fiable para predecir la probabilidad de POI tras gastrectomía radical D2 por CG.

Palabras clave:

Cáncer gástrico. Índice pronóstico nutricional. Cociente linfocito-plaquetario. Infección pulmonar. Nomograma.

INTRODUCTION

In 2020, gastric cancer (GC) had more than one million new cases and caused around 769,000 deaths worldwide. It ranked fifth in regards to new cases and fourth in regards to causing mortality among all types of cancer (1). In China, GC is the third leading cause of cancer-related deaths (2). The definitive and possibly curative treatment for GC without distant metastases is radical stomach resection combined with regional lymphadenectomy. In eastern Asia, the D2 radical gastrectomy is the established method for treating curable GC (3). Although the prognosis of patients after radical gastrectomy has improved considerably with advances in operative technology and perioperative care, postoperative complications, including postoperative pulmonary infections (POIs), continue to be clinically significant events, particularly within aged patients or those with poorer immune status (4,5). The postoperative complications have been illustrated to be linked to elevated medical expenses, prolonged stays in hospitals, and raised mortality during the perioperative period (6,7). Furthermore, there is an increasing amount of data indicating that postoperative infectious complications, such as POI, impact the overall survival of GC patients (8-11). Hence, it is crucial to elucidate the risk factors linked to the development of POI to identify high-risk patients and provide early, specific medicinal interventions to decrease the occurrence of POI and improve postoperative clinical results.

Previous studies have examined the predictive significance of various nutritional and inflammation-related indicators derived from blood tests, involving the controlling nutritional status (CONUT) score (12), prognostic nutritional index (PNI) (13), platelet-to-lymphocyte ratio (PLR) (14), neutrophil-to-lymphocyte ratio (NLR), and others (15,16), for postoperative complications and long-term survival in GC. However, the existing preoperative predictive investigations have mainly concentrated on individual nutritional or inflammatory indicators, with a limited number of researches exploring the combined predictive value of both nutritional and inflammatory markers concerning postoperative complications for GC patients. Furthermore, as far as we know, no study currently focuses on creating a nomogram that combines nutritional and inflammation-related markers to accurately forecast the individual risk of POI after radical gastrectomy for GC.

This study examines the relationship between preoperative nutrition, inflammation-related biomarkers, and postoperative POI in individuals who undergo D2 radical gastrectomy for GC. Further, we developed a nomogram that combines the PNI and PLR as an intuitive and easy-to-use tool for clinicians to accurately assess the likelihood of POI after D2 radical gastrectomy. This nomogram may assist clinicians in tailoring treatment approaches to enhance patient outcomes.

METHODS

PATIENTS

This study comprised 404 patients with GC who had D2 radical gastrectomy at the Department of Gastrointestinal Surgery, Lu'an Hospital, Anhui Medical University, between January 2019 and December 2021. Each of the individuals matched the essential inclusion standards: 1) Patients who were diagnosed with GC through a biopsy before surgery and deemed appropriate for D2 radical resection based on a thorough preoperative assessment; 2) Patients who underwent D2 radical resection; 3) Patients with complete medical and pathological information; 4) Patients who received no neoadjuvant therapy; 5) Patients with tumours other than GC were excluded from this study. Each patient had a whole or partial gastrectomy, accompanied by D2 lymph node dissections, according to the tumour's position and size. The surgical management of GC was performed following the Japanese recommendations for treating this condition.

The study was authorised by the Lu'an Hospital Ethics Committee of Anhui Medical University, complying with the principles of the Declaration of Helsinki. Simultaneously, before conducting the study, each patient provided fully informed written permission.

DATA COLLECTION

This study examined clinicopathological variables like baseline demographics, preoperative lab tests, intra-operative factors, and pathological tumour characteristics (according to the American Joint Committee on Cancer TNM staging system 8th edition). The serum albumin (ALB) level, total cholesterol, and blood cell counts, namely neutrophils, platelets, and lymphocytes, were obtained from the medical records before therapy. This study analysed preoperative indicators of nutrition and inflammation, including the prognosis nutritional index (PNI), controlling nutritional status (CONUT) score, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR). The NLR and PLR were determined by dividing the number of neutrophils and platelets by the number of lymphocytes (17). The PNI was derived using the formula: (10 × albumin level [g/dL]) + (0.005 × lymphocyte count [number/mm^3]) (18). The CONUT score was estimated following the approach described in table I (19). The primary measure evaluated was the occurrence of postoperative pulmonary infection (POI) during 30 days after the surgical procedure. The diagnosis of POI was established based on the criteria put forward by the United States Centres for Disease Control and Prevention (20). The researchers in this study meticulously reviewed each patient's medical records to validate the POI diagnosis.

STATISTICAL ANALYSIS

Statistical analyses were conducted using SPSS version 26.0 and R version 4.3.0. The appropriate cutoff values for PNI, CONUT score, PLR, and NLR were identified using the receiver operating characteristic (ROC) curve. The categorical data are represented as the number of instances (%) and analysed using either the Chi-square or Fisher's exact test. Quantitative variables were measured as the median with the interquartile range and were compared using either the student's t-test or the Mann-Whitney U-test. The binary logistic regression model included Variables with a significance level of $p < 0.05$ obtained from univariate analysis. A nomogram was created to estimate the probability of occurrence of a specific result. The nomogram's predictive capability was evaluated by computing the concordance index (C-index) and the area under the receiver operating characteristic curve (AUC). A calibration chart was created to conduct concordance testing, comparing expected and actual values. Finally, decision curve analysis (DCA) was used to evaluate the practical value of the nomogram in a clinical setting. A *p*-value less than 0.05 indicates a statistically significant difference.

