European Journal of Surgical Oncology 45 (2019) 425–431

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Prognostic impact of preoperative prognostic nutritional index in resected advanced gastric cancer: A multicenter propensity score analysis

Zeyu Luo [a, 1], Lin Zhou [a, 1], Alpha I. Balde [a, **], Zhou Li [a, *], Linyun He [a], Cai ZhenWei [a], ZeNan Zou [a], ShengYi Huang [a], Shuai Han [a], Min Wei Zhou [b], Gang Qing Zhang [c], Zhai Cai [a]

[a] Department of General Surgery, Zhujiang Hospital, Southern Medical University, Guangzhou, Guangdong Province, China
[b] Department of General Surgery, General Hospital of Guangzhou Military Command of PLA, China
[c] Department of General Surgery, Guangdong No. 2 Provincial People's Hospital, Guangzhou, Guangdong Province, China

ARTICLE INFO

Article history:
Received 20 April 2018
Received in revised form
24 July 2018
Accepted 26 September 2018
Available online 19 October 2018

Keywords:
Advanced gastric cancer
Prognostic nutritional index
Prognosis
Inflammation
Propensity score matching

ABSTRACT

Background: Advanced gastric cancer (AGC) causes debilitating malnutrition and leads to deterioration of the immune response. However, the concept of the prognostic nutritional index (PNI) is controversial when applied to patients with AGC. The aim of the present study was to evaluate the effect of the PNI after gastrectomy in patients with AGC.
Materials and methods: A multicenter retrospective study was conducted using propensity score matching (PSM) in gastric adenocarcinoma patients who underwent resection via laparoscopic or open surgery between 2014 and 2017. To overcome selection bias, we performed 1:1 matching using 5 covariates.
Results: The resection margins ($P < 0.001$) and LNM ($P = 0.004$) were significantly different between the two groups. In univariate analysis, poor tumor differentiation ($P = 0.038$) (R1+R2, $P = 0.004$), vascular and neural invasion ($P < 0.001$), and a PNI<50 ($P < 0.001$) were associated with poor recurrence-free survival (RFS). In multivariate analysis, a PNI<50 (hazard ratio (HR), 12.993; $P < 0.001$) was a risk factor for RFS. Univariate analysis for overall survival (OS) revealed that a PNI<50 ($P < 0.001$) (R1+R2,$P = 0.006$) and vascular and neural invasion ($P < 0.001$) were risk factors. In subsequent multivariate analysis, a PNI<50 (HR, 24.501; $P < 0.001$) was a significant risk factor for OS. Clinical assessments performed during a 12.34 (±5.050) month follow-up revealed that OS ($P < 0.001$) and RFS ($P < 0.001$) were worse in patients with a low PNI (<50) than in matched patients with a high PNI.
Conclusion: A low PNI is a strong predictor of unfavorable RFS and OS in patients with AGC.

Introduction

Worldwide, gastric cancer (GC) remains the fifth most common malignancy [1,2]. Even with a decrease in the overall incidence, the frequency of cancer in the upper third of the stomach and gastroesophageal junction (GEJ) has been increasing in both Asian and western countries [3–7] The lack of symptoms in early-stage disease or the presence of nonspecific symptoms mainly contributes to the diagnosis of GC at an advanced stage [8], leading to a poor prognosis [9]. Therefore, evaluation of the perioperative prognostic nutritional index (PNI), immunocompetence and inflammatory process can be useful in ameliorating symptoms or optimizing patient care.

Since the first study on the PNI in 1980, many studies have evaluated the impact of immunocompetence and nutritional conditions compared with that of single variables [10,11]; these factors were associated with many other malignancies [10,12,13]. Previous studies have investigated the role of the PNI and postoperative outcomes. In a study investigating the postoperative outcomes of GC in elderly patients, the PNI was useful in predicting long-term

* Corresponding author.
** Corresponding author.
E-mail addresses: kitimmaibrahima@yahoo.fr (A.I. Balde), gzlizhou@smu.edu.cn (Z. Li).
[1] Zeyu Luo and Lin Zhou contributed equally to this work, including the design of the study and the preparation of the manuscript; they should be considered co-first author.

https://doi.org/10.1016/j.ejso.2018.09.004
0748-7983/

related factors. Another study demonstrated that preoperative nutrition may impact the short and long-term outcomes of patients with certain types of disease.

