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Original Article

Systemic immunoinflammatory index and prognostic nutrition index for predicting pathologic responses of patients with advanced gastric cancer after neoadjuvant therapy for advanced gastric cancer

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Abstract: To investigate the value of prognostic nutrition index (PNI) and systemic immunoinflammatory index (SII) for predicting pathological responses of patients with advanced gastric cancer (GC) after neo-adjuvant chemotherapy (NACT). The clinicopathological data of 326 patients with advanced GC who received NACT in Xiangya School of Medicine, Central South University (The First People's Hospital of Changde City) from January 2017 to December 2021 were retrospectively collected. The SII and PNI of patients were calculated. The receiver operating characteristics (ROC) curve was leveraged for getting the optimal cutoff values of SII and PNI. The pathological response of patients after NACT, as obtained from their postoperative pathological examinations, was evaluated based on the tumor regression grade (TRG) criteria. Multivariate regression analysis was employed for identifying factors that led to various pathological responses after NACT in advanced GC patients. The log-rank test was utilized for between-group comparison of patients' survival curves. The SII and PNI were 507.45 and 48.48 respectively, and their levels were divided into high and low groups. Pathological response (TRG 0-1) was observed in 66 cases (20.25%), while non-pathological response (TRG 2-3) was observed in 260 cases (79.75%). The results of multivariate logistic regression analysis showed that tumor diameter < 5 cm, ypT T0-T2, ypN N0, chemotherapy regimen XELOX (capecitabine combined with oxaliplatin), SII < 507.45 (P=0.002), PNI > 48.48 were all independent factors affecting the pathological responses of advanced GC patients after NACT (all P < 0.05). With SII and PNI being included, the AUC was 0.821 (95% CI: 0.765-0.876), and the specificity was 87.90% and the sensitivity was 64.20%. The Kaplan-Meier survival curve analysis showed that NACT patients with tumor diameter < 5 cm, ypT T0-T2, ypN N0, XELOX chemotherapy regimen, SII < 507.45 and SII ≥ 507.45 had a higher survival rate. (P < 0.001). Before treatment, tumor diameter < 5 cm, ypT T0-T2, ypN N0, chemotherapy regimen XELOX, SII < 507.45, PNI > 48.48 were all independent factors affecting the pathological response of advanced GC patients after NACT. Moreover, the inclusion of SII and PNI increased the accuracy of predicting the pathological response of patients after NACT.

Keywords: Advanced gastric cancer, neo-adjuvant chemotherapy, pathological response, prognostic nutritional index, systemic inflammatory index

Introduction

Gastric cancer (GC) is one of the most common highly heterogeneous tumor diseases worldwide. According to statistics, there will be over 1 million new cases of GC globally in 2020, with approximately 769,000 deaths, ranking its morbidity and mortality among various cancer in the world at 5th and 4th respectively [1]. Compared to women, men have a higher incidence of GC. Due to hard-to-detect nature of GC, it is challenging for the majority of patients to notice their clinical symptoms before the disease progresses into severe, and many patients are diagnosed at the advanced or even terminal stage, resulting in a frequently poor prognosis [2, 3].

At present, the treatments for GC encompass surgical resection, neo-adjuvant chemotherapy (NACT), radiotherapy, immunotherapy and targeted therapy [4]. However, the survival rate of

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patients with locally advanced GC remains low after regional lymph node dissection/radical surgical resection. As NACT is capable of degrading the tumor and enhancing the R0 resection rate, its clinical application is on the rise day by day. A 2018 clinical meta-review indicated that NACT combined with radical surgical resection reduced the recurrence rate of tumors and effectively lowered the mortality of patients at 1, 3, and 5 years post-treatment (Risk Ratio: 0.78, 0.81, 0.88, respectively) [5]. The underlying mechanism might be that the use of chemotherapy before surgery can shrink tumor size, optimize tumor stage, prevent mild tumor cell metastases in the body, and provide patients with an opportunity to receive radical resection [6, 7]. Additionally, studies have confirmed that NACT can effectively enhance the remission rate of patients with tumors and increase their chance to undergo surgery, with higher safety and prolonged survival rate [8, 9]. Several studies have shown that patients receiving NACT have better OS (overall survival) and PFS (progression-free survival) [10, 11]. At present, NACT has emerged as a crucial component of the standardized treatment regimen for advanced GC. However, due to the significant individual differences, there are still some patients who cannot present ideal pathological response after NACT. Hence, identifying factors to predict pathological responses of patients to chemotherapy for tumors and offering individualized treatment so as to improve patients' prognosis has become a hot research topic over recent years.