RESULTS

PATIENT CHARACTERISTICS

Table I displays the clinical and pathological features of the 404 patients. Of the total, 294 individuals (72.8 %) were male, while 110 individuals (27.2 %) were female. The median age of the individuals was 68.0 years, with a range of 39.0 to 88.0 years. Among the 404 instances, hypertension was present in 129 patients (31.9 %), chronic obstructive pulmonary disease (COPD) in 19 patients (4.7 %), and diabetes mellitus in 40 patients (9.9 %). Two hundred twenty-two patients, 55.0 % of the sample, had laparoscopically assisted gastrectomy. One hundred four people, accounting for 25.7 % of the 404 participants, were diagnosed with pulmonary infection based on the diagnostic criteria.

THE CORRELATION OF PNI AND PLR WITH CLINICOPATHOLOGIC VARIABLES

The optimal cutoff values for the PNI and PLR in predicting POI were determined to be 48.55 and 142.89, respectively, by the maximum Youden index (Fig. 1A-B). The CONUT score had a cutoff value 2.50, while the NLR had a cutoff value of 2.515, as seen in figure 1C-D. Among the 404 patients, 172 (42.6 %) patients had a PNI ≤ 48.55, while 198 (49.0 %) patients had a PLR ≤ 142.89. On the other hand, 232 patients (57.4 %) had a PNI > 48.55, and 206 patients (51.0 %)

Table I. Computing of CONUT score

Variables	Levels of malnutrition			
	Normal	Mild	Moderate	Severe
Albumin, g/dL	≥ 3.5	3.0 ≤ ALB < 3.5	2.5 ≤ ALB < 3.0	< 2.5
Score	0	2	4	6
Total lymphocyte count, mg/mL	≥ 1600	1200 ≤ TLC < 1600	800 ≤ ALB < 1200	< 800
Score	0	1	2	3
Total cholesterol, mg/dL	≥ 180	140 ≤ TC < 180	100 ≤ TC < 140	< 100
Score	0	1	2	3
Total score	0-1	2-4	5-8	9-12

had a PLR > 142.89. The PNI ≤ 48.55 group and the PNI > 48.55 group exhibited significant differences in age, BMI, COPD, haemoglobin, albumin, CA199, maximal tumour diameter, *p* T stage, *p* N stage, *p* TNM stage, vascular infiltration, neural infiltration, and postoperative pulmonary infection, as indicated in table II. The PLR ≤ 142.89 group and the PLR > 142.89 group showed significant differences in BMI, diabetes, haemoglobin, albumin, maximal tumour diameter, *p* T stage, *p* TNM stage, and postoperative pulmonary infection.

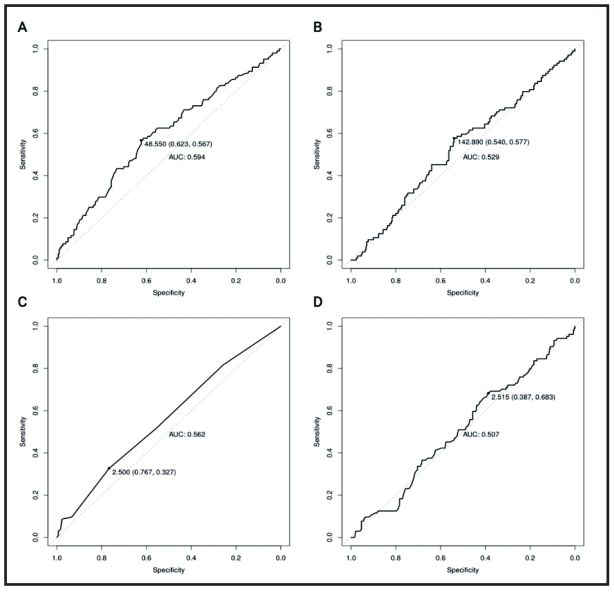

Figure 1.

ROC curve analysis of PNI, PLR, CONUT score and NLR for predicting POI (A. PNI; B. PLR; C. CONUT score; D. NLR).

UNIVARIATE AND MULTIVARIATE LOGISTIC REGRESSION ANALYSIS

The univariate logistic analysis demonstrated substantial correlations between many covariates and the incidence of POI following D2 radical gastrectomy for GC. These variables include age, hypertension, diabetes, haemoglobin levels, albumin levels, PNI, PLR, CA199 levels, American Society of Anesthesiologists (ASA) score, operation time, and postoperative intensive care unit (ICU) treatment ($p < 0.001$ or 0.05). Additional multivariate logistic regression analyses revealed that age, PNI, PLR, CA199 levels, ASA score, and postoperative ICU treatment were determined to be independent risk variables for POI after D2 radical gastrectomy for GC ($p < 0.001$ or 0.05) (Table III).

CONSTRUCTING VALIDATING THE NOMOGRAM

We used the outcomes of logistic regression analysis to develop an intuitive and effective nomogram for evaluating the probability of POI after D2 radical gastrectomy for GC (Fig. 2). The area under the curve (AUC), sensitivity, and specificity of the nomogram were 0.736 (95 % CI = 0.678-0.794), 61.7 %, and 76.2 %, respectively (Fig. 3A). The internal validation was conducted using the Bootstrap approach, which included doing self-help repeated sampling 1000 times. The c-index was determined to be 0.707 (95 % CI = 0.705-0.709). The calibration curve demonstrated a strong agreement between the nomogram's estimation of the risk of POI following D2 radical gastrectomy for GC and the actual observed risk (Fig. 3B).