Advanced gastric cancer (AGC) can cause malnutrition and deterioration [14] because of obstruction and bleeding, which may lead to impaired immunocompetence and decreased nutritional conditions [15]. The PNI can be a good tool to predict outcomes; however, the clinical significance of the PNI in AGC remains controversial. Propensity score matching (PSM) increases the reliability of results and helps overcome selection bias in retrospective studies. Thus, an appropriate way to estimate the exposure effect without increasing bias is to include all variables related to outcomes regardless of exposure. Therefore, we conducted the present study to evaluate the role of the PNI in outcomes related to AGC.

Materials and methods

The present study is a multicenter retrospective analysis of 260 gastric adenocarcinoma patients who underwent open or laparoscopy-assisted gastrectomy (LAG) surgery with radical resection from 2014 to 2017 at three different institutions. However, only 230 patients met the study criteria and were enrolled in the present study. The following inclusion criteria were considered: gastric adenocarcinoma diagnosed via computed tomography (CT), GC confirmed via pathology, and the presence or absence of lymph node (LN) metastasis. The following exclusion criteria were considered: infection and history of inflammatory disease, including vasculitis, systemic lupus erythematosus (SLE), and rheumatologic condition ($n = 7$); history of preoperative anticancer chemotherapy or any cancer-related surgery ($n = 20$); and history of steroid medication use ($n = 3$). The flow diagram for study subject screening and grouping is shown in Fig. 1. Patients underwent detailed laboratory evaluation, including blood count, medical history review, endoscopic ultrasonography (EUS) and abdominal CT. Standard demographic and clinicopathological data, including sex, age, body-mass index (BMI), symptoms, tumor location and size, and pathological results, were collected. Surgical details, including operation time and data from the last follow-up, including tumor recurrence and death, were collected and analyzed.

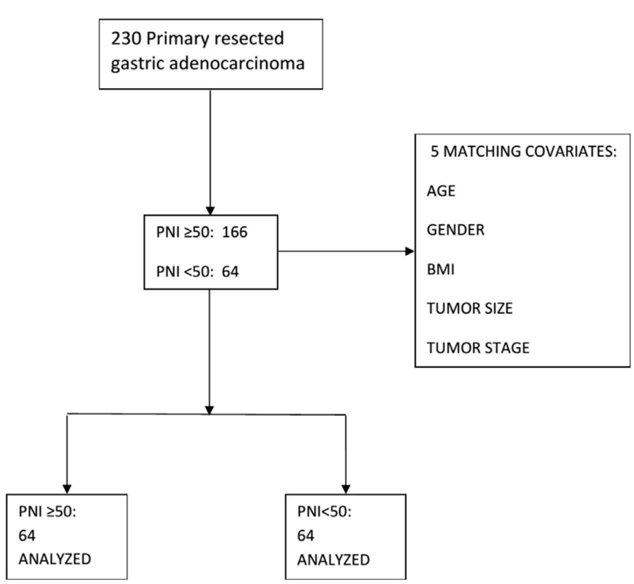

Fig. 1. Flow chart.

Tumors were staged according the International Agency Cancer Classification for GC. Tumor-node-metastasis (TNM) stages II to IV (with resectable liver metastasis) of patients with primary gastrectomy were included in the present study. All patients underwent potentially curative radical resection with D2 lymphadenectomy. Based on a previous study, PNI was calculated as follows: $10 \times$ serum albumin (g/dl)$+0.005 \times$ lymphocyte count (per mm^3). All patients were reviewed by a multidisciplinary team (MDT) that included surgical oncologists, pathologists, and medical oncologists. All patients provided written informed consent. The present study was approved by the Ethics Committee of Zhujiang Hospital.

PSM

To overcome selection biases, we performed a 1:1 matching for each patient using 5 covariates—age, tumor size, BMI, tumor stage, and sex—to generate propensity scores. A total of 64 patients with a PNI<50 and 166 patients with a PNI≥50 were divided into 64 pairs. The overall survival (OS) and disease-free survival (DFS) rates were compared between the two matched groups. The best way to estimate the exposure effect without increasing the bias is to include all variables that are related to outcomes regardless of exposure.

