Original Article

Predictive value of prognostic nutritional index on infection after radical gastrectomy: a retrospective study

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Background: The prognostic nutritional index (PNI) is a useful tool to evaluate nutritional status, which is associated with postoperative complications and prognosis of patients with cancer. Recent studies have shown that PNI has important predictive value for postoperative infection in cancer patients. However, the role and clinical value of PNI in infection after radical gastrectomy remains unclear. This study investigated the relationship between PNI and infection after radical surgery for gastric cancer (GC), focusing on the predictive value of PNI.

Methods: A total of 1,111 patients with primary gastric cancer who underwent radical surgery in our hospital from December 2010 to December 2020 were included in this retrospective study. The demographic and clinicopathological data of all patients were acquired through hospital information system (HIS). Preoperative serum albumin (ALB) level and peripheral blood lymphocyte count were obtained for PNI calculation. We selected 812 patients by propensity score matching to reduce biases due to the different distributions of co-variables among the comparable groups. The factors influencing postoperative infection in the matched patients were explored using univariate and multivariate analyses.

Results: Baseline characteristics significantly differed among patients with different PNI scores. After one-to-one matching, the clinicopathological data of the 2 groups were comparable, and 812 patients were included for further analysis. Among these patients, 101 developed infections, with an infection rate of 12.4%, which were mainly caused by gram-negative bacteria. The incidence of infection was significantly higher in the low PNI group than in the high PNI group. Univariate and multivariate analyses identified body mass index (BMI) ≥25 kg/m^2 [odds ratio (OR) =2.314, P=0.004], diabetes mellitus (OR =1.827, P=0.042), PNI score <45 (OR =2.138, P=0.037), combined multi-organ resection (OR =2.946, P<0.001), operation time ≥240 minutes (OR =2.744, P=0.023), and perioperative blood transfusion (OR =2.595, P=0.025) as risk factors for infection after radical surgery for GC.

Conclusions: Infection is the most common complication after radical gastrectomy for GC, and a low preoperative PNI score is a risk factor for postoperative infection.

Keywords: Radical surgery for gastric cancer (GC); prognostic nutritional index (PNI); infection; propensity score matching (PSM)

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Introduction

Gastric cancer (GC) is one of the most common and deadly malignancies worldwide (1,2). In China, the high incidence of GC has become a serious public health concern, with the country accounting for about half of all new cases in the world (3,4). Currently, radical surgery remains the gold standard treatment for GC, and relatively complete resection of the tumor can result in good outcomes. However, most patients experience postoperative complications due to their old age, advanced disease stage, declining physical function, and poor immunological status and surgical tolerance. Infection, the most common complication after radical gastrectomy, can lead to prolonged hospital stays, increased risk of intensive care unit (ICU) admission/rehospitalization, and a higher mortality rate (5-7).

Previous studies have shown that the incidence of infection after radical gastrectomy is 11.3–15.5%, with higher rates in the elderly and in immunocompromised patients (8,9). In a retrospective analysis, Xiao *et al.* (10) found that abdominal infection was the main postoperative complication (with an incidence rate of 10.2%) of patients undergoing radical surgery for GC, followed by pulmonary infection. Postoperative infection remains a challenge despite proactive preventive measures. Therefore, it is important to identify the risk factors and implement early interventions accordingly to minimize the occurrence of postoperative infection.

In recent years, nutrition- and inflammation-related indicators have been used to predict surgical risk and postoperative complications. One of these is the prognostic nutritional index (PNI), a simple tool calculated by combining the total peripheral blood lymphocyte count with the serum albumin (ALB) concentration. PNI can be used to assess the nutritional level and immune status of a patient and predict postoperative complications and survival time (11,12). Several clinical studies have found a close relationship between PNI and the prognosis of cancers, including gastric, colorectal, and pancreatic cancers (13,14). Shi *et al.* (15) further revealed that PNI score is an important factor in the occurrence and development of post-surgical infections. Another recent study showed that lower PNI is associated with increased susceptibility to postoperative infection of prostate cancer. Patients with severe malnutrition had more postoperative complications compared to well-nourished patients (16). However, few studies have investigated the relationship between PNI and infection after radical surgery for GC, and most of the available studies have small sample sizes and notable biases in study design, making it difficult to provide high-quality evidence for clinical practice.

In our current study, we explored the role of preoperative PNI in predicting the occurrence of infection after radical surgery for GC to inform the development of targeted measures for the further prevention and control of postoperative infections. We present the following article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-192/rc).