Table II. Correlation of patient characteristics with PNI and PLR

Characteristics	Total (*n* = 404)	PNI			PLR		
		< 48.55 (*n* = 172)	≥ 48.55 (*n* = 232)	*p*-value	< 142.8 (*n* = 198)	≥ 142.89 (*n* = 206)	*p*-value
Age, years*	68.0 (63.0-74.0)	71.0 (66.0-75.0)	67.0 (60.0-72.0)	*< 0.001*	68.0 (62.0-73.0)	69.0 (64.0-75.0)	0.334
Male sex	294 (72.8)	124 (72.1)	170 (73.3)	0.792	150 (75.8)	144 (69.9)	0.186
Smoking	68 (16.8)	34 (19.8)	34 (14.7)	0.174	37 (18.7)	31 (15.0)	0.329
Drinking	64 (15.8)	28 (16.3)	36 (15.5)	0.836	38 (19.2)	26 (12.6)	0.071
BMI*	21.8 (19.5-24.1)	21.1 (19.0-23.7)	22.2 (19.9-24.2)	*0.003*	22.2 (20.0-24.2)	21.3 (19.2-23.8)	*0.018*
Hypertension	129 (31.9)	55 (32.0)	74 (31.9)	0.986	72 (36.4)	57 (27.7)	0.061
COPD	19 (4.7)	13 (7.6)	6 (2.6)	*0.020*	7 (3.5)	12 (5.8)	0.277
Diabetes	40 (9.9)	16 (9.3)	24 (10.3)	0.729	29 (14.6)	11 (5.3)	*0.002*
Prior abdominal surgery	61 (15.1)	30 (17.4)	31 (13.4)	0.257	28 (14.1)	33 (16.0)	0.598

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Table II (cont.). Correlation of patient characteristics with PNI and PLR

Characteristics	Total (*n* = 404)	PNI			PLR		
		< 48.55 (*n* = 172)	≥ 48.55 (*n* = 232)	*p*-value	< 142.8 (*n* = 198)	≥ 142.89 (*n* = 206)	*p*-value
Hemoglobin, g/L*	122.0 (97.3-135.8)	102.0 (83.0-120.0)	132.0 (118.0-141.0)	*< 0.001*	129.0 (113.0-138.3)	112.5 (86.8-133.0)	*< 0.001*
Albumin, g/L*	41.8 (38.0-45.3)	37.4 (34.8-40.0)	44.9 (42.3-46.7)	*< 0.001*	42.3 (39.0-45.7)	41.4 (37.2-44.9)	*0.010*
CEA, ng/mL < 5 > 5	 307 (76.6) 94 (23.4)	 129 (75.9) 41 (24.1)	 178 (77.1) 53 (22.9)	0.784	 155 (78.7) 42 (21.3)	 152 (74.5) 52 (25.5)	0.324
CA125, U/mL < 35 > 35	 392 (97.8) 9 (2.2)	 164 (96.5) 6 (3.5)	 228 (98.7) 3 (1.3)	0.136	 195 (99.0) 2 (1.0)	 197 (96.6) 7 (3.4)	0.102
CA199, U/mL < 37 > 37	 346 (86.3) 55 (13.7)	 140 (82.4) 30 (17.6)	 206 (89.2) 25 (10.8)	0.050	 173 (87.8) 24 (12.2)	 173 (84.8) 31 (15.2)	0.381
Tumor location Upper Middle Lower	 183 (45.3) 89 (22.0) 132 (32.7)	 74 (43.0) 36 (20.9) 62 (36.0)	 109 (47.0) 53 (22.8) 70 (30.2)	0.461	 97 (49.0) 42 (21.2) 59 (29.8)	 86 (41.7) 47 (22.8) 73 (35.4)	0.322
Maximum tumour diameter, cm < 4 > 4	 204 (50.5) 200 (49.5)	 71 (41.3) 101 (58.7)	 133 (57.3) 99 (42.7)	*0.001*	 119 (60.1) 79 (39.9)	 85 (41.3) 121 (58.7)	*< 0.001*
p T stage T1 + T2 T3 + T4	 127 (31.4) 277 (68.6)	 37 (21.5) 135 (78.5)	 90 (38.8) 142 (61.2)	*< 0.001*	 76 (38.4) 122 (61.6)	 51 (24.8) 155 (75.2)	*0.003*
p N stage N0 N1 + N2 + N3	 168 (41.6) 236 (58.4)	 60 (34.9) 112 (65.1)	 108 (46.6) 124 (53.4)	*0.019*	 88 (44.4) 110 (55.6)	 80 (38.8) 126 (61.2)	0.253
p TNM stage I II III	 108 (26.7) 103 (25.5) 193 (47.8)	 29 (16.9) 49 (28.5) 94 (54.7)	 79 (34.1) 54 (23.3) 99 (42.7)	*0.001*	 65 (32.8) 45 (22.7) 88 (44.4)	 43 (20.9) 58 (28.2) 105 (51.0)	*0.024*
Tumor differentiation Well Moderate Poor	 42 (10.4) 69 (17.1) 293 (72.5)	 12 (7.0) 26 (15.1) 134 (77.9)	 30 (12.9) 43 (18.5) 159 (68.5)	0.073	 23 (11.6) 33 (16.7) 142 (71.7)	 19 (9.2) 36 (17.5) 151 (73.3)	0.730
Vascular infiltration	184 (45.5)	93 (54.1)	91 (39.2)	*0.003*	81 (40.9)	103 (50.0)	0.067
Neural infiltration	190 (47.0)	91 (52.9)	99 (42.7)	*0.042*	85 (42.9)	105 (51.0)	*0.105*
Pulmonary infection	104 (25.7)	59 (34.3)	45 (19.4)	*0.001*	60 (30.3)	44 (1.4)	*0.040*