Statistical analyses

Continuous variables are presented as the mean ± standard deviation or median (interquartile range), depending on their normality, and categorical variables are presented as frequencies and percentages. The differences between clinicopathological characteristics grouped by the preoperative PNI were compared using Pearson's $\chi 2$ test for categorical variables and the Wilcoxon rank sum test for continuous variables. Survival curves and 3-year OS rates were determined using the Kaplan-Meier method with univariate analysis, and differences were compared using the log-rank test. A Cox proportional hazard model of multivariate analysis was used for the calculation of independent prognostic factors. Variables with $P < 0.05$ by univariate analysis were subjected to multivariate analyses. Each test was two tailed. Data management and statistical analyses were performed using SPSS software (SPSS 20.0, Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

Patient population and clinicopathological characteristics

The patient population and clinicopathological characteristics are presented in Table 1. After PSM, there were no significant differences between the groups in terms of age, sex, American Society of Anesthesiologists (ASA) grade, tumor size, number of LNs retrieved, or TNM stage. However, operation time and LN metastasis were significantly different ($P = 0.029$ and $P = 0.044$, respectively) between the two groups. Positive resection margins (P<**0.001)** were significantly different between the two groups. Blood transfusion ($P = 0.593$) and complications ($P = 0.818$) were not significantly different between the two groups.

Univariate and multivariate analyses for RFS and OS

In univariate analysis, poor tumor differentiation (hazard ratio (HR), 2.311; 95% confidence interval (CI), 1.045, 5.108; P = 0.038), positive resection margins (R1+R2) (HR, 2.131; 95% CI, 1.278,3.555; P = **0.004**) and a low PNI (HR, 12.993; 95% CI, 5.911, 28.560; $P < 0.001$) were associated with a poor prognosis. Cox multivariate analysis demonstrated that only a low PNI ($P < 0.001$) was independently associated with poor RFS as shown in Table 2.

Table 1
Clinicopathological characteristic of low versus high PNI for gastric cancer after propensity score matching.

Characteristic	Total	PNI≥50	PNI<50	Statistic (χ^2/Z)	*P*
	($n = 128$)	($n = 64$)	($n = 64$)		
Age (year)[a]	54.0 ± 12.3	53.4 ± 12.5	54.6 ± 12.2	−0.381	0.703
Sex				0.034	0.855
female	47(36.7)	24(51.1)	23(48.9)		
male	81(63.3)	40(49.4)	41(50.6)		
ECOG score [f]				0.898	0.728
0	6(4.7)	2(33.3)	4(66.7)		
1	104(81.3)	52(50.0)	52(50.0)		
2 + 3	18(14.1)	10(55.6)	8(44.4)		
ASA score				0.956	0.620
1	47(36.7)	26(55.3)	21(44.7)		
2	59(46.1)	27(45.8)	32(54.2)		
3	22(17.2)	11(50.0)	11(50.0)		
Symptoms				0.508	0.476
yes	72(56.3)	34(47.2)	38(52.8)		
no	56(43.8)	30(53.6)	26(46.4)		
Comorbidity				1.647	0.199
yes	47(36.7)	27(57.4)	20(42.6)		
no	81(63.3)	37(45.7)	44(54.3)		
Operation method				0.150	0.699
total gastrectomy	38(29.7)	18(47.4)	20(52.6)		
distal + partial gastrectomy	90(70.3)	46(51.1)	44(48.9)		
Tumor size (cm)				0.667	0.414
<5	96(75.0)	50(52.1)	46(47.9)		
≥5	32(25.0)	14(43.8)	18(56.3)		
Tumor differentiation				4.616	0.099
well	21(16.4)	15(71.4)	6(28.6)		
moderate	26(20.3)	12(46.2)	14(53.8)		
poor	81(63.3)	37(45.7)	44(54.3)		
Serosal invasion				2.213	0.331
T2	19(14.8)	8(42.1)	11(57.9)		
T3	22(17.2)	14(63.6)	8(36.4)		
T4	87(68.0)	42(48.3)	45(51.7)		
Number of retrieved LNs[b]	22.0(21.0, 25.0)	22.0(21.0, 25.0)	22.5(21.0, 27.8)	−0.591	0.554
LN metastasis				8.112	**0.044**
N0	31(24.2)	18(58.1)	13(41.9)		
N1	34(26.6)	13(38.2)	21(61.8)		
N2	24(18.8)	17(70.8)	7(29.2)		
N3	39(30.5)	16(41.0)	23(59.0)		
TNM staging				0.401	0.818
II	41(32.0)	20(48.8)	21(51.2)		
III	71(55.5)	37(52.1)	34(47.9)		
IV	16(12.5)	7(43.8)	9(56.3)		
Tumor location				2.677	0.262
U	26(20.3)	14(53.8)	12(46.2)		
M	41(32.0)	24(58.5)	17(41.5)		
L	61(47.7)	26(42.6)	35(57.4)		
Chemotherapy				0.076	0.783
yes	113(88.3)	57(50.4)	56(49.6)		
no	15(11.7)	7(46.7)	8(53.3)		
Operation time (min)[b]	270.0(195.5, 317.8)	270.0(202.5, 327.5)	269.5(192.0, 311.5)	−0.458	0.647
Intraoperative bleeding (ml)[b]	167.5(100.0, 261.3)	192.0(127.3, 276.5)	142.0(100.0, 238.3)	−2.177	**0.029**
Length of hospital stay (day)[b]	10.0(10.0, 11.0)	10.0(10.0, 11.0)	10.0(9.0, 11.0)	−0.705	0.481
Time to first ambulation (day)[b]	2.0(1.0, 2.0)	2.0(1.0, 2.0)	1.0(1.0, 2.0)	−1.477	0.140
Time to first flatus (day)[b]	3.0(2.0, 3.0)	2.0(2.0, 3.0)	3.0(2.0, 3.0)	−1.745	0.081
Time to first liquid intake (day)[b]	6.0(5.0, 6.0)	6.0(5.0, 6.0)	6.0(5.0, 6.0)	−0.265	0.791
Resection margins				14.366	**<0.001**
R0	103(80.5)	60(58.3)	43(41.7)		
R1+R2	25(19.5)	4(16.0)	21(84.0)		
Blood transfusion				0.286	0.593
yes	16(12.5)	7(43.8)	9(56.3)		
no	112(87.5)	57(50.9)	55(49.1)		
Complication				0.053	0.818
yes	23(18.0)	11(47.8)	12(52.2)		
no	105(82.0)	53(50.5)	52(49.5)		