Methods

Study design

This is a single-center, retrospective, observational, and cohort study based on the hospital information system. It was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the ethics committee of Minhang Hospital, Fudan University (2021-012-01K). Informed consent was taken from all the patients.

Subjects

The demographic and clinicopathological data of patients who underwent radical surgery for GC in our center from December 2010 to December 2020 were retrieved from the hospital information system. The inclusion criteria were as follows: (I) all patients were diagnosed with primary GC by gastric mucosal histopathology; (II) patients were diagnosed with clinical TNM stage I–III, which met the indications for radical surgery; (III) patients were aged >18 years; and (IV) patients were assigned an American Society of Anesthesiologists (ASA) score of ≤III. The exclusion criteria were as follows: (I) remnant GC; (II) cardiac, cerebral, pulmonary, and/or other vital organ dysfunction; (III) other malignant tumors, hematological diseases, and/or autoimmune diseases; (IV) preoperatively confirmed acute and chronic infectious disease(s) that were still under treatment; (V) use of immunosuppressive drugs or hormones within 1 month before enrollment; (VI) a history of laparotomy or other major surgery within 1 month before enrollment; and (VII) loss to follow-up, perioperative deaths, or incomplete clinical data. A total of 1,111 postoperative inpatients were finally included and grouped according to their PNI scores (*Figure 1*). Pathological diagnosis and staging of the tumors were performed for each patient.

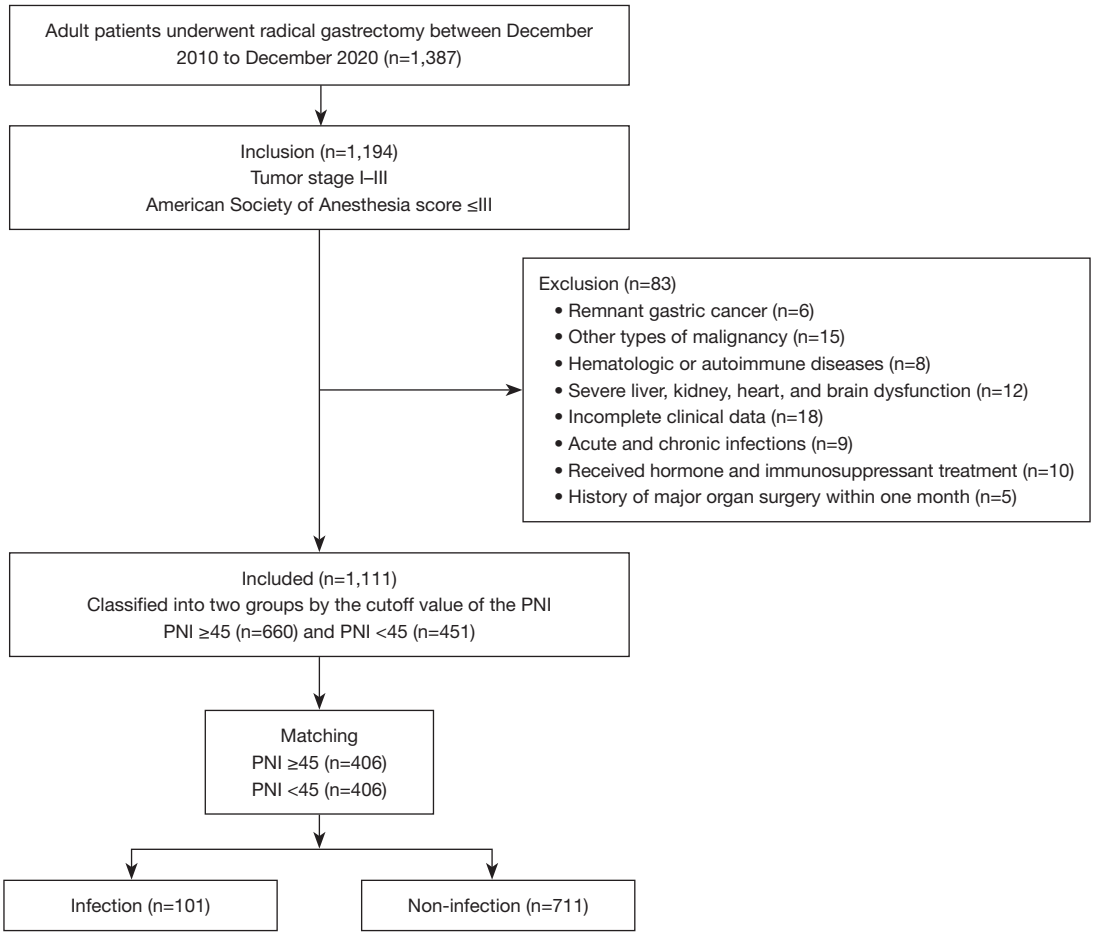

Figure 1 Flow chart of subject enrollment. PNI, prognostic nutritional index.