The inflammatory response within the host and the characteristics of tumors themselves play an important role in their progression, which might influence the pathological response of patients after NACT by affecting the microenvironment around the tumors, especially the systemic inflammatory response and the nutritional status within the body [12, 13]. Studies have shown that the increase in indexes that reflect systemic inflammatory response such as systemic immunoinflammatory index (SII) indicates poor prognosis in patients [14-17]. PNI is a comprehensive indicator showing immune and nutritional status in patients, which is also capable of predicting and evaluating the prognosis of patients with digestive tract malignant tumors [18]. Takao et al. [19] studied the correlation between PNI and the prognosis of 263 patients with esophageal squamous cell carcinoma who received NACT combined with radical surgical resection, and found that the PNI of patients post-NACT was higher than that of theirs pre-NACT, accompanied by better improvement in their prognosis as PNI increased. It was found that PNI was an independent risk factor affecting the prognosis of GC patients. At present, there have been studies on the relationship between SII and PNI and the prognosis and survival of GC patients undergoing NACT, but their clinical application value is still controversial. Therefore, the purpose of this study was to explore the prediction effect of SII and PNI on the pathological response of patients with advanced GC after NACT.

Materials and methods

Case selection

The clinicopathological data of 326 patients with advanced GC who received NACT in Xiangya School of Medicine, Central South University (The First People's Hospital of Changde City) from January 2017 to December 2021 were retrospectively collected.

Inclusion criteria: patients were eligible for the study if they had advanced GC confirmed by pathological examinations; they had undergone NACT for 2 to 4 cycles; their tumors showed no distant or peritoneal metastasis; they were performed with radical surgical resection after the completion of NACT; they had received no other treatments for the tumor before being enrolled; they underwent post-operative pathological biopsy, and their pathological data and follow-up data were complete.

Exclusion criteria: patients were excluded from the study if their physical conditions did not fit for the surgery; they had recurrent GC or other kinds of malignant tumors; they had hematological tumors, hepatitis and autoimmune related diseases; they had undergone other anti-tumor therapies, including radiotherapy, targeted therapy and immunotherapy, instead of NACT prior to surgery; they underwent emergency surgery due to gastrointestinal perforation bleeding.

This study was approved by the Ethics Committee of the Xiangya School of Medicine, Central South University (The First People's

Hospital of Changde City) (Approval number: 2024-086-01).

SII and PNI calculation methods

Peripheral venous blood was collected from all patients on an empty stomach within 1 week before NACT. Peripheral blood neutrophils, lymphocytes, and platelets were measured using an automated blood analyzer (Beckman Coulter LH750, USA). Peripheral blood albumin levels were measured using an automated blood analyzer (Beckman Coulter AU5800, USA). SII = platelet count × neutrophil/lymphocyte; PNI = albumin value + 5× lymphocytes.

Data collection

The general data of GC patients, including age, sex, smoking habit, alcohol consumption, chemotherapy regimen [SOX (S-1 combined with oxaliplatin) or XELOX (capecitabine combined with oxaliplatin)] and so on were collected and analyzed. The pathological data of the enrolled patients, such as tumor size, tumor location, degree of tumor cell differentiation, Lauren classification, Borrmann classification, ypT, ypN, vascular invasion, the number of lymph node metastasis, tumor regression grade (TRG), were collected and analyzed as well. The information of what kind of surgery, either partial or total gastrectomy, of the enrolled patients was determined, too.

Follow-up

The survival time of patients was obtained by telephone follow-up, and all patients were followed up for two years (until December 2023). In this study, the factors influencing pathological response after new NACT in advanced GC patients were the main outcome, and survival analysis was the secondary outcome.

Efficacy evaluation

According to the results of postoperative pathological examinations, the pathological response of patients was assessed based on the TRG criteria [20]: (1) TRG 0 was defined as a pathological complete response (pCR), that is, the complete regression of the tumor with no tumor cells visible under the microscope. (2) TRG 1 was defined as a moderate response, that is, only single or small focal cancer cells observed under the microscope. (3) TRG 2 was defined as a mild response, that is, the tumor had significant regression but a certain number of tumor cells remained. (4) TRG 3 was defined as the observation of extensive residual cancer cells, indicating an adverse reaction. The pathological response of patients after NACT was between TRG 0 and 1, indicating that patients' tumor presented a good response to treatment. TRG 2 and 3 indicated a poor response from patients after NACT, meaning patients had non-pathological response (non-pCR).

Statistical method

SPSS version 29.0 was used for statistical analysis in the study. The cutoff values of SII and PNI were calculated by ROC curve analysis. The area under the ROC curve (AUC) was employed to evaluate the predictive values and identify the optimal cutoff values of SII and PNI. The classification data and n (%) were described by χ^2 test. Multivariate logistic regression analysis was performed to analyze the pathological response after NACT. Differences in survival curves between groups were compared using the Log-Rank test, and statistical significance was set at $P < 0.05$.