PNI: Prognostic Nutritional Index; ECOG: Eastern Cooperative Oncology Group; ASA: American Society of Anesthesiologists; LN: Lymph Node; TNM: Tumor-Node-Metastasis; U: Upper; M: Middle; L: Lower.

[a] Values are shown as the means±standard deviations.

[b] Values are shown as median (interquartile range).

[f] Fisher's exact test.

Table 2
Univariate and multivariate analyses of risk factors related to recurrence-free survival after propensity score matching.

Characteristic	Univariate analysis			Multivariate analysis		
	HR	*95% CI*	*P*	*HR*	*95% CI*	*P*
Age (year)	1.001	(0.980, 1.022)	0.940			
Sex						
female	ref					
male	1.062	(0.654, 1.724)	0.807			
Symptoms						
yes	1.072	(0.670, 1.715)	0.771			
no	ref					
Operation method						
distal + partial gastrectomy	ref					
total gastrectomy	1.226	(0.735, 2.045)	0.434			
Tumor differentiation						
well	ref					
moderate	1.734	(0.706, 4.259)	0.230			
poor	2.311	(1.045, 5.108)	**0.038**			
State at diagnosis						
asymptomatic	ref					
symptomatic	1.237	(0.755, 2.024)	0.398			
LN metastasis						
N0	ref					
N1	1.444	(0.750, 2.779)	0.272			
N2	1.193	(0.535, 2.661)	0.667			
N3	1.337	(0.703, 2.540)	0.376			
PNI						
≥50	ref			ref		
<50	12.993	(5.911, 28.560)	**<0.001**	12.993	(5.911, 28.560)	**<0.001**
Vascular and neural invasion						
yes	5.762	(3.068, 10.822)	**<0.001**			
no	ref					
Operation time (min)	1.000	(0.997, 1.003)	0.866			
Resection margins						
R0	ref					
R1+R2	2.131	(1.278, 3.555)	**0.004**			
Blood transfusion						
yes	1.137	(0.596, 2.171)	0.696			
no	ref					
Complication						
yes	1.067	(0.593, 1.920)	0.828			

LN: Lymph Node; PNI: Prognostic Nutritional Index; HR: Hazard Ratio; CI: Confidence Interval; ref: Reference.

