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ORIGINAL RESEARCH

Preoperative Neutrophil-to-Albumin Ratio as a Prognostic Indicator in Advanced Gastric Cancer Undergoing Radical Gastrectomy

Huaping Ye[1,*], Rong Kang[2,*], Mao Chen[3], Si Zhang[3], Jinfeng Yang[1]

[1]Department of Gastrointestinal Surgery, The First Affiliated Hospital of Chengdu Medical College, Chengdu, People's Republic of China; [2]Department of Urology, The First Affiliated Hospital of Chengdu Medical College, Chengdu, People's Republic of China; [3]Department of Emergency Medicine, The First Affiliated Hospital of Chengdu Medical College, Chengdu, People's Republic of China

*These authors contributed equally to this work

Correspondence: Jinfeng Yang, Department of Gastrointestinal Surgery, The First Affiliated Hospital of Chengdu Medical College, No. 278, The Middle Section of Baoguang Avenue, Xindu District, Chengdu City, Sichuan Province, 610500, People's Republic of China, Email yangjinfeng13@163.com; Si Zhang, Department of Emergency Medicine, The First Affiliated Hospital of Chengdu Medical College, No. 278, The Middle Section of Baoguang Avenue, Xindu District, Chengdu City, Sichuan Province, 610500, People's Republic of China, Email 692653629@qq.com

Objective: This study aimed to evaluate the prognostic significance of the preoperative neutrophil-to-albumin ratio (NAR) in patients with advanced gastric cancer undergoing radical gastrectomy.

Methods: A retrospective analysis was conducted involving 526 patients diagnosed with locally advanced gastric adenocarcinoma who underwent radical gastrectomy between January 2017 and December 2019. Preoperative NAR values were calculated using neutrophil count and serum albumin levels obtained within 24 hours of admission. Patients were stratified into high-NAR and low-NAR groups using an optimal cut-off value determined by receiver operating characteristic analysis. Kaplan-Meier curves, univariate, and multivariate Cox regression analyses were used to evaluate overall survival and recurrence-free survival.

Results: The optimal NAR cut-off value was identified as 2.8. Patients with high NAR exhibited significantly worse overall survival and recurrence-free survival compared to the low-NAR group. High NAR was significantly associated with advanced tumor stage, incomplete resection status, administration of chemotherapy and radiotherapy, and poor histological differentiation (all $P < 0.0001$). Multivariate analyses confirmed NAR as an independent prognostic factor for both overall survival (HR=2.67; 95% CI, 1.97–4.25; $p = 0.002$) and recurrence-free survival (HR=3.51; 95% CI, 1.58–5.26; $p = 0.003$).

Conclusion: The preoperative neutrophil-to-albumin ratio is an independent and reliable prognostic biomarker for overall and recurrence-free survival in patients with advanced gastric cancer undergoing radical gastrectomy. Due to its accessibility, simplicity, and predictive value, the neutrophil-to-albumin ratio can effectively facilitate risk stratification, personalized clinical decision-making, and targeted interventions to improve patient outcomes.

Keywords: gastric cancer, neutrophil-to-albumin ratio, prognostic biomarker, radical gastrectomy, systemic inflammation

Introduction

Gastric cancer remains one of the leading causes of cancer-related morbidity and mortality worldwide, largely due to its late-stage diagnosis and aggressive clinical course.[1,2] Despite significant advancements in surgical techniques and multimodal treatment strategies including chemotherapy, radiotherapy, and targeted therapies, the prognosis for advanced gastric cancer remains poor, with five-year survival rates below 50%.[3,4] Consequently, identifying reliable and accessible prognostic biomarkers for accurate risk stratification and individualized treatment planning is crucial for improving clinical outcomes in patients with advanced gastric cancer.