Radical surgery for GC

All subjects underwent laparoscopic or open surgery according to their condition after admission, and all operations were performed by the same surgical team. In the laparoscopic surgery group, patients were placed in a supine position after induction of general anesthesia and endotracheal intubation. A 1 cm incision was made at the lower edge of the umbilicus. After CO_2 pneumoperitoneum was established, the corresponding trocar was placed, and the abdominal cavity was explored to locate the tumor. In the open surgery group, a 5–8 cm incision was made in the middle of the abdomen for routine exploration, mobilization, and lymph node dissection. Depending on the location of the tumors, the surgical approaches included total gastrectomy, distal gastrectomy, and proximal gastrectomy, along with D2/D2 plus superior mesenteric lymph node dissection. Combined multi-organ resection was performed for patients with tumors invading adjacent organs. For total gastrectomy, the lymph nodes stations dissected were 1, 2, 3, 4d, 4sa, 4sb, 5–10, 11p, 12a, and 14v. For proximal gastrectomy, the lymph nodes stations dissected were 1–4, 7, 8a, 9, 10, and 11, with the preservation of vascular arcades on the lesser and greater curvatures. For distal gastrectomy, the lymph node stations dissected were 1, 3, 4d, 4sb, 5–9, 11p, 12a, and 14v. For proximal gastrectomy, end-to-side anastomosis between the anterior wall of the remnant stomach and the esophageal stump was performed. For distal gastrectomy, Billroth I or II GI reconstruction was performed. For total gastrectomy, Roux-en-Y GI reconstruction was performed. The abdominal cavity was washed using distilled water, and the tumor condition was examined. Antibiotics were applied perioperatively to prevent infection. Postoperatively, a small number of patients with advanced GC were given adjuvant chemotherapy with capecitabine plus oxaliplatin or with S-1

plus oxaliplatin according to the National Comprehensive Cancer Network (NCCN) guidelines.

Diagnostic criteria

Postoperative infections at various sites in patients undergoing radical surgery for GC were assessed according to the *Diagnostic Criteria for Hospital-Acquired Infections (Trial)* formulated by China's Ministry of Health in 2001. The responsible physician monitored and recorded the patient's body temperature, peripheral blood leukocyte count, and clinical signs. Intra-abdominal infection was defined as follows: (I) the presence of fever, abdominal pain, abdominal distension, or obvious signs of peritonitis, with an elevated neutrophil to lymphocyte ratio (NLR); (II) culture positive abdominal fluid (drainage fluid or puncture fluid); or (III) radiologically confirmed intra-abdominal infectious lesions (e.g., abscesses and purulent exudates). A diagnosis of pulmonary infection was made if the patient experienced persistent elevated body temperature (>38.0 ℃) for more than 24 hours after surgery, which might be accompanied by cough and sputum production, with or without positive sputum bacterial culture, and/or the presence of new infiltrates, solid changes, and other signs on chest images. Incisional infection was defined as postoperative infection involving the skin and subcutaneous tissue at the surgical site and featuring redness, swelling, heat, pain, and/or purulent discharge. Lower urinary tract infection was defined as cystitis and urethritis in postoperative patients, with pus and/or hematuria on routine urinalysis and pathogenic bacteria on urine culture. Catheter-associated infections were identified based on the patient's clinical presentation (bacteremia, with hyperthermia and/or chills) and a positive tip culture. In all patients with infections, specimens of pathogenic bacteria were collected for isolation and culture of the pathogen, and antibiotics were administered.

Information collection

The data of patients who met the inclusion criteria were retrieved through the hospital information system. Baseline demographic information, pathologic features of tumors, preoperative laboratory measurements, and surgery-related indicators were collected by reviewing the patients' medical records. The baseline demographic data included age, gender, body mass index (BMI), ASA score, history of abdominal surgery, chronic diseases, and smoking status. The pathologic features of tumors included histologic type, stage, location, and size. Surgery-related indicators consisted of surgical modality, operation time, intraoperative blood loss, blood transfusion, and neoadjuvant chemotherapy. The tumor stage and disease grade were classified according to the 7th edition of the TNM classification of the International Union Against Cancer (UICC), while gross staging and surgical approach and scope were based on the 3rd edition of the Japanese Gastric Cancer Treatment Guidelines.