Univariate analysis for OS showed that a low PNI (HR, 24.501; 95% CI, 5.994, 100.149; P < 0.001), positive resection margins (R1+R2) (HR, 2.096; 95% CI, 1.242,3.536; P = **0.006**) and vascular and neural invasion (HR; 95% CI, 17.933,2193.970; P < 0.001) were associated with a reduction in OS. However, Cox multivariate analysis showed that only a low PNI (P < 0.001) was independently associated with decreased OS as shown in Table 3.

Follow-up

After AGC resection, clinical assessments were conducted for an average of 12.34 (±5.050) months. During this follow-up period, the OS (P < 0.001) and RFS (P**<0.001**) were worse in patients with a low PNI than in patients with a high PNI between the two matched groups (Fig. 2 and Fig. 3). The means±standard deviations of the total follow-up time for a PNI ≥50 and a PNI <50 were 11.55 ± 5.15 months and 13.14 ± 4.86 months, respectively.

Discussion

The findings of this study indicated that a low PNI may be an independent predictor of prognosis in AGC. The results demonstrated the importance of the PNI in estimating OS and RFS, which were significantly different between patients with a low and high PNI. Our findings are consistent with those of previous studies [16–18], which also indicated differences between these two groups. Hematogenous metastasis is a common concern during initial recurrence in patients who experience anorexia and cachexia. In this study, the tumor stage was not associated with PNI, which is in accordance with the findings of Katsunobo et al. These authors did not find differences between the low and high PNI groups in terms of stage II and III disease but found differences among patients with stage I disease. In our study, only patients with stage II to IV resectable disease were included. LN metastasis was different between the two groups (P = 0.0440), which supported the findings of a previous study by Yoshimoto et al. [19] who demonstrated that PNI was related to invasion depth and LN metastasis.

GC can sometimes cause nonspecific symptoms or can even be asymptomatic at a very early stage. This condition can be a strong factor that can negate a clinical or oncological treatment and its results. Complete tumor removal after surgery or the possibility of disease remission during treatment with curative intent is impossible. The resection margins are crucial in determining the success of an adopted definitive treatment. The residual tumor (R) classification denotes the absence or presence of residual tumor specifically after surgical resection. In this study, there was a significance difference between R0 and R1+R2 in the two matched groups. R1+R2 was associated with adverse prognostic factors in univariate and multivariate analysis of OS and RFS. The R classification, which can be used in many conditions including after surgery alone, chemo radiotherapy alone, or MDT therapy, remains subject to

Table 3
Univariate and multivariate analysis of risk factors related to overall survival after propensity score matching.

Characteristic	Univariate analysis			Multivariate analysis		
	HR	*95% CI*	*P*	*HR*	*95% CI*	*P*
Age (year)	0.996	(0.975, 1.018)	0.727			
Sex						
female	ref					
male	1.220	(0.723, 2.061)	0.456			
Symptoms						
yes	1.257	(0.768, 2.058)	0.362			
no	ref					
Operation method						
distal + partial gastrectomy	ref					
total gastrectomy	1.433	(0.841, 2.441)	0.186			
Tumor differentiation						
well	ref					
moderate	1.436	(0.547, 3.773)	0.463			
poor	1.963	(0.831, 4.636)	0.124			
State at diagnosis						
asymptomatic	ref					
symptomatic	1.469	(0.868, 2.484)	0.152			
LN metastasis						
N0	ref					
N1	2.011	(0.998, 4.054)	0.051			
N2	1.870	(0.781, 4.481)	0.160			
N3	1.860	(0.922, 3.752)	0.083			
PNI						
≥50	ref			ref		
<50	24.501	(5.994, 100.149)	**<0.001**	24.501	(5.994, 100.149)	**<0.001**
Vascular and neural invasion						
yes	3.560	(1.862, 6.807)	**<0.001**			
no	ref					
Operation time (min)	1.000	(0.996, 1.003)	0.878			
Resection margins						
R0	ref					
R1+R2	2.096	(1.242, 3.536)	**0.006**			
Blood transfusion						
yes	0.987	(0.488, 1.998)	0.971			
no	ref					
Complication						
yes	0.996	(0.531, 1.867)	0.989			

LN: Lymph Node; PNI: Prognostic Nutritional Index; HR: Hazard Ratio; CI: Confidence Interval; ref: Reference.