Systemic inflammation and nutritional status play pivotal roles in tumor progression, immune response modulation, and metastasis.[5,6] In recent years, inflammation-based biomarkers, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and fibrinogen-to-prealbumin ratio (FPAR), have demonstrated prognostic

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significance in various malignancies, including gastric cancer.[6–8] More recently, the neutrophil-to-albumin ratio (NAR), derived from neutrophil count and serum albumin levels, has emerged as a promising prognostic biomarker due to its ability to reflect systemic inflammation and nutritional status concurrently.[9–11] NAR has been validated as an independent prognostic factor in several cancers, including pancreatic adenocarcinoma, hepatocellular carcinoma, and esophageal cancer, highlighting its potential clinical relevance.[12–15]

Some studies have demonstrated that inflammatory and nutritional markers have prognostic value for many cancers, such as oral squamous cell carcinoma, esophageal cancer, nasopharyngeal carcinoma, and hepatocellular carcinoma.[11,16–18] However, the clinical utility of the preoperative NAR in prognostic evaluation of advanced gastric cancer remains unexplored. Given its accessibility, cost-effectiveness, and biological significance, further investigation into the prognostic impact of NAR in patients with advanced gastric cancer could provide valuable insights into its role in clinical decision-making. Therefore, this study aims to evaluate whether preoperative NAR independently predicts overall survival and recurrence-free survival in patients with advanced gastric cancer undergoing radical gastrectomy. By elucidating its prognostic significance, this study seeks to establish NAR as a novel and practical biomarker for risk stratification, ultimately guiding personalized therapeutic strategies and improving patient outcomes.

Patients and Methods

Study Population

The research was conducted following the ethical principles of the Declaration of Helsinki and received approval from the Ethics Committee of The First Affiliated Hospital of Chengdu Medical College (Approval No. 23526424). A retrospective review was conducted on data from 617 patients diagnosed with advanced gastric adenocarcinoma who underwent radical gastrectomy at the First Affiliated Hospital of Chengdu Medical College between January 2017 and December 2019.

The inclusion criteria were as follows: (1) a pathological diagnosis of advanced gastric cancer, specifically locally advanced cases without distant metastasis; (2) received radical gastrectomy; (3) absence of prior chemotherapy or immunotherapy before surgery; (4) no evidence of distant metastases; and (5) no history of severe cardiovascular or cerebrovascular diseases. Patients were excluded if they met any of the following conditions: (1) underwent non-radical gastrectomy; (2) primary carcinomas were out of the gastric; (3) had incomplete clinical or follow-up data. According to the inclusion and exclusion criteria, 91 patients were excluded because 20 patients received non-radical gastrectomy, 32 patients received prior chemotherapy before surgery, and 39 patients were lost to follow-up. Ultimately, 526 patients were enrolled in this study.

Data Collection

Clinicopathologic and demographic data were retrospectively retrieved from the electronic medical record system of the study hospital. Blood samples were collected within 24 hours of the patient's admission for operation, and neutrophil count and albumin concentration were analyzed within two hours of sample collection. The neutrophil-to-albumin ratio was calculated by dividing the neutrophil count (percentage) by the albumin concentration (g/L) and multiplying by 100. Tumor infiltration depth, lymph node involvement, metastatic status, and overall pathological staging were assessed based on the NCCN guidelines.[19]

Patient Treatment

All patients enrolled in this study were diagnosed with advanced gastric cancer, specifically locally advanced cases without distant metastasis, and underwent radical gastrectomy. Treatment strategies were implemented in accordance with NCCN guidelines.[19] The chemotherapy protocols included the following regimens: (1) monotherapy with fluorouracil-based anticancer agents such as Capecitabine, Tegafur, Gimeracil, and Oteracil potassium capsules; (2) a combination of Capecitabine and Oxaliplatin; (3) a regimen combining 5-FU, Leucovorin Calcium, and Oxaliplatin; and (4) a combination of 5-FU and Oxaliplatin. Indications for radiotherapy included: (1) positive surgical margins and (2) R0 resection with lymph node dissection covering less than the D2 range. The radiotherapy was performed by

fluoropyrimidine-based chemoradiation, and the recommended radiation dose was 45–50.4 Gy, administered at 1.8 Gy per session over a total of 25–28 fractions.