Results

Clinical data

The clinicopathological data of 358 patients with advanced GC admitted to our hospital from January 2017 to December 2021 were included. Thirty-two cases were excluded because 10 were not treated with NACT. Remote metastasis and peritoneal metastasis were found in 8 GC patients. Five patients did not receive radical surgical resection after NACT. Four patients had received radiotherapy or combined with chemoradiotherapy or targeted therapy before this treatment. The pathological data and follow-up data of 5 patients were missing. A total of 326 cases meeting the inclusion criteria were screened out as study subjects, whose clinicopathological characteristics were shown in **Figure 1** and **Table 1**.

The cutoff values of SII and PNI

According to the ROC curve, the cutoff values of SII and PNI corresponding to the maximum Jorden index were 507.45 and 48.48, respectively. See **Figure 2**.

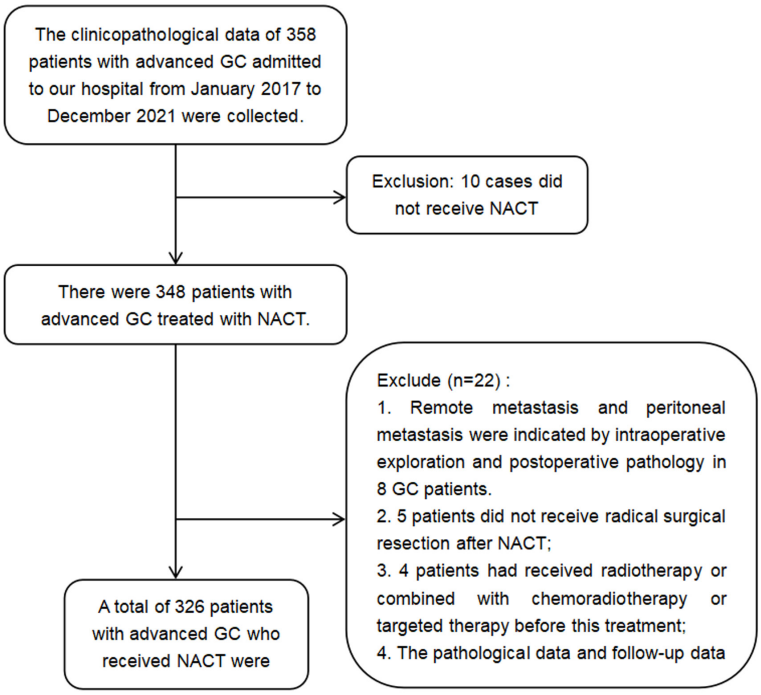

Figure 1. Patient screening process. GC: gastric cancer; NACT: neo-adjuvant chemotherapy.

Table 1. Clinicopathological features of the enrolled patients

Variable	Group	N (%)
Sex		
Male	199	61.04
Female	127	38.96
Age (years)		
≥ 60	160	49.08
< 60	166	50.92
Smoking		
Yes	144	44.17
No	182	55.83
Drinking		
Yes	76	23.31
No	250	76.69
Tumor site		
Antrum of stomach	138	42.33
Body of stomach	128	39.26
Cardia fundus	60	18.40
Tumor size (cm)		
< 5	157	48.16
≥ 5	169	51.84
Degree of tumor cell differentiation		
Poorly differentiated	199	61.04
Moderately differentiated	116	35.58
Highly differentiated	11	3.37

Univariate analysis of factors influencing pathological responses of patients with advanced GC after NACT

According to the results of the univariate analysis, 30 GC patients out of the 326 (9.20%) were in TRG 0, 36 (11.04%) in TRG 1, 131 (40.18%) in TRG 2, and 129 (39.57%) in TRG 3. Therefore, 66 patients (20.25%) whose TRG were 0 and 1 were considered having presented pathological response and 260 patients whose TRG were 2 and 3 (79.75%) presented otherwise results. No significant differences were identified between the pathological response of patients with advanced GC after NACT and their gender (P=0.841), age (P=0.914), smoking habits (P=0.381), alcohol consumption (P=0.239), tumor site (P=0.050), degree of tumor cell differentiation (P=0.645), Borrmann classification (P=0.299), Lauren classification (P=0.646), vascular invasion degree (P=0.107) and operation type (P=0.401). Before treatment, tumor size < 5 cm (P=0.002), ypT (P < 0.001), ypN (P=0.025), chemotherapy regimen (P=0.001), SII (P=0.002) and PNI (P < 0.001) were all associated with a low pathological response rate of patients with advanced GC after NACT. See **Table 2**.