**Values are median (interquartile range). ASA: American society of anesthesiology; BMI: body mass index; CA199: carbohydrate antigen 199; CA125: carbohydrate antigen 125; CEA: carcinoembryonic antigen; COPD: chronic obstructive pulmonary disease; PLR: platelet-to-lymphocyte ratio; PNI: prognostic nutritional index.*

Table III. Univariate and multivariate logistic regression analysis of POI risk factors

Characteristics	UV OR (95 % CI)	UV *p-value*	MV OR (95 % CI)	*MV p-value**
Age, > 71.5 years	2.766 (1.749-4.374)	*< 0.001*	1.796 (1.067-3.024)	*0.028*
Gender, male *vs* female	1.249 (0.746-2.091)	0.397		
Smoking	0.954 (0.523-1.740)	0.878		
Drinking	1.052 (0.574-1.928)	0.870		
Hypertension	2.074 (1.306-3.292)	*0.002*	NS	0.744
COPD	1.352 (0.500-3.653)	0.552		
Diabetes	2.353 (1.202-4.606)	0.012	NS	0.606
Prior abdominal surgery	1.504 (0.835-2.709)	0.174		
BMI, < 18.5 kg/m^2	1.347 (0.724-2.507)	0.347		
Hemoglobin, < 110/120 g/L	1.655 (1.055-2.595)	*0.028*	NS	0.624
Albumin, < 35 g/L	2.206 (1.154-4.217)	*0.017*	NS	0.933
PNI, > 48.55	0.461 (0.293-0.725)	*0.001*	0.529 (0.313-0.893)	*0.017*
CONUT score, > 2.5	1.596 (0.978-2.603)	0.061		
PLR, > 142.89	0.625 (0.398-0.980)	*0.041*	0.489 (0.290-0.822)	*0.007*
NLR, > 2.515	0.737 (0.459-1.184)	0.207		
CEA, > 5 ng/mL	1.456 (0.873-2.428)	0.150		
CA125, > 35 U/mL	0.365 (0.045-2.955)	0.345		
CA199, > 37 U/mL	1.869 (1.023-3.417)	*0.042*	2.005 (1.025-3.924)	*0.042*
Tumor location Middle *vs* upper Lower *vs* upper	 0.845 (0.469-1.521) 0.949 (0.570-1.579)	 0.574 0.840		
ASA score 2 *vs* 1 3 *vs* 1	 4.714 (2.635-8.436) 14.371 (2.918-70.779)	 *< 0.001* *0.001*	 3.391 (1.789-6.426) 6.949 (1.284-37.615)	 *< 0.001* *0.024*
Surgical approach, open *vs* laparoscopy	1.178 (0.754-1.843)	0.472		
Type of resection, total *vs* subtotal	1.002 (0.627-1.602)	0.992		
Multi-visceral resection	0.792 (0.389-1.610)	0.519		
Operation time, > 261 min	1.731 (1.105-2.713)	0.017	NS	0.062
Intraoperative blood loss, > 325 ml	1.637 (0.880-3.047)	0.120		
Perioperative blood transfusion	1.394 (0.855-2.273)	0.182		
Postoperative ICU treatment	12.417 (2.592-59.472)	0.002	6.588 (1.199-36.198)	*0.030*
Maximum tumor diameter, > 4 cm	1.082 (0.692-1.690)	0.730		
p T stage, T3 + T4 vs T1 + T2	1.043 (0.644-1.689)	0.865		
p N stage, N1 + N2 + N3 *vs* N0	1.484 (0.933-2.360)	0.095		

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Table III (cont.). Univariate and multivariate logistic regression analysis of POI risk factors

Characteristics	UV OR (95 % CI)	UV *p-value*	MV OR (95 % CI)	*MV p-value**
p TNM stage				
II *vs* I	1.120 (0.601-2.088)	0.720		
III *vs* I	1.133 (0.657-1.953)	0.654		
Tumor differentiation				
Moderate *vs* well	2.118 (0.765-5.859)	0.148		
Poor *vs* well	2.254 (0.915-5.552)	0.077		
Vascular infiltration	0.883 (0.564-1.385)	0.589		
Neural infiltration	0.734 (0.467-1.152)	0.179		

**Variables found to be significant at $p < 0.05$ in the univariate analysis were entered into the multivariate logistic regression analysis. ASA: American society of anesthesiology; BMI: body mass index; CA199: carbohydrate antigen 199; CA125: carbohydrate antigen 125; CEA: carcinoembryonic antigen; CONUT: controlling nutritional status; COPD: chronic obstructive pulmonary disease; MV: multivariable; NLR: neutrophil-to-lymphocyte ratio; NS: not significant; PLR: platelet-to-lymphocyte ratio; PNI: prognostic nutritional index; UV: univariate; OR: odds ratio; CI: confidence interval.*

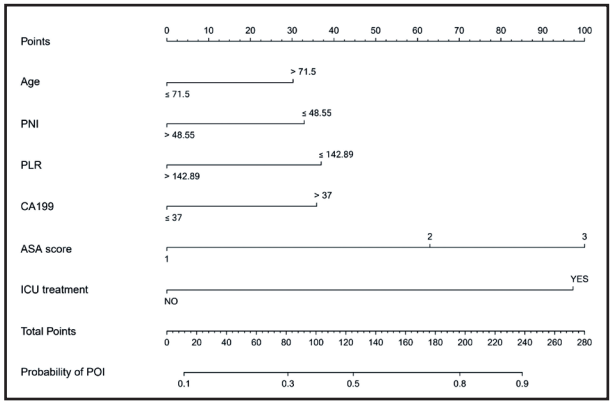

Figure 2.