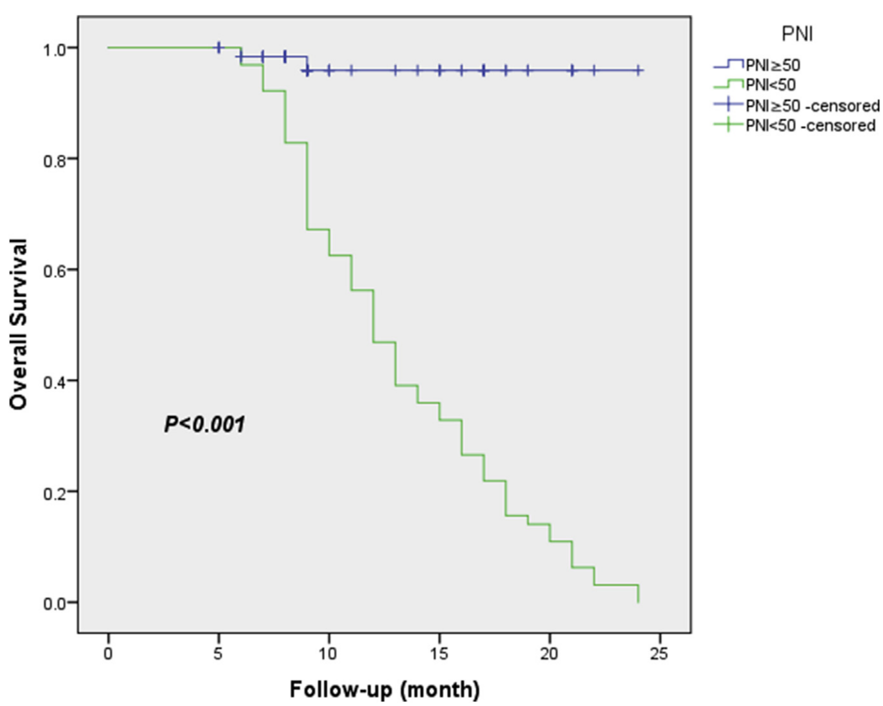

Fig. 2. OS.

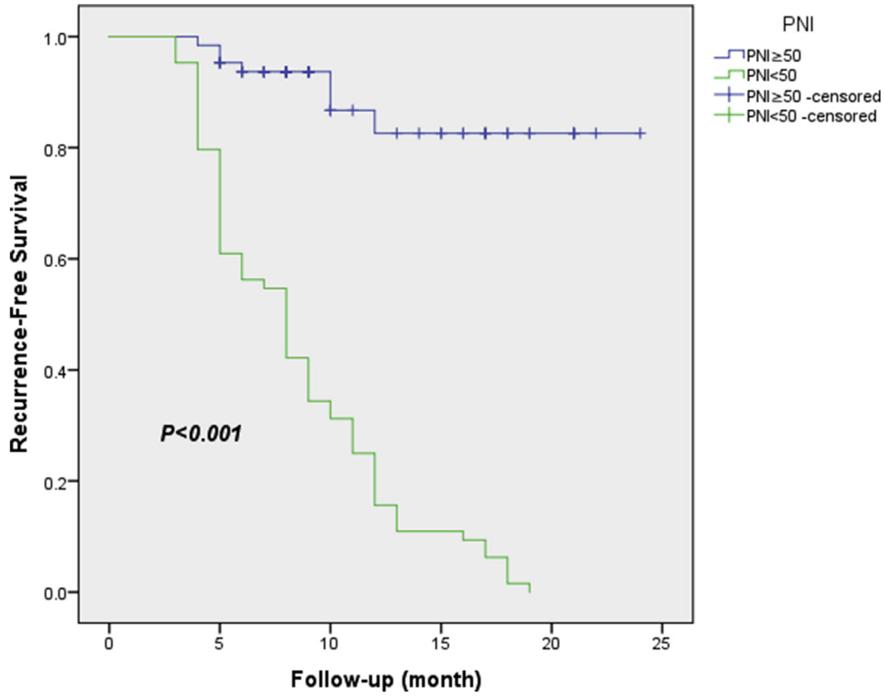

Fig. 3. RFS.

misinterpretation and inconsistent use despite the importance of the resection margin status in the management of cancer patients. These issues can negatively impact or negate the clinical value and utility of the R classification.