Patient Follow-Up

Patient follow-up was carried out through outpatient visits and telephone interviews, with monitoring continuing until December 2024. Each follow-up visit included clinical evaluations and tumor marker assessments, supplemented by imaging studies such as ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI) when necessary. Recurrence was determined based on histopathological confirmation via tumor biopsy and/or the detection of new lesions on imaging. Overall survival was defined as the time from the initial diagnosis to death from any cause or the last recorded follow-up in December 2024. Recurrence-free survival referred to the period following radical gastrectomy during which patients remain free of detectable disease on imaging or until death from any cause.

Statistical Analysis

A receiver operating characteristic (ROC) curve analysis was conducted to assess the sensitivity and specificity of the NAR in predicting a 5-year overall survival, and the Youden index was calculated to determine the optimal cut-off value. Categorical variables were analyzed using either the Chi-square test or Fisher's exact test. Kaplan–Meier curves were employed to evaluate overall and recurrence-free survival, with comparisons between groups performed using the Log rank test. A Cox regression model was applied to identify factors influencing overall and recurrence-free survival, followed by multivariate analysis to determine independent prognostic variables. Statistical significance was defined as $p < 0.05$. All data analyses were conducted using SPSS software.

Results

Patient Characteristics of the Study Population

Patient characteristics of the study population are shown in Table 1. A total of 526 patients were enrolled in this study, the median age at diagnosis was 60 years old, with 237 (45.06%) patients younger than 60 years and 289 (54.94%) patients aged 60 years or older. Among them, 273 (51.90%) patients were male and 253 (48.10%) patients were female. Regarding tumor stage, 95 (18.06%) patients had stage I disease, 220 (41.83%) patients had stage II disease, and 211

Table 1 Patient Characteristics of the Study Population

Characteristics	n	%
Total	526	100
Age		
<60	237	45.06
≥60	289	54.94
Gender		
Male	273	51.90
Female	253	48.10
Tumor stage		
I	95	18.06
II	220	41.83
III	211	40.11
Resection status		
R0	475	90.30
R1	40	7.60
R2	11	2.10

(*Continued*)

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Table 1 (Continued).

Characteristics	n	%
Chemotherapy		
No	23	4.37
Yes	503	95.63
Radiotherapy		
No	465	88.40
Yes	61	11.60
Surgical type		
Proximal gastrectomy	154	29.28
Distal gastrectomy	300	57.03
Total gastrectomy	72	13.69
Pathological type		
Papillary adenocarcinoma	78	14.83
Mucinous adenocarcinoma	269	51.14
Tubular adenocarcinoma	127	24.14
Signet ring cell carcinoma	52	9.89
Histological differentiation		
Well	244	46.39
Moderate	193	36.70
Poor	89	16.91

(40.11%) patients had stage III disease. Surgical resection status included R0 gastrectomy in 475 (90.30%) patients, R1 gastrectomy in 40 (7.60%) patients, and R2 gastrectomy in 11 (2.10%) patients.

Chemotherapy was administered to 503 (95.63%) patients, whereas 23 (4.37%) patients did not receive chemotherapy due to an early disease stage. Radiotherapy was given to 61 (11.60%) patients, while the remaining 465 (88.40%) patients did not receive radiotherapy. Regarding the types of gastrectomy performed, 154 (29.28%) patients underwent proximal gastrectomy, 300 (57.03%) underwent distal gastrectomy, and 72 (13.69%) underwent total gastrectomy. Histopathological analysis revealed papillary adenocarcinoma in 78 (14.83%) patients, mucinous carcinoma in 269 (51.14%) patients, tubular adenocarcinoma in 127 (24.14%) patients, and signet ring cell carcinoma in 52 (9.89%) patients. Regarding histological differentiation, 244 (46.39%) tumors were well differentiated, 193 (36.70%) moderately differentiated, and 89 (16.91%) poorly differentiated.

Determination of the Optimal Cut-off Value of the Preoperative NAR for Predicting 5-year Overall Survival

Using ROC curve analysis with 5-year overall survival as the endpoint, the optimal preoperative NAR cut-off value was determined to be 2.8 (Figure 1). The area under the ROC curve (AUC) for NAR was 0.672, with a sensitivity of 84.61% and a specificity of 75.23%. Based on this threshold, patients were categorized into two groups: those with an NAR exceeding 2.8 were placed in the high-NAR group, while those with an NAR below this value were classified into the low-NAR group.