The PNI was calculated as 10 × serum ALB value (g/dL) + 0.005 × peripheral lymphocyte count (per mm^3). Based on a previous study, a cutoff value of 45 was used to divide patients into low and high PNI groups (17).

PSM

PSM was performed to balance the distribution of baseline characteristics. A logistic regression model was established with high/low PNI score as the dependent variables and with age, gender, BMI, ASA score, smoking status, neoadjuvant chemotherapy, tumor stage, tumor differentiation, tumor location, laboratory measurements, tumor size, surgical modality, operation time, and blood loss as independent variables. A 1:1 matching was performed according to the principle of proximity matching (caliper value: 0.05), without alternatives. The differences in each indicator between the high PNI group and low PNI group before and after matching were compared.

Statistical analysis

Statistical analysis was performed using the SPSS 22.0 software package (IBM Corp., Armonk, NY, USA). The normally distributed measurement data [presented as mean ± standard deviation ($\bar{x}$±SD)], and the non-normally distributed measurement data [presented as median (interquartile spacing)] were compared using independent sample *t*-test or Mann-Whitney U test. The categorical variables were compared using chi-square test or Fisher's exact probability test and are expressed as number of cases (%). Propensity score matching was performed to adjust for differences in baseline characteristics between high PNI and low PNI groups. The resulting score-matched pairs were analyzed subsequently. Univariate analysis was performed to evaluate potential factors for postoperative infection; subsequently, multivariate Logistic regression analysis was performed to obtain the odds ratio (OR) and

95% confidence interval (95% CI) for each factor. All P values reported are two-tailed. A P value of <0.05 was set as the threshold for statistical significance.

Results

Clinicopathological features before matching

A total of 1,111 patients [693 males (62.4%) and 418 females (37.6%), with an average age of 63.8 years] were included in this study. Most patients had ASA scores of 2 (74.3%) and stage I–II disease (72.9%). Laparoscopic surgery was performed in 59.6% of patients, while open surgery was performed in 40.4% of patients. Total gastrectomy was performed in 257 patients, partial gastrectomy in 775 patients, and combined multi-organ resection in 79 patients (including splenectomy in 33 cases, transverse colectomy in 18 cases, partial hepatectomy in 12 cases, and partial pancreatectomy in 16 cases). The mean operation time was 248.4±50.2 minutes, and the average intra-operative blood loss was 210.4±132.1 mL.

The patients were divided into a low PNI group (n=451) and a high PNI group (n=660), with the mean PNI value of patients in the low PNI group significantly lower than that of patients in the high PNI group (39.4±4.5 *vs.* 49.8±4.6). The clinicopathological features of these 2 groups before matching are summarized in *Table 1*. Differences in gender, number of smokers, previous surgical history, number of patients receiving neoadjuvant chemotherapy, and tumor location were not statistically significant between the 2 groups (all P>0.05), whereas differences in mean age, BMI, ASA score, tumor grade, tumor differentiation, preoperative laboratory measurements, tumor size, surgical modality, type of resection, mean operation time, and mean intraoperative blood loss were statistically significant (all P<0.05).

Clinicopathological features after matching

After PSM, the mean age, BMI, ASA score, tumor grade, tumor differentiation, tumor size, surgical modality, type of resection, mean operation time, and mean intraoperative blood loss were not significantly different between the low PNI group and the high PNI group (all P>0.05), although the ALB level, hemoglobin level, and lymphocyte count were still significantly lower in the low PNI group than in the high PNI group (all P<0.05). The mean PNI value was 50.4±3.7 in the high PNI group after matching, which was higher than that in the low PNI group. The clinicopathological features after matching are listed in *Table 2*.

Distribution of infections and detection of pathogenic bacteria after matching

Among the 812 patients, 101 experienced infections after surgery (*Table 3*), including intra-abdominal infections (n=46), pulmonary infections (n=27), and surgical site infections (n=25). In addition, 1 patient had a urinary tract infection, and 2 had catheter-related infections. The incidence of infection was 15.0% in the low PNI group, which was significantly higher than that in the high PNI group (P=0.026). The number of patients with noninfectious complications was also significantly higher in the low PNI group (P=0.029), although there was no statistical difference in the composition ratio of infected cases (P>0.05).

Microbiological specimens were collected for culture in 92 cases (91.1%), among which 77 (83.7%) were culture positive. A total of 82 pathogenic strains were identified, including 56 strains of gram-negative bacteria (68.3%), most of which were *Escherichia coli*; 23 strains of gram-positive bacteria (28.0%), most of which were *Enterococcus faecalis*; and 3 strains of fungi (3.7%), all of which were *Candida albicans* (*Table 4*).