The use of chemotherapy to ameliorate symptoms or extend lifespan represents an important aspect of the postoperative management of GC. However, Kanda et al. [16] did not find any benefit of adjuvant chemotherapy for patients with a low PNI. These authors found that an impaired immune nutritional status reflected a reduction in the tolerance of the adverse effects of chemotherapy, increasing the likelihood of disease progression and deterioration of immunocompetence. A relation between chemotherapy or radiation and immunologic cell death (ICD) has been reported [20,21]. Similarly, systematic inflammation and antitumor responses are related to the activity of cytotoxic T lymphocytes, which detect cancer cells. Therefore, with regard to patient immune functions, the chemotherapy response in patients with increased inflammation may be indicative of a poor prognosis.

As a predictive value, the PNI should be used to distinguish stage I from III GC to select adjuvant chemotherapy to treat patients with AGC. The expectation of better outcomes in stage I GC than in stage III GC may indicate the need for intensive nutritional care for patients with stage II GC. Cancer cachexia syndrome [22,23] during the progression of AGC may be related to obstruction that leads to reduced food intake, hypoalbuminemia, weight loss and muscle wasting. This condition is associated with nutritional impairment and immune suppression [24,25] Moreover, anorexia-cachexia syndrome is associated with shortened OS [26]. Therefore, the PNI may be useful for the assessment of perioperative malnutrition status to determine the strategy of nutritional care in AGC patients. The postoperative nutritional status plays a role in the decision to support or maintain nutritional status in the catabolic period after tumor resection. Malnutrition substantially decreased after surgery in 435 patients with GC [27]. Thus, the improvement of the nutritional status before surgery may ameliorate the outcomes of GC patients.

Several limitations of our study must be considered. First, this study was retrospective; thus, selection bias might exist for the two groups despite the use of PSM. Second, the follow-up period was relatively short. Additionally, patients with different disease stages and invasion statuses may not be well distributed between the two groups because of the relatively small number of T2 and stage IV cases. Nevertheless, the PNI was associated with OS, RFS, LN metastasis and tumor infiltration.

Conclusion

The PNI is associated with OS and RFS. Thus, evaluation of the preoperative nutritional status may provide better strategies for long-term follow-up and indicate the need to adapt adjuvant chemotherapy to improve the management of patients with AGC.

Funding

There was no funding for this study.

Declarations of interest

Drs. Alpha I. Balde, Lin Zhou, Zhai Cai, Zhou Li, Linyun He, Cai ZhenWei, ZeNan Zou, ShengYi Huang, Zeyu Luo, Shuai Han, Min Wei Zhou, and Gang Qing Zhang have no conflicts of interest or financial ties to disclose.

References

[1] Ferlay J, Soerjomataram I. Cancer incidence and mortality worldwide: sources, method and major patterns in GLOBACAN 2012. In.t J. Cancer 2015;136: E359–86.
[2] Torre LA, Bray F, Siegel RL. Global cancer statistics, 2012. Ca - Cancer J Clin 2012;65:87–108.
[3] Deans C, Yeo MS, Soe MY, Shabbir A, Ti TK, So JB. Cancer of the gastric cardia is rising in incidence in an Asian population and is associated with adverse outcome. World J Surg 2011;35:617–24.
[4] Steevens J, Botterweck AA, Dirx MJ. Trends in incidence of oesophageal and