Association of the Patients' Clinicopathological Characteristics with the NAR

High NAR values were significantly associated with tumor stage ($p < 0.0001$), resection status ($p < 0.0001$), chemotherapy ($p < 0.0001$), radiotherapy ($p < 0.0001$), and histological differentiation ($p < 0.0001$). However, age, gender, surgical type, and pathological type are not associated with the NAR value (Table 2).

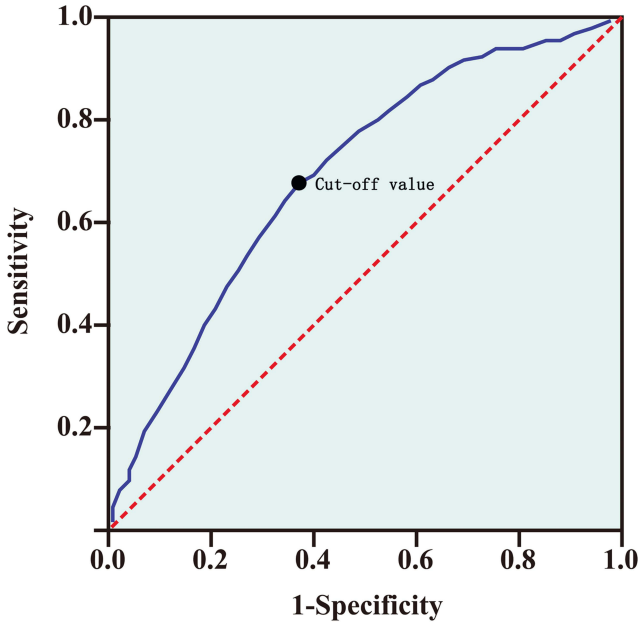

Figure 1 Receiver operating characteristic curves of the neutrophil to albumin ratio in gastric cancer patients for predicting 5-year overall survival, the Youden index is 0.183, AUC is 0.672, cut-off value is 2.8, sensitivity is 84.61%, and specificity is 75.23%.

High NAR Values Were Associated with Decreased Overall Survival in Gastric Cancer Patients

Kaplan-Meier analysis demonstrated that gastric cancer patients with high NAR values exhibited a shorter overall survival than those with low NAR values (Figure 2). To determine the factors affecting overall survival, univariate and multivariate Cox proportional hazards regression analyses were performed.

Table 2 Association of the Patients' Clinicopathological Characteristics with the NAR

Characteristics	Low NAR	High NAR
Age		0.255
<60	122	115
≥60	134	155
Gender		0.256
Male	156	117
Female	132	121
Tumor stage		< **0.0001**
I	63	32
II	83	137
III	62	149
Resection status		< **0.0001**
R0	362	113
R1	11	29
R2	2	9
Chemotherapy		< **0.0001**
No	17	6
Yes	152	351

(*Continued*)

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Table 2 (Continued).

Characteristics	Low NAR	High NAR
Radiotherapy		**< 0.0001**
No	347	118
Yes	13	48
Surgical type		0.662
Proximal gastrectomy	74	80
Distal gastrectomy	140	160
Total gastrectomy	30	42
Pathological type		0.269
Papillary adenocarcinoma	31	47
Mucinous adenocarcinoma	131	138
Tubular adenocarcinoma	67	61
Signet ring cell carcinoma	24	28
Histological differentiation		**< 0.0001**
Well	190	54
Moderate	75	118
Poor	23	66

Note: The statistical significance was analyzed by a chi-square test or Fisher's exact test. A p <0.05 was considered statistical significance and was highlighted in bold text.

The univariate analysis identified age, tumor stage, resection status, chemotherapy, radiotherapy, histological differentiation, and NAR values as factors significantly associated with overall survival (Table 3). After adjusting for confounding factors, including age, resection status, tumor stage, radiotherapy, chemotherapy, and histological differentiation, the multivariate analysis confirmed that NAR values, tumor stage, and resection status were independent prognostic factors influencing overall survival (Table 3).