Risk factors for infection in patients after radical surgery for GC

In the univariate analysis (*Table 5*), age ≥65 years (P=0.037), BMI ≥25 kg/m^2 (P=0.031), smoking (P=0.048), diabetes mellitus (P=0.023), low PNI value (P=0.026), combined multi-organ resection (P=0.017), operation time ≥240 minutes (P=0.009), blood loss ≥200 mL (P=0.011), and perioperative blood transfusion (P=0.021) were associated with the occurrence of infection after radical surgery for GC. Further multivariate logistic regression analysis (*Table 6*) showed that BMI ≥25 kg/m^2 (P=0.004), diabetes mellitus (P=0.042), PNI value <45 (P=0.037), combined multi-organ resection (P<0.001), operation time ≥240 minutes (P=0.023), and perioperative blood transfusion (P=0.025) were risk factors for infection after radical surgery for GC.

Discussion

Radical gastrectomy is the mainstay of curative treatment for GC. Most patients with early-stage GC and 40–50% of patients with advanced GC can be treated with

Table 1 Clinicopathological data in the 2 groups before matching

Variables	All	Low PNI	High PNI	P
n	1,111	451	660	
Age, years	63.8±9.4	64.5±9.1	63.2±9.7	0.025
Gender, male, n (%)	693 (62.4)	293 (65.0)	400 (60.6)	0.141
BMI, kg/m^2	22.4±2.6	22.2±2.6	22.6±2.7	0.014
ASA classification, n (%)				
I	102 (9.2)	44 (9.8)	58 (8.8)	0.035
II	826 (74.3)	318 (70.5)	508 (77.0)	
III	183 (16.5)	89 (19.7)	94 (14.2)	
Smoking, n (%)	478 (43.0)	208 (46.1)	270 (40.9)	0.085
Previous surgical history, n (%)	179 (16.1)	65 (14.4)	114 (17.3)	0.203
Neo-adjuvant chemotherapy, n (%)	78 (7.0)	28 (6.2)	50 (7.6)	0.381
Tumor location, n (%)				
Upper	201 (18.1)	89 (19.7)	112 (17.0)	0.079
Middle	240 (21.6)	108 (23.9)	132 (20.0)	
Lower	670 (60.3)	254 (56.3)	416 (63.0)	
Tumor stage, n (%)				
I	464 (41.8)	173 (38.4)	291 (44.1)	0.015
II	346 (31.1)	135 (29.9)	211 (32.0)	
III	301 (27.1)	143 (31.7)	158 (23.9)	
Differentiation, n (%)				
Well	207 (18.6)	68 (15.1)	139 (21.1)	0.011
Moderate	446 (40.1)	177 (39.2)	269 (40.8)	
Poor	458 (41.2)	206 (45.7)	252 (38.2)	
Pre-operative measurements				
White blood cell count, ×10^9/L	6.27±2.4	6.19±2.6	6.48±2.1	0.041
Albumin, g/L	37.5±4.4	35.2±4.9	39.3±3.6	<0.001
Hemoglobin, g/L	118.0±25.8	111.3±26.8	124.1±22.4	<0.001
Lymphocyte count, ×10^9/L	1.74±0.6	1.51±0.5	1.96±0.6	<0.001
Tumor size, mm	49.5±27.4	51.2±26.6	47.6±27.9	0.032
Operation modality, n (%)				
Laparoscopy	662 (59.6)	288 (63.9)	374 (56.7)	0.016
Laparotomy	449 (40.4)	163 (36.1)	286 (43.3)	
Type of resection, n (%)				
Subtotal	775 (69.8)	296 (65.6)	479 (72.6)	0.043
Total	257 (23.1)	117 (25.9)	140 (21.2)	
Combined multi-organ resection	79 (7.1)	38 (8.4)	41 (6.2)	
Operation time, min	248.4±63.6	253.5±60.6	244.7±65.4	0.023
Intra-operative blood loss, mL	210.4±132.1	217.4±146.2	198.7±118.1	0.019

PNI, prognostic nutritional index; BMI, body mass index; ASA, American Society of Anesthesiologists.