Multivariate logistic regression analysis of factors influencing pathological responses of advanced GC patients after NACT

Before treatment, tumor size < 5 cm, ypT T0-T2, ypN N0, the application of chemotherapy regimen XELOX, SII < 507.45

Borrmann typing		
I Type	15	4.60
II Type	82	25.15
III Type	212	65.03
IV Type	17	5.21
Lauren typing		
Intestinal pattern	114	34.97
Diffuse type	116	35.58
Mixed type	96	29.45
ypT		
T0-T2	145	44.48
T3-T4	181	55.52
ypN		
N0	143	43.87
N1-N3	183	56.13
Vascular invasion		
Yes	125	38.34
No	201	61.66
Chemotherapy regimen		
SOX	201	61.66
XELOX	125	38.34
Operation		
Partial gastrectomy	91	27.91
Total gastrectomy	235	72.09
Pathological response	199	61.04
Pathological response	127	38.96
Nonpathological response		

Note: NACT: neo-adjuvant chemotherapy.

(P=0.002), and PNI > 48.48 were all independent factors affecting the pathological responses of patients with advanced GC after NACT (all P < 0.05). See **Table 3**.

The effects of SII and PNI on predicting pathological responses in patients with advanced GC after NACT

A prediction model was constructed in accordance with indexes listed in **Table 3** for forecasting pathological responses of patients with advanced GC. Without counting SII and PNI in, the AUC of the prediction model was 0.734 (95% CI: 0.664-0.803), and the specificity and sensitivity were 71.20% and 71.50%, respectively. However, after taking SII and PNI into consideration, the AUC of the prediction model was 0.821 (95% CI: 0.765-0.876), and the specificity and sensitivity were 87.90% and 64.20%, respectively, suggesting that the addition of SII and PNI effectively improved the predictive validity of pathological responses in patients with advanced GC after NACT. See **Table 4** and **Figure 3**.

Survival analysis

All patients were followed up for two years. During the follow-up, 5 deaths were reported in the pCR group and 73 deaths in the non-pCR group. The Kaplan-Meier survival curve analysis showed that the survival time of patients with tumor size < 5 cm was longer than that of patients with tumor size ≥ 5 cm (P=0.005; **Figure 4A**); The survival time of ypT patients with T0-T2 was longer than that of ypT patients with T3-T4 (P=0.040; **Figure 4B**); The survival time of patients with ypN N0 was longer than that with ypN T1-T3 (P=0.036; **Figure 4C**); The survival time of patients undergoing chemotherapy regimen XELOX was longer than that of patients receiving SOX (P= 0.007; **Figure 4D**); The survival time of patients whose SII < 507.45 was longer than that of patients whose SII ≥ 507.45 (P < 0.001; **Figure 4E**); The survival time of patients whose PNI > 48.48 was longer than that of patients whose PNI ≤ 48.48 (P=0.044; **Figure 4F**).

Discussion

At present, the treatment of advanced GC remains a comprehensive approach based on multidisciplinary collaboration [21]. NACT can reduce the treatment duration, enhances the rate of radical resection, eliminate tumor metastases and improve the long-term survival rate of patients, while postoperative chemotherapy or radiotherapy can minimize postoperative recurrence and significantly improve the prognosis of patients [22, 23]. At present, there is no unified standard for evaluating the efficacy of GC patients after NACT, and their prognosis is the ultimate objective in assessing the effectiveness of adjuvant therapy. However,