The nomogram for predicting POI (ASA: American Society of Anesthesiology; CA199: carbohydrate antigen 199; PLR: platelet-to-lymphocyte ratio; PNI: prognostic nutritional index).

DECISION CURVE ANALYSIS

The nomogram's clinical value was evaluated using a decision curve (Fig. 4). The DCA indicated that the nomogram has a significant positive net effect and is clinically valuable for accurately predicting the occurrence of POI following D2 radical gastrectomy for GC.

DISCUSSION

Gastrectomy is the primary and most effective therapy for curing GC. Nevertheless, radical resection for GC is intricate and time-consuming, posing a significant risk of infection after surgery. The incidence of POI after radical gastrectomy exhibits significant variation across different nations and regions. This retrospective study analyzed 404 GC patients who had D2

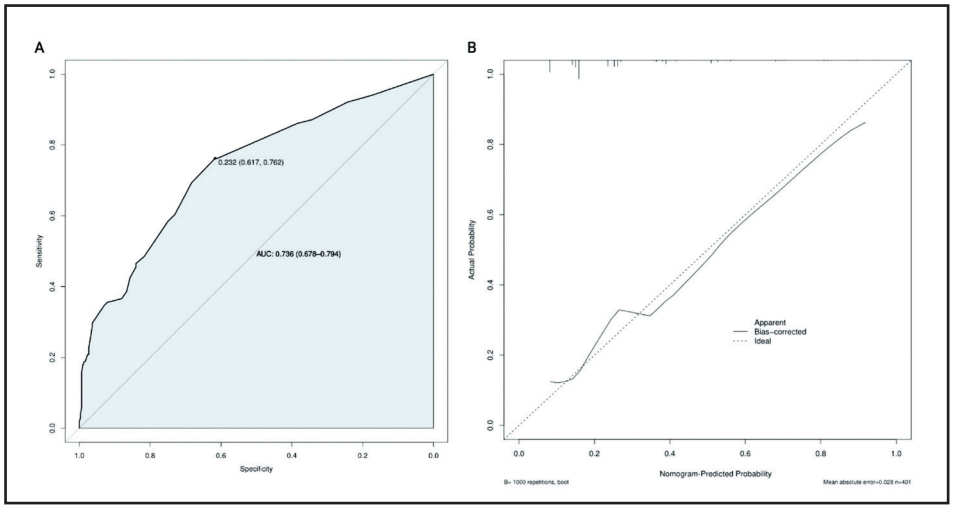

Figure 3.

The ROC curve and the calibration curve of the nomogram (A. The ROC curve; B. The calibration curve).

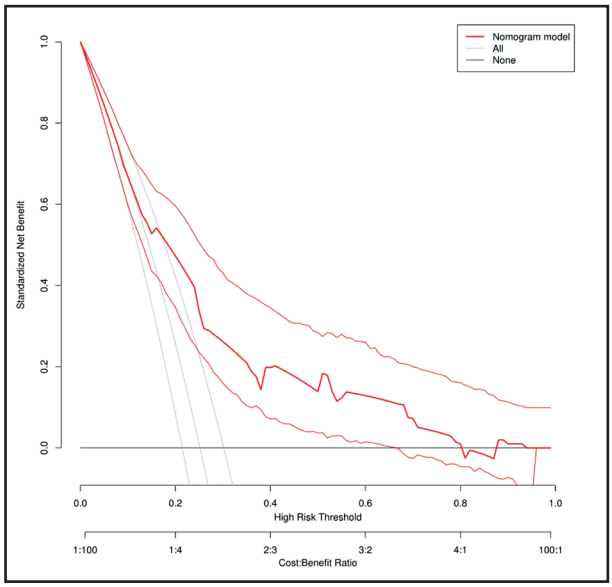

Figure 4.

The DCA curve of the nomogram.

radical gastrectomy. The study found that the incidence of POI was 25.7 %, which was significantly higher compared to the rates of 12.8 % (9) and 14.7 % (21) reported in earlier studies. Possible explanations for this divergence might be attributed to variations in the diagnostic criteria for POI, heterogeneity in the features of the research cohorts, and disparities in surgical procedures. Postoperative infection carries a substantial economic cost for patients and hampers their recovery. Hence, it is crucial to determine the risk factors and promptly adopt measures to minimise the likelihood of such infections (7,22). Several recent studies have shown a strong correlation between the patient's nutritional state and levels of inflammation with the occurrence of postoperative infection in various illnesses. The need to evaluate nutrition and inflammation in cancer patients is widely acknowledged (22-24). Recently, several studies have examined the risk variables associated with POI after radical gastrectomy (25,26). However, these studies have not sufficiently included all relevant risk factor variables, and few studies considered preoperative nutritional and inflammation-related variables in patients. Consequently, these studies provide restricted guidance for clinical practice.

In this work, we create a nomogram that combines the PNI and PLR to accurately predict the probability of POI after D2 radical gastrectomy for GC. This work represents the first endeavour to integrate patients' nutritional and inflammatory-related indicators to individually predict the likelihood of POI after D2 radical gastrectomy for GC. The findings of our study suggest that Age, PNI, PLR, CA199 level, ASA score, and ICU treatment were identified as separate risk factors for POI. In addition, we developed a nomogram incorporating independent risk variables obtained from multivariate analysis, which effectively predicts the probability of POI. The nomogram model exhibited a significant level of discrimination, as shown by its C-index of 0.707. The calibration curves for predicting the probability of POI demonstrated a strong agreement between the anticipated values from the nomogram and the observed values. Hence, our nomogram may serve as an intuitive tool for determining the probability of POI after D2 radical gastrectomy for GC and for implementing preventive medical measures to mitigate the occurrence of POI and improve patients' clinical outcomes.