Table 2 Clinicopathological data in the 2 groups after matching

Variables	All	Low PNI	High PNI	P
n	812	406	406	
Age, years	63.6±9.2	64.1±9.4	63.0±8.9	0.087
Gender, male, n (%)	543 (66.9)	268 (66.0)	275 (67.7)	0.602
BMI, kg/m^2	21.5±2.3	21.8±2.5	22.1±2.2	0.070
ASA classification, n (%)				
I	79 (9.7)	42 (10.3)	37 (9.1)	0.119
II	595 (73.3)	285 (70.2)	310 (76.4)	
III	138 (17.0)	79 (19.5)	59 (14.5)	
Smoking, n (%)	360 (44.3)	188 (46.3)	172 (42.4)	0.258
Previous surgical history, n (%)	125 (15.4)	57 (14.0)	68 (16.7)	0.285
Neo-adjuvant chemotherapy, n (%)	51 (6.3)	24 (5.9)	27 (6.7)	0.770
Tumor location, n (%)				
Upper	152 (18.7)	79 (19.5)	73 (18.0)	0.083
Middle	177 (21.8)	100 (24.6)	77 (19.0)	
Lower	483 (59.5)	227 (55.9)	256 (63.0)	
Tumor stage, n (%)				
I	313 (38.5)	147 (36.2)	166 (40.9)	0.062
II	248 (30.5)	118 (29.1)	130 (32.0)	
III	251 (30.9)	141 (34.7)	110 (27.1)	
Differentiation, n (%)				
Well	130 (16.0)	57 (14.0)	73 (18.0)	0.124
Moderate	326 (40.1)	158 (38.9)	168 (41.4)	
Poor	356 (43.8)	191 (47.0)	165 (40.6)	
Pre-operative detection				
White blood cell count, ×10^9/L	6.24±2.0	6.16±2.3	6.35±1.8	0.190
Albumin, g/L	37.3±4.2	34.6±4.8	39.1±3.4	<0.001
Hemoglobin, g/L	116.0±23.5	110.7±26.3	121.6±20.9	<0.001
Lymphocyte count, ×10^9/L	1.77±0.6	1.48±0.5	2.07±0.7	<0.001
Tumor size, mm	50.5±27.8	51.6±26.3	48.4±28.1	0.094
Operation method, n (%)				
Laparoscopy	504 (62.1)	264 (65.0)	240 (59.1)	0.083
Laparotomy	308 (37.9)	142 (35.0)	166 (40.9)	
Type of resection, n (%)				
Subtotal	545 (67.1)	265 (65.3)	280 (69.0)	0.290
Total	197 (24.3)	108 (26.6)	89 (21.9)	
Combined multi-organ resection	70 (8.6)	33 (8.1)	37 (9.1)	
Operation time, min	253.7±64.5	250.9±61.2	257.6±68.0	0.140
Intra-operative blood loss, mL	207.2±129.6	215.4±147.3	202.5±114.8	0.164

PNI, prognostic nutritional index; BMI, body mass index; ASA, American Society of Anesthesiologists.

Table 3 Distribution of infections after radical surgery for GC in patients with different PNI scores

Variables	All	Low PNI	High PNI	P
n	812	406	406	
Noninfectious complications, n (%)	37 (4.6)	25 (6.2)	12 (3.0)	0.029
Infection, n (%)	101 (12.4)	61 (15.0)	40 (9.9)	0.026
Intra-abdominal infection	46 (5.7)	28 (6.9)	18 (4.4)	0.767
Pneumonia	27 (3.3)	17 (4.2)	10 (2.5)	
Wound infection	25 (3.1)	15 (3.7)	10 (2.5)	
Urinary tract infection	1 (0.1)	0	1 (0.2)	
Catheter-related infections	2 (0.2)	1 (0.2)	1 (0.2)	

GC, gastric cancer; PNI, prognostic nutritional index.

Table 4 Composition ratio of pathogenic bacteria isolated from patients experiencing infections after radical surgery for GC

Pathogens	Number of strains	Constituent ratio (%)
n	82	100.0
Gram-negative	56	68.3
Escherichia coli	25	30.5
Klebsiella pneumonia	14	17.1
Pseudomonas aeruginosa	10	12.2
Enterobacter cloacae	4	4.9
Acinetobacter baumannii	2	2.4
Proteus mirabilis	1	1.2
Gram-positive	23	28.0
Enterococcus	11	13.4
Staphylococcus aureus	8	9.8
Staphylococcus haemolyticus	2	2.4
Staphylococcus epidermidis	2	2.4
Fungus	3	3.7
Candida albicans	3	3.7

GC, gastric cancer.

radical resection. However, radical resection for GC is a complicated and time-consuming procedure with a high rate of postoperative infection. Postoperative infection poses a significant financial burden on patients and affects postoperative recovery; therefore it is clinically important to identify its risk factors (18). Many recent studies have demonstrated that the nutritional and immunological status of the human body is closely related to postoperative infection in a variety of diseases, and the value of nutritional assessment in oncology patients has increasingly been recognized (19,20). Many nutritional screening/assessment tools are available, including the Nutritional Risk Screen 2002, the Mini-Nutritional Assessment, and the Subjective Global Assessment. However, these tools are often cumbersome and susceptible to subjective factors, which may lead to less accurate results (21).