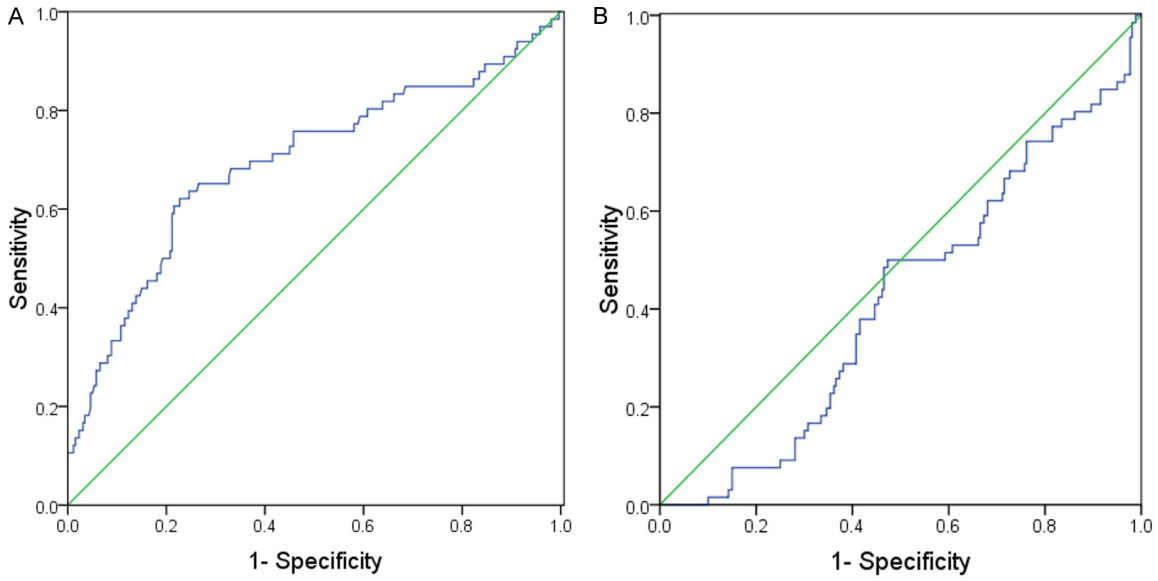

Figure 2. The selection of cutoff values of SII and PNI. A. ROC curve corresponding to SII; B. ROC curve corresponding to PNI. SII: systemic immunoinflammatory Index; PNI: prognostic nutritional index.

Table 2. Univariate analysis of factors influencing pathological responses of patients with advanced GC after NACT

Factors	Pathological response		χ^2	P
	Yes (n=35)	No (n=65)		
Sex			0.040	0.841
Male	41 (62.12)	158 (60.77)		
Female	25 (37.88)	102 (39.23)		
Age (years)			0.012	0.914
≥ 60	32 (48.48)	128 (49.23)		
< 60	34 (51.52)	132 (50.77)		
Smoking			0.766	0.381
Yes	26 (39.39)	118 (45.38)		
No	40 (60.61)	142 (54.62)		
Drinking			1.388	0.239
Yes	19 (27.79)	57 (21.92)		
No	47 (71.21)	203 (78.08)		
Tumor site			5.994	0.050
Antrum of stomach	20 (30.30)	118 (45.38)		
Body of stomach	34 (51.52)	94 (36.15)		
Cardia fundus	12 (18.18)	48 (18.46)		
Tumor size (cm)			9.570	0.002
< 5	43 (65.15)	114 (43.85)		
≥ 5	23 (34.85)	146 (56.15)		
Degree of cell differentiation			0.878	0.645
Poorly differentiated	41 (62.12)	92 (35.38)		
Moderately differentiated	24 (36.36)	158 (60.77)		
Highly differentiated	1 (1.52)	10 (3.85)		

accurate prognosis assessment requires a prolonged follow-up, with continuous periodic efficacy evaluations throughout the entire GC treatment process, to make informed decisions for subsequent treatment. Therefore, the evaluation of NACT efficacy may be beneficial in the selection of postoperative chemotherapy regimen.

Following adjuvant therapy, tumors often show pathological morphological changes, such as degeneration, necrosis, tissue fibrosis and inflammatory cell infiltration. TRG, also known as pathological response grade, is a therapeutic evaluation standard for assessing the pathological morphological changes after adjuvant therapy. It is commonly employed to evaluate the efficacy of preoperative radiotherapy, chemotherapy, and targeted therapy for tumors, and assess patients'

Borrmann typing			3.670	0.299
I Type	5 (5.71)	10 (4.62)		
II Type	20 (31.43)	26 (23.08)		
III Type	39 (60.00)	173 (67.69)		
IV Type	2 (2.86)	15 (4.62)		
Lauren typing			0.874	0.646
Intestinal pattern	20 (30.30)	94 (36.15)		
Diffuse type	26 (39.39)	90 (34.62)		
Mixed type	20 (30.30)	76 (29.23)		
ypT			12.299	< 0.001
T0-T2	42 (63.64)	103 (39.62)		
T3-T4	24 (36.36)	157 (60.38)		
ypN			4.999	0.025
N0	37 (56.06)	106 (40.77)		
N1-N3	29 (43.94)	154 (59.23)		
Vascular invasion			2.605	0.107
Yes	31 (46.97)	94 (36.15)		
No	35 (53.03)	166 (63.85)		
Chemotherapy regimen			10.273	0.001
SOX	14 (97.14)	111 (95.38)		
XELOX	52 (2.86)	149 (4.62)		
Operation			0.706	0.401
Partial gastrectomy	14 (21.21)	77 (29.62)		
Total gastrectomy	52 (78.79)	183 (70.38)		
SII			10.006	0.002
≤ 507.45	60 (90.91)	188 (72.31)		
> 507.45	6 (9.09)	72 (27.69)		
PNI			38.482	< 0.001
≤ 48.48	25 (37.88)	201 (77.31)		
> 48.48	41 (62.12)	59 (22.69)		

Notes: NACT: neo-adjuvant chemotherapy; SII: systemic immunoinflammatory Index; PNI: prognostic nutritional index.