A rising percentage of clinicians are beginning to recognise the significance of nutrition for patients diagnosed with GC. Hence, it is crucial to assess the nutritional condition of individuals diagnosed with GC precisely. Among various clinical factors, the patient's nutritional status stands out as a modifiable factor, unlike age, tumor status, and comorbidities, which are essentially unchangeable. Hence, to enhance a patient's postoperative outcome, it is crucial to focus on modifiable risk factors that may be partly or completely changed. Timely recognition and intervention for patients who suffer from malnutrition or are at high nutritional risk is essential for the efficient treatment of tumor patients during the perioperative period. Several nutritional risk screening/assessment methods are accessible, such as the Nutritional Risk Screen 2002, the Malnutrition Universal Screening Tool, the Subjective Global Assessment, and the Patient-generated Subjective Global Assessment. Nevertheless, such methods often need to be more convenient and susceptible to subjective influences, resulting in less precise outcomes (27). The PNI is a quantitative nutritional assessment tool that may be readily determined by measuring the serum ALB level and the peripheral blood lymphocyte count. Serum ALB, a hepatically synthesised protein, is crucial in transporting substances and regulating plasma osmolality. Additionally, Serum ALB concentration serves as an indicator of the body's nutritional status (28). Peripheral blood lymphocytes play a crucial role in the elimination and programmed cell death of tumour cells, thereby serving as a critical component of the body's immunological defence against cancer. A reduced lymphocyte count indicates a decline in the body's immunological activity against tumours (29). Xi et al. (22) demonstrated using PNI in predicting postoperative infection following radical surgery for GC. Their study revealed that a PNI value below 45 was a significant risk variable for infection following radical surgery for GC. Xiao et al. (30) found that infection is an essential complication after gastrectomy, and a PNI value of less than 43.9 is an independent risk factor for infection after stage II/III radical gastric resection. This study determined that a PNI value of 48.55 is the optimal cutoff value for predicting the occurrence of POI following D2 radical gastrectomy. Furthermore, a multivariate analysis demonstrated that a PNI value below 48.55 is an independent risk factor for POI.

Neutrophils, lymphocytes, and platelets are easily accessible via standard blood count tests and have essential functions in reducing inflammation, responding to infections, and maintaining proper blood coagulation (31). The PLR, derived from the combined platelet and lymphocyte counts, is a reliable indicator of systemic inflammation and immunological function (32).

Consequently, a lower PLR score indicates the presence of both systemic inflammation and weakened immune response. Mounting data suggests that a widespread inflammatory response may have a significant impact on the initiation and advancement of cancer. While several studies have established PLR as a prognostic indicator for various solid tumours (16,33), acute ischemic stroke, and acute renal damage (34,35), there is less data about its possible correlation with POI after radical gastrectomy for GC. This study found a strong correlation between preoperative PLR and POI. Multivariate analysis showed that the preoperative PLR ≤ 142.89 is an independent risk factor for POI. The specific mechanism by which preoperative PLR affects POI in individuals with GC is likely intricate yet not fully understood. A diminished PLR indicates a reduction in the total lymphocyte count and an elevation in platelet count. A reduced total lymphocyte count indicates compromised cell-mediated immunity and malnutrition in the body. In contrast, an elevated platelet count indicates inflammation and a predisposition to blood clotting (36). A diminished lymphocyte-mediated antibacterial immune response may reduce the lymphocyte-mediated antibacterial cellular immunological response, hence facilitating bacterial invasion and proliferation (14,37). The platelet count is acknowledged as an indicator of a widespread inflammatory reaction and the possibility of tiny blood vessel clotting. The prevalence of inflammatory cytokine cascades, such as those associated with tumour necrosis factor-a and interleukin (IL)-1, IL-6, and IL-8, is enhanced by systemic inflammatory responses, including a low PLR. These immune modulators can potentially influence the activity and regulation of natural killer cells, cytotoxic T lymphocytes, and antigen-presenting cells (38-40). Eventually, the interaction between these intricate elements raises infectious complications following surgery.

An advantage of our research is that the nomograms were constructed using PNI and PLR indicates derived from standard laboratory tests of plasma albumin, platelet, and lymphocyte counts. These procedures are often used in clinical practice. Nevertheless, there are some limitations to this research. Initially, as this is a single-centre retrospective study, it was impossible to exclude some potential biases completely. Furthermore, this study did not collect data to analyse the nutritional supplements provided to patients after their surgery. The outcomes of this research need to offer more proof regarding the effect of postoperative nutritional supplementation and oral diet on POI. Ultimately, this research did not have external validation, and it is necessary to confirm the predictive effectiveness of this nomogram model in other populations. Therefore, we will conduct multicenter research, including a broader population, to further validate our findings.