PNI is an objective nutritional assessment tool that is easily calculated based on the serum ALB concentration and the peripheral blood lymphocyte count. Serum ALB, which is synthesized by the liver, maintains colloid osmotic pressure and nutritional metabolism, and its level reflects the nutritional status of the body (22). Peripheral blood lymphocytes are involved in the destruction and apoptosis of tumor cells and thus constitute a critical component of anti-tumor immunity. A lower lymphocyte count suggests a decrease in the body's anti-tumor immune function (23). Early studies have found that PNI value has potential as a prognostic marker of colorectal cancer, as patients with low PNI values tend to have poor long-term prognosis (14-16) Sakurai *et al.* (24) showed that PNI was useful in predicting prognosis and immunological and nutritional status in patients with GC, and that a PNI of <45 was predictive of anastomotic edema and peritoneal effusion. Although many studies have evaluated the role of PNI in patients with gastrointestinal (GI) cancer, most have focused on the prognostic value of PNI, with few studies analyzing the impact of PNI value on postoperative infection. In addition, baseline clinical features often differ among patients with different PNI scores. Thus, PSM analysis was adopted in this study to avoid potential confounding variables. Based

Table 5 Univariate analysis of infections after radical surgery for GC after matching

Variables	Subgroups	Infection	Non-infection	χ^2	P
n	812	101	711		
Age, years	≥65/<65	34/67	171/540	4.330	0.037
Gender	Male/female	72/29	471/240	1.015	0.314
BMI, kg/m^2	≥25/<25	16/85	64/647	4.659	0.031
ASA score	III/I–II	23/78	115/596	2.729	0.099
Smoking	Yes/no	54/47	306/405	3.896	0.048
Diabetes	Yes/no	16/85	62/649	5.165	0.023
Hypertension	Yes/no	11/90	49/662	2.067	0.151
Heart disease	Yes/no	5/96	24/687	0.637	0.425
Chronic liver disease	Yes/no	15/86	114/597	0.093	0.761
White blood cell count, ×10^9/L	≥4/<4	94/7	647/64	0.475	0.491
Albumin, g/L	≥35/<35	69/32	533/178	2.039	0.153
Hemoglobin, g/L	≥100/<100	70/31	540/171	2.088	0.148
Lymphocyte count, ×10^9/L	≥1.5/<1.5	52/49	405/306	1.078	0.299
Operation method	Open/laparoscopic-assisted	46/55	262/449	2.840	0.092
Type of resection	Subtotal/total	60/29	485/168	1.888	0.169
Combined multi-organ resection	Yes/no	15/86	55/656	5.685	0.017
PNI	≥45/<45	40/61	366/345	4.987	0.026
Tumor stage	III/I–II	36/29	215/241	1.210	0.271
Operation time, min	≥240/<240	41/60	199/512	6.749	0.009
Intra-operative blood loss, mL	≥200/<200	42/59	207/504	6.468	0.011
Perioperative blood transfusion	Yes/no	30/71	140/571	5.356	0.021

GC, gastric cancer; BMI, body mass index; ASA, American Society of Anesthesiologists; PNI, prognostic nutritional index.

Table 6 Multivariate logistic analysis of infections after radical surgery for GC after matching

Variables	OR	95% confidence interval	P
Age ≥65 years	1.752	0.497–6.187	0.375
BMI ≥25 kg/m^2	2.314	1.557–3.438	0.004
Diabetes	1.827	1.039–3.213	0.042
Smoking	1.763	0.969–2.296	0.061
PNI score <45	2.138	1.077–4.246	0.037
Combined multi-organ resection	2.946	1.589–5.462	<0.001
Operation time ≥240 min	2.744	1.253–6.010	0.023
Blood loss ≥200 mL	1.682	0.768–3.684	0.218
Peri-operative blood transfusion	2.595	1.117–6.028	0.025

GC, gastric cancer; OR, odds ratio; BMI, body mass index; PNI, prognostic nutritional index.

on dimensionality reduction algorithms, PSM incorporates the information provided by multiple confounding factors into 1 propensity score and then stratifies, matches, or weights individuals from different comparison groups based on the propensity score to improve the balance of variables among nonrandomized groups. This method has been widely used in observational and nonrandomized studies. In our study, there were significant differences in the mean age, BMI, ASA score, tumor grade, tumor differentiation, surgical modality, and type of resection between the high and low PNI groups before matching, making a comparison of infection rates unfeasible. After matching, there were no significant differences in preoperative baseline data between these 2 groups (except for ALB level, hemoglobin level, and lymphocyte count), thus improving comparability.