stomach cancer subtypes in Europe. Eur J Gastroenterol Hepatol 2010;22: 669–78.
[5] Dassen AE, Lemmens VE, van de Poll-Franse LV. Trends in incidence, treatment and survival of gastric adenocarcinoma between 1990 and 2007: a population-based study in The Netherlands. Eur J Canc 2010;46:1101–10.
[6] Crew KD, Neugut AI. Epidemiology of gastric cancer. World J Gastroenterol 2006;12:354–62.
[7] Shang J, Pena AS. Multidisciplinary approach to understand the pathogenesis of gastric cancer. World J Gastroenterol 2005;11:4131–9.
[8] Sohda M, Kuwano H. Current status and future prospects for esophageal cancer treatment. Ann Thorac Cardiovasc Surg 2017;23:1–11.
[9] Coussens LM, Werb Z. Inflammation and cancer. Nature 2002;420:860–7.
[10] Okamura Y, Ashida R, Ito T, Sugiura T, Mori K, Uesaka K. Preoperative neutrophil to lymphocyte ratio and prognostic nutritional index predict overall survival after hepatectomy for hepatocellular carcinoma. World J Surg 2015;39:1501–9.
[11] Jiang N, Deng JY, Ding XW, Ke B, Liu N, Zhang RP, et al. Prognostic nutritional index predicts postoperative complications and long-term outcomes of gastric cancer. World J Gastroenterol 2014;20:10537–44.
[12] Watanabe M, Iwatsuki M, Iwagami S, Ishimoto T, Baba Y, Baba H. Prognostic nutritional index predicts outcomes of gastrectomy in the elderly. World J Surg 2012;36:1632–9.
[13] Kanda M, Fujii T, Kodera Y. Nutritional predictors of postoperative outcomes in pancreatic cancer. Br J Surg 2011;98:268–74.
[14] Shen L, Shan YS, Hu HM. Management of gastric cancer in Asia: ressource-stratified guidelines. Lancet Oncol 2013;14:e535–547.
[15] Hartgrink HH, Jansen EPM, van Grieken NCT, van de Velde CJH. Gastric cancer. Lancet 2009;374:477–90.
[16] Kanda M, Mizuno A, Tanaka C, Kobayashi D, Fujiwara M, Iwata N, et al. Nutritional predictors for postoperative short-term and long-term outcomes of patients with gastric cancer. Med. (Balt.) 2016;95:e3781.
[17] Sun KY, Xu JB, Chen SL, Yuan YJ, Wu H, Peng JJ, et al. Novel immunological and nutritional-based prognostic index for gastric cancer. World J Gastroenterol 2015;21:5961–71.
[18] Lee Y, Auh SL, Wang Y, Burnette B, Wang Y, Meng Y, et al. Therapeutic effects of ablative radiation on local tumor require CD8+ T cells: changing strategies for cancer treatment. Blood 2009;114:589–95.
[19] Yoshimoto Y, Suzuki Y, Mimura K. Radiotherapy-induced anti-tumor immunity contributes to the therapeutic efficacy of irradiation and can be augmented by CTLA-4 blockade in a mouse model. PLoS One 2014;9, e92572.
[20] Garg AD, Galluzzi L, Apetoh L, Baert T, Birge RB, Bravo-San Pedro JM, et al. Molecular and translational classifications of DAMPs in immunogenic cell death. Front Immunol 2015;6:588.
[21] Suzuki Y, Mimura K, Yoshimoto Y, Watanabe M, Ohkubo Y, Izawa S, et al. Immunogenic tumor cell death induced by chemoradiotherapy in patients with esophageal squamous cell carcinoma. Cancer Res 2012;72:3967–76.
[22] Tomita M, Shimizu T, Ayabe T, Yonei A, Onitsuka T. Preoperative neutrophil to lymphocyte ratio as a prognostic predictor after curative resection for non-small cell lung cancer. Anticancer Res 2011;31:2995–8.
[23] Smith RA, Bosonnet L, Raraty M, Sutton R, Neoptolemos JP. Preoperative platelet-lymphocyte ratio is an independent significant prognostic marker in resected pancreatic ductal adenocarcinoma. Am J Surg 2009;197:466–72.
[24] Shibata M, Cachexia K Gonda. Immunological participation. Horizons in Cancer Research. New York: Nova Science Publishers, Inc.; 2015.
[25] Tisdale MJ. Biology of cachexia. J Natl Cancer Inst (Bethesda) 1997;89: 1763–73.
[26] Dong YW, Shi YQ, He LW, Su PZ. Prognostic significance of neutrophil-to-lymphocyte ratio in rectal cancer: a meta-analysis. Onco Targets Ther 2016;9:3127–34.
[27] Shim H, Cheong JH, Lee KY, Lee H. Perioperative nutritional status changes in gastrointestinal cancer patients. Yonsei Med J 2013;54:1370–6.