CONCLUSION

In conclusion, our research concluded that age, PNI, PLR, CA199, ASA score, and postoperative ICU treatment were identified as independent risk factors for POI following radical gastrectomy for GC. Furthermore, the nomogram combining PNI and PLR may aid in precisely predicting the probability of POI following radical gastrectomy for GC, assisting clinicians in developing individualised treatment plans.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-49. DOI: 10.3322/caac.21660
2. Cao W, Chen HD, Yu YW, Li N and Chen WQ. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. Chin Med J (Engl) 2021;134:783-91. DOI: 10.1097/CM9.0000000000001474
3. Japanese Gastric Cancer Association. Japanese Gastric Cancer Treatment Guidelines 2021 (6th edition). Gastric Cancer 2023;26:1-25. DOI: 10.1007/s10120-022-01331-8
4. Shibata C, Ogawa H, Nakano T, Koyama K, Yamamoto K, Nagao M, et al. Influence of age on postoperative complications especially pneumonia after gastrectomy for gastric cancer. BMC Surg 2019;19:106. DOI: 10.1186/s12893-019-0573-x
5. Kiuchi J, Komatsu S, Ichikawa D, Kosuga T, Okamoto K, Konishi H, et al. Putative risk factors for postoperative pneumonia which affects poor prognosis in patients with gastric cancer. Int J Clin Oncol 2016;21:920-6. DOI: 10.1007/s10147-016-0987-8
6. Lawrence VA, Hilsenbeck SG, Mulrow CD, Dhanda R, Sapp J and Page CP. Incidence and hospital stay for cardiac and pulmonary complications after abdominal surgery. J Gen Intern Med 1995;10:671-8. DOI: 10.1007/BF02602761
7. Thompson DA, Makary MA, Dorman T and Pronovost PJ. Clinical and economic outcomes of hospital acquired pneumonia in intra-abdominal surgery patients. Ann Surg 2006;243:547-52. DOI: 10.1097/01.sla.0000207097.38963.3b
8. Tu RH, Lin JX, Li P, Xie JW, Wang JB, Lu J, et al. Prognostic significance of postoperative pneumonia after curative resection for patients with gastric cancer. Cancer Med 2017;6:2757-65. DOI: 10.1002/cam4.1163
9. Suzuki S, Kanaji S, Matsuda Y, Yamamoto M, Hasegawa H, Yamashita K, et al. Long-term impact of postoperative pneumonia after curative gastrectomy for elderly gastric cancer patients. Ann Gastroenterol Surg 2018;2:72-8. DOI: 10.1002/ags3.12037
10. Kanda M, Ito S, Mochizuki Y, Teramoto H, Ishigure K, Murai T, et al. Multi-institutional analysis of the prognostic significance of postoperative complications after curative resection for gastric cancer. Cancer Med 2019;8:5194-201. DOI: 10.1002/cam4.2439
11. Li QG, Li P, Tang D, Chen J and Wang DR. Impact of postoperative complications on long-term survival after radical resection for gastric cancer. World J Gastroenterol 2013;19:4060-5. DOI: 10.3748/wjg.v19.i25.4060
12. Sun F, Zhang C, Liu Z, Ai S, Guan W and Liu S. Controlling Nutritional Status (CONUT) score as a predictive marker for short-term complications following gastrectomy of gastric cancer: a retrospective study. BMC Gastroenterol 2021;21:107. DOI: 10.1186/s12876-021-01682-z
13. Lee JY, Kim HI, Kim YN, Hong JH, Alshomimi S, An JY, et al. Clinical Significance of the Prognostic Nutritional Index for Predicting Short- and Long-Term Surgical Outcomes After Gastrectomy: A Retrospective Analysis of 7781 Gastric Cancer Patients. Medicine (Baltimore) 2016;95:e3539. DOI: 10.1097/MD.0000000000003539
14. Inaoka K, Kanda M, Uda H, Tanaka Y, Tanaka C, Kobayashi D, et al. Clinical utility of the platelet-lymphocyte ratio as a predictor of postoperative complications after radical gastrectomy for clinical T2-4 gastric cancer. World J Gastroenterol 2017;23:2519-26. DOI: 10.3748/wjg.v23.i14.2519
15. Kwak JS, Kim SG, Lee SE, Choi WJ, Yoon DS, Choi IS, et al. The role of postoperative neutrophil-to-lymphocyte ratio as a predictor of postoperative major complications following total gastrectomy for gastric cancer. Ann Surg Treat Res 2022;103:153-9. DOI: 10.4174/astr.2022.103.3.153
16. Gulmez S, Senger A, Uzun O, Ozduman O, Ofluoglu C, Subasi I, et al. Comparative Analysis of Preoperative Ratio Based Markers in Predicting Postoperative Infectious Complications After Gastrectomy. Pol Przegl Chir 2022;95:1-5. DOI: 10.5604/01.3001.0015.9662