prognosis [24, 25]. However, compared with tumors such as breast cancer and colorectal cancer, the pCR rate of GC after NACT is lower [26, 27]. A domestic meta-analysis showed that despite perioperative, operation-centered comprehensive treatment being considered the standard of care for locally advanced GC, the average pCR rate across 7 comparable studies was 6.74%, with a range from 3% to 15% [28]. Patients who failed to meet the pCR target tended to have advanced tumor stages, display low or even non-responsive sensitivity to the chemotherapy regimen, and exhibit low tumor cell differentiation. In this study, 9.20% was in TRG 0, 20.25% showed a pathological response. These results conformed to previous clinical studies, which found differences in pathological response rates between different study groups as well as between different study programs. Therefore, this study underscores the importance of devising tailored treatment programs for diverse patients groups to enhance their pathological responses. Identifying effective predictors for assessing post-NACT pathological response, by administering specific NACT regimens tailored to distinct patients populations, holds paramount significance.

Becker et al. [29] analyzed the clinical data of 480 patients with advanced GC, and found that age and gender had nothing to do with the efficacy of NACT, and the tumor located in the upper 1/3 of the stomach and intestinal type gastric cancer were more likely to achieve good treatment efficacy. In addition, it was reported that [30] tumor size and degree of tumor differentiation are closely related to the efficacy of NACT for patients with advanced GC. The results of this study found that tumor size < 5 cm, ypT T0-T2, ypN N0, the application of chemotherapy regimen XELOX, SII < 507.45, PNI > 48.48 before treatment were all independent factors affecting the pathological response of patients with advanced GC after NACT. It can be seen that patients with small lesions and in early disease stage exhibit a great likelihood of achieving pCR and favorable pathological responses, which is consistent with the concept of radical radiotherapy for esophageal cancer. A European study on the effect of surgical interval time on pCR rate and surgery-related safety of esophagogastric junction cancer after concurrent chemoradiotherapy [31] showed that 906 of 3 091 (29%) patients realized pCR, suggesting that pCR rate was mainly related to tumor type, surgery, duration of synchronous chemoradiotherapy interval and cT staging. One study found that

Table 3. Multivariate Logistic regression analysis of factors affecting pathological responses of patients with advanced GC after NACT

Variables	*B*	*SE*	*Wald*	*P*	*OR*	*95% CI*
Tumor size	0.881	0.328	7.220	0.007	2.413	1.269-4.589
ypT	0.928	0.324	8.206	0.004	2.531	1.341-4.777
ypN	0.812	0.324	6.264	0.012	2.252	1.193-4.253
Chemotherapy regimen	1.026	0.364	7.950	0.005	0.789	1.367-5.691
SII	1.282	0.487	6.919	0.009	3.605	1.387-9.371
PNI	1.628	0.321	25.659	< 0.001	5.092	2.713-9.560
Constant	-1.374	0.389	12.506	< 0.001	0.253	-

Notes: NACT: neo-adjuvant chemotherapy; SII: systemic immunoinflammatory Index; PNI: prognostic nutritional index.

Table 4. Predictive validity of pathological responses following NACT in patients with advanced gastric cancer before and after incorporating SII and PNI

Index	AUC (90% CI)	Sensitivity	Specificity	95% CI
Without SII and PNI	0.734	71.50%	71.20%	0.664-0.803
With SII and PNI	0.821	62.40%	87.90%	0.765-0.876

Notes: NACT: neo-adjuvant chemotherapy; SII: systemic immunoinflammatory Index; PNI: prognostic nutritional index; AUC: area under the curve.