Malnutrition leads to prolonged wound healing and altered immune function, both of which are associated with the occurrence of postoperative infections. In our study, postoperative infections occurred in 101 of 812 patients with GC. The most common infections were abdominal infection, pulmonary infection, surgical site infection, and urinary tract infection, which was consistent with the distribution of postoperative infection sites in patients with GC reported by Cai *et al.* (25). After one-to-one matching, we found that the incidence of infection was significantly higher in the low PNI group than in the high PNI group, suggesting that PNI can identify patients at high risk for postoperative infection. Our study also showed that the pathogenic bacteria were predominantly gram-negative bacteria, among which *Escherichia coli* was the most common pathogen, which may be related to the opening of the GI tract during the surgery. In a study of a large cohort of patients undergoing radical treatment for GC in China, the most common pathogens of abdominal infection after radical surgery were *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococci*, and *Candida albicans* (26). This was similar to our findings. Many studies suggest that infections after radical surgery for GC are often caused by multidrug-resistant strains (2). Therefore, antimicrobial drugs must be applied rationally to reduce the occurrence of infection in clinical settings.

Infections after radical surgery for GC can be caused by multiple risk factors, which vary somewhat among different studies depending on the disease characteristics, surgical modality, and underlying conditions. The reported risk factors include diabetes mellitus, long operation time, perioperative blood transfusion, intraoperative blood loss, combined multi-organ resection, and high BMI (27-30). The univariate analysis in our current study showed that age ≥65 years, BMI ≥25 kg/m^2, diabetes mellitus, low PNI value, combined multi-organ resection, operation time ≥240 minutes, blood loss ≥200 mL, and perioperative blood transfusion were risk factors. Further multivariate analyses identified BMI ≥25 kg/m^2, diabetes mellitus, PNI score <45, combined multi-organ resection, operation time ≥240 minutes, and intra-operative blood loss as risk factors. The risk of postoperative infection was significantly higher in GC patients with a BMI of ≥25 kg/m^2 compared to that in patients with a normal BMI, probably due to the poor surgical exposure and long operation time in patients with obesity, as well as the high incidence of chronic diseases like diabetes and hypertension in such patients (31). According to Wang *et al.* (32), diabetes mellitus is an important risk factor for abdominal infection after radical surgery for GC because diabetic patients have more hyperactive catabolism and impaired protein synthesis, which results in poor healing of anastomosis and incision and thus high incidence rates of complications such as incisional infection and pulmonary infection. The development of surgical techniques has lowered the proportion of patients requiring blood transfusion during surgery, although some patients still require a blood transfusion to improve their anemic condition. However, as shown by Xu *et al.* (33), allogeneic blood transfusion mediates immunosuppression and impairs immune function, leading to the development of postoperative inflammatory reactions. Low PNI is a risk factor for infection after radical surgery for GC, which can be attributed to the following two reasons. First, reduced serum ALB level and decreased or insufficient activities of antibody synthetases contribute to decreased immunity and a high rate of infections (34,35). Second, lymphocytes are the prime movers of the immune system, and a low lymphocyte count indicates an inadequate immune response to a tumor. Therefore, based on the PNI score, clinicians may assess the risk of infection after radical surgery for GC, develop an intervention plan, and monitor the implementation of the plan. Patients with a PNI score of <45 can be actively treated with nutritional and immune interventions to reduce the incidence of postoperative infection.

Our current study has some limitations, including a retrospective, single-center design and possible selection bias. The negative impact of low preoperative PNI score on infection needs to be further validated in prospective studies.

In conclusion, infection is the most common complication after radical surgery for GC, with gram-

negative bacteria being the most common pathogens. The rate of postoperative infection is higher in patients with low PNI values, and PNI <45 is a risk factor for postoperative infection. Therefore, appropriate nutritional interventions can be given for patients with low-PNI, thus reducing the incidence of postoperative infection.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-192/rc

Data Sharing Statement: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-192/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-192/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the ethics committee of Minhang Hospital, Fudan University (2021-012-01K). Informed consent was taken from all the patients.

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