17. Sun X, Liu X, Liu J, Chen S, Xu D, Li W, et al. Preoperative neutrophil-to-lymphocyte ratio plus platelet-to-lymphocyte ratio in predicting survival for patients with stage I-II gastric cancer. Chin J Cancer 2016;35:57. DOI: 10.1186/s40880-016-0122-2
18. Nozoe T, Ninomiya M, Maeda T, Matsukuma A, Nakashima H and Ezaki T. Prognostic nutritional index: a tool to predict the biological aggressiveness of gastric carcinoma. Surg Today 2010;40:440-3. DOI: 10.1007/s00595-009-4065-y
19. Ignacio de Ulibarri J, Gonzalez-Madrono A, de Villar NG, Gonzalez P, Gonzalez B, Mancha A, et al. CONUT: a tool for controlling nutritional status. First validation in a hospital population. Nutr Hosp 2005;20:38-45. DOI:
20. Horan TC, Andrus M and Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. Am J Infect Control 2008;36:309-32. DOI: 10.1016/j.ajic.2008.03.002
21. Meng Y, Zhao P and Yong R. Modified Frailty Index Independently Predicts Postoperative Pulmonary Infection in Elderly Patients Undergoing Radical Gastrectomy for Gastric Cancer. Cancer Manag Res 2021;13:9117-26. DOI: 10.2147/CMAR.S336023
22. Xi X, Yang MX, Wang XY and Shen DJ. Predictive value of prognostic nutritional index on infection after radical gastrectomy: a retrospective study. J Gastrointest Oncol 2022;13:569-80. DOI: 10.21037/jgo-22-192
23. Bora Makal G and Yildirim O. Are the C-reactive protein/albumin ratio (CAR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (NLR) novel inflammatory biomarkers in the early diagnosis of postoperative complications after laparoscopic sleeve gastrectomy? Obes Res Clin Pract 2020;14:467-72. DOI: 10.1016/j.orcp.2020.07.003
24. Muscaritoli M, Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, et al. ESPEN practical guideline: Clinical Nutrition in cancer. Clin Nutr 2021;40:2898-913. DOI: 10.1016/j.clnu.2021.02.005
25. Xiao H, Zhou H, Liu K, Liao X, Yan S, Yin B, et al. Development and validation of a prognostic nomogram for predicting post-operative pulmonary infection in gastric cancer patients following radical gastrectomy. Sci Rep 2019;9:14587. DOI: 10.1038/s41598-019-51227-4
26. Cho H, Tsuchida K, Iwasaki K and Maezawa Y. Risk factors of post-operative pneumonia in elderly patients with gastric cancer: a retrospective cohort study. Jpn J Clin Oncol 2021;51:1044-50. DOI: 10.1093/jjco/hyab032
27. Xiao Q, Li X, Duan B, Li X, Liu S, Xu B, et al. Clinical significance of controlling nutritional status score (CONUT) in evaluating outcome of postoperative patients with gastric cancer. Sci Rep 2022;12:93. DOI: 10.1038/s41598-021-04128-4
28. Arroyo V, Garcia-Martinez R and Salvatella X. Human serum albumin, systemic inflammation, and cirrhosis. J Hepatol 2014;61:396-407. DOI: 10.1016/j.jhep.2014.04.012
29. Zhang H, Tao Y, Wang Z and Lu J. Evaluation of nutritional status and prognostic impact assessed by the prognostic nutritional index in children with chronic kidney disease. Medicine (Baltimore) 2019;98:e16713. DOI: 10.1097/MD.0000000000016713
30. Xiao Y, Wei G, Ma M, Liu D, Chen P, Quan H, et al. Association among prognostic nutritional index, post-operative infection and prognosis of stage II/III gastric cancer patients following radical gastrectomy. Eur J Clin Nutr 2022;76:1449-56. DOI: 10.1038/s41430-022-01120-7
31. Mungan I, Dicle CB, Bektas S, Sari S, Yamanyar S, Cavus M, et al. Correction to: Does the preoperative platelet-tolymphocyte ratio and neutrophil-tolymphocyte ratio predict morbidity after gastrectomy for gastric cancer? Mil Med Res 2020;7:12. DOI: 10.1186/s40779-020-00242-y
32. Kim EY, Lee JW, Yoo HM, Park CH and Song KY. The Platelet-to-Lymphocyte Ratio Versus Neutrophil-to-Lymphocyte Ratio: Which is Better as a Prognostic Factor in Gastric Cancer? Ann Surg Oncol 2015;22:4363-70. DOI: 10.1245/s10434-015-4518-z
33. Mungan I, Dicle CB, Bektas S, Sari S, Yamanyar S, Cavus M, et al. Does the preoperative platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio predict morbidity after gastrectomy for gastric cancer? Mil Med Res 2020;7:9. DOI: 10.1186/s40779-020-00234-y
34. Zheng CF, Liu WY, Zeng FF, Zheng MH, Shi HY, Zhou Y, et al. Prognostic value of platelet-to-lymphocyte ratios among critically ill patients with acute kidney injury. Crit Care 2017;21:238. DOI: 10.1186/s13054-017-1821-z
35. Chen C, Gu L, Chen L, Hu W, Feng X, Qiu F, et al. Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio as Potential Predictors of Prognosis in Acute Ischemic Stroke. Front Neurol 2020;11:525621. DOI: 10.3389/fneur.2020.525621
36. Zhou X, Du Y, Huang Z, Xu J, Qiu T, Wang J, et al. Prognostic value of PLR in various cancers: a meta-analysis. PLoS One 2014;9:e101119. DOI: 10.1371/journal.pone.0101119
37. Mohri Y, Tanaka K, Toiyama Y, Ohi M, Yasuda H, Inoue Y, et al. Impact of Preoperative Neutrophil to Lymphocyte Ratio and Postoperative Infectious Complications on Survival After Curative Gastrectomy for Gastric Cancer: A Single Institutional Cohort Study. Medicine (Baltimore) 2016;95:e3125. DOI: 10.1097/MD.0000000000003125
38. Miyamoto R, Inagawa S, Sano N, Tadano S, Adachi S and Yamamoto M. The neutrophil-to-lymphocyte ratio (NLR) predicts short-term and long-term outcomes in gastric cancer patients. Eur J Surg Oncol 2018;44:607-12. DOI: 10.1016/j.ejso.2018.02.003
39. Kubota T, Hiki N, Nunobe S, Kumagai K, Aikou S, Watanabe R, et al. Significance of the inflammation-based Glasgow prognostic score for short- and long-term outcomes after curative resection of gastric cancer. J Gastrointest Surg 2012;16:2037-44. DOI: 10.1007/s11605-012-2036-x
40. Horn F, Henze C and Heidrich K. Interleukin-6 signal transduction and lymphocyte function. Immunobiology 2000;202:151-67. DOI: 10.1016/S0171-2985(00)80061-3