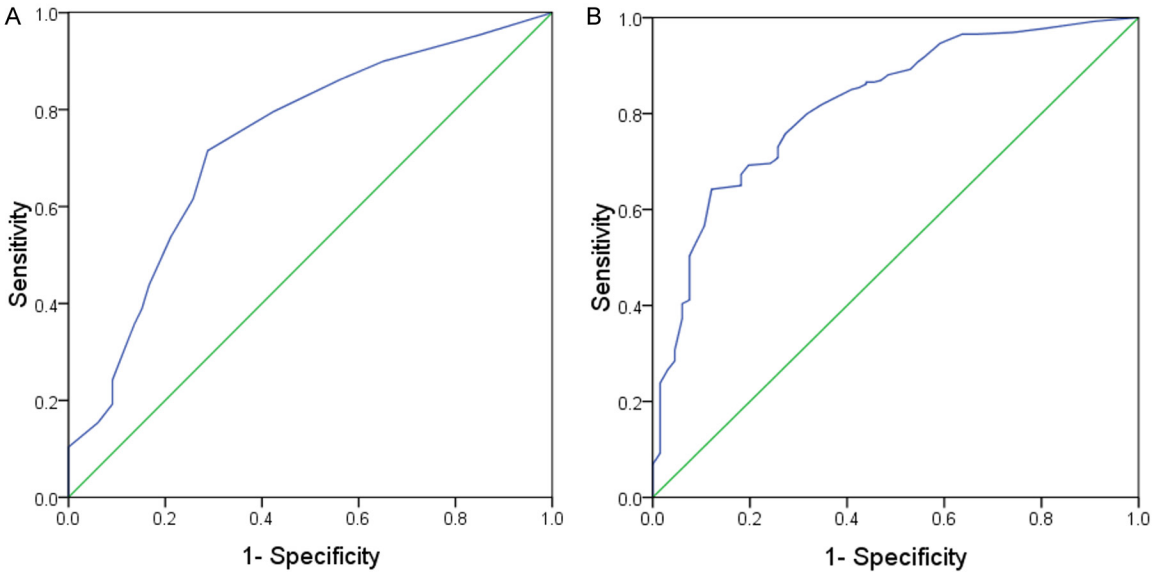

Figure 3. Effects of the pathological response prediction model for patients with advanced gastric cancer after NACT. A. Effects of the prediction model before including SII and PNI; B. Effects of the prediction model after including SII and PNI. SII: systemic immunoinflammatory Index; PNI: prognostic nutritional index.

patients with adenocarcinoma and an interval greater than 13 weeks between surgery and concurrent chemoradiotherapy, and in ealry cT stage were more likely to have high pCR rates. At the same time, it was found that the mortality rate of patients during 30-day hospitalization significantly increased in the groups with intervals ranging from 10 to 12 weeks and over 15 weeks.

Inflammation frequently correlates with an unfavorable prognosis across multiple tumor types, as it fosters tumor progression through various mechanisms, notably genetic muta-

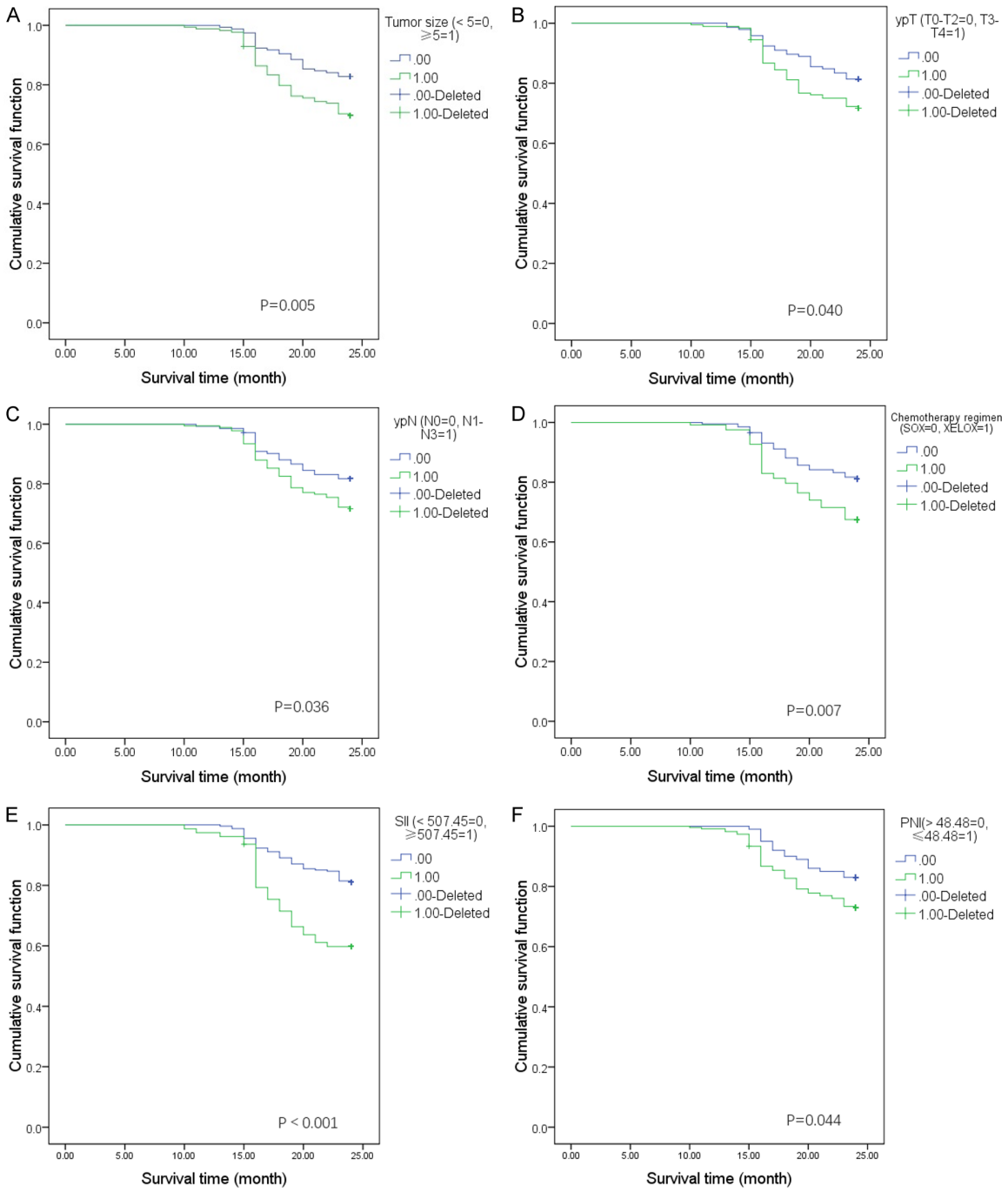

Figure 4. Survival curve analysis. A. Survival curve based on tumor size; B. Survival curve based on ypT; C. Survival curve based on ypN; D. Survival curve of chemotherapy regimen; E. Survival curve based on SII; F. Survival curve based on PNI. SII: systemic immunoinflammatory Index; PNI: prognostic nutritional index.

tions, tumor cell proliferation, and angiogenesis. In addition, cancer has been associated with systemic inflammation, often leading to malnutrition and cachexia, accompanied by loss of muscle mass, which increases morbidity and mortality. Wang Kang et al. [32] analyzed the data of 444 GC patients who underwent gastrectomy and found that the risk of death in patients with SII ≥ 660 was 1.551 times higher than that in patients with SII < 660, and compared to NLR and PLR, SII had a better effect in evaluating the prognosis of GC patients follow-

ing treatment. Therefore, SII can be deemed as an independent risk factor. However, due to the influence of preoperative TNM stage, there are few studies on the prognosis of GC patients who receive NACT before surgery. Chen Li et al. [33] included the data of 107 patients with advanced GC who received NAC and 185 patients with pathologically confirmed GC as controls. In Cox regression analysis, radical resection, pathological stage, total lymph nodes, positive lymph nodes, Borrmann typing, lymphocytes, and SII were important prognostic factors for predicting DFS and OS. The incidence of DFS and OS at 1, 3, and 5 years was high in GC patients with SII < 600. As people pay more attention to SII, more and more prognostic studies have been conducted on esophageal cancer [34], liver cancer [35], sig-ring cell carcinoma of stomach [36], small cell lung cancer [37] and other cancers, and SII has guiding significance for the treatment of various types of tumors.

Nozoe et al. [38] studied the relationship between preoperative PNI and the clinicopathological features of 148 GC patients. Their results showed that the mean value of PNI in patients with lymph node metastasis, large tumor depth, venous infiltration and lymphatic vessel infiltration was significantly lower than that in patients without these manifestations. In multivariate analysis, the independent correlation factors for poor prognosis in GC patients were tumor stage (P=0.006) and low preoperative PNI (P=0.004). Takahashi et al. [39] discussed the significance of PNI in predicting the long-term prognosis of GC patients over 80 years old. A total of 127 elderly GC patients undergoing surgical treatment were included, among which 86 were selected for survival analysis through propensity score matching, with the cut-off value of PNI score set at 46.5. Of the 86 GC patients, 38.2% whose PNI < 46.5 and 49.3% whose PNI ≥ 46.5 achieved 5-year survival. According to multivariate analysis, PNI and pathological stage were independent prognostic factors. In addition, there are several studies on the predictive value of PNI in the prognosis of patients with pancreatic cancer [40] and ovarian cancer [41].

In this study, it was found that the AUC of the prediction model with SII and PNI included was 0.821, which was significantly higher than that of the prediction model without the addition of SII and PNI (0.734), suggesting that the addition of SII and PNI effectively improved the predictive accuracy of pathological responses in patients with advanced GC after NACT. Meanwhile, on the basis of follow-up results, the survival time of patients in the pCR group was significantly longer than that of patients in the non-pCR group, hence pathological response is an ideal measurement for the recurrence and metastasis of tumors in patients as well as their survival time. There are some shortcomings in this study, including but not limited to small sample size, single data source, possible sampling errors, and unrepresentative pathological responses of GC patients after NACT. At the same time, the data requirements were not adequately estimated at the beginning of the study design, so that the data collection in practice may not be as comprehensive as expected. Therefore, in subsequent studies, we will expand the sample size, optimize the data collection methods, strengthen the data analysis capabilities, or conduct multi-center and prospective studies to further optimize.

Conclusion

Before treatment, tumor size < 5 cm, ypT T0-T2, ypN N0, the application of chemotherapy regimen XELOX, SII < 507.45, PNI > 48.48 were independent factors affecting the pathological response of patients with advanced GC after NACT, among which the addition of SII and PNI could increase the accuracy in predicting the pathological responses as well.

Disclosure of conflict of interest

None.

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