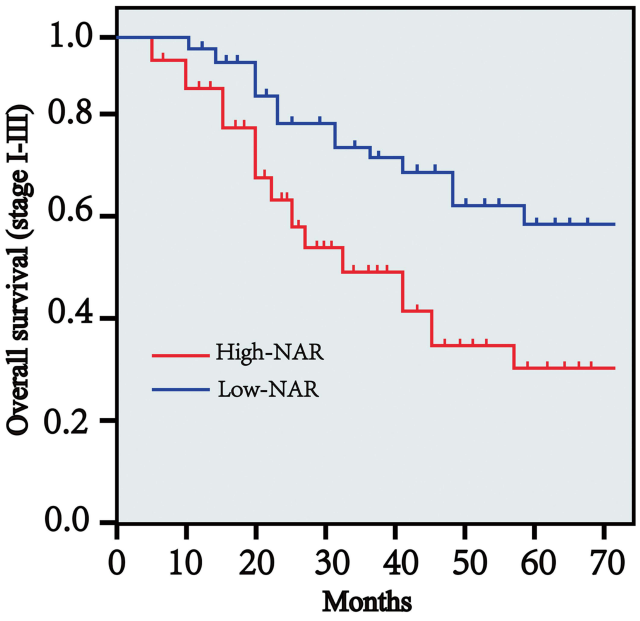

Figure 2 The association between NAR values and overall survival in gastric cancer patients, with an HR=3.37, 95% CI: 1.64–5.82, and p = 0.003.

Table 3 Univariate and Multivariate Cox Proportional Hazards Regression Analyses of Prognostic Factors for Overall Survival

Variables	Univariate Analysis HR (95% CI)	*p-value*	Multivariate Analysis HR (95% CI)	Adjusted *p-value*
Age (year)				
<60	1.00 (Reference)		1.00 (Reference)	
≥60	2.16 (1.24–3.68)	**0.003**	0.92 (0.81–1.32)	0.135
Gender				
Male	1.00 (Reference)		1.00 (Reference)	
Female	1.12 (0.87–1.25)	0.342	0.98 (0.82–1.24)	0.276
Tumor stage				
I	1.00 (Reference)		1.00 (Reference)	
II	2.64 (1.37–4.15)	**0.002**	2.17 (1.42–3.55)	**0.007**
III	3.25 (2.26–5.17)	**0.001**	2.89 (1.23–4.51)	**0.002**
Resection status				
R0	1.00 (Reference)		1.00 (Reference)	
R1	3.62 (2.54–5.39)	**0.011**	3.05 (1.92–5.47)	**0.017**
R2	4.89 (2.82–6.83)	**0.005**	4.36 (2.51–6.04)	**0.012**
Chemotherapy				
No	1.00 (Reference)		1.00 (Reference)	
Yes	3.26 (1.42–4.26)	**0.006**	1.01 (0.88–2.27)	0.231
Radiotherapy				
No	1.00 (Reference)		1.00 (Reference)	
Yes	3.37 (2.18–5.13)	**0.001**	1.05 (0.79–1.51)	0.413
Surgical type				
Proximal gastrectomy	1.00 (Reference)		1.00 (Reference)	
Distal gastrectomy	0.92 (0.73–1.34)	0.312	1.06 (0.87–1.27)	0.242
Total gastrectomy	1.12 (0.92–1.75)	0.125	0.97 (0.81–1.31)	0.352
Pathological type				
Papillary adenocarcinoma	1.00 (Reference)		1.00 (Reference)	
Mucinous adenocarcinoma	1.03 (0.97–1.34)	0.441	0.87 (0.65–1.23)	0.315
Tubular adenocarcinoma	1.04 (0.83–1.42)	0.322	1.12 (0.91–1.36)	0.091
Signet ring cell carcinoma	0.82 (0.71–1.27)	0.121	0.94 (0.83–1.24)	0.217
Histological differentiation				
Well	1.00 (Reference)		1.00 (Reference)	
Moderate	2.47 (1.42–4.25)	**0.001**	1.04 (0.87–1.47)	0.313
Poor	3.25 (2.01–5.45)	**0.002**	1.12 (0.89–1.52)	0.402
NAR values				
Low	1.00 (Reference)		1.00 (Reference)	
High	3.32 (1.43–5.82)	**0.001**	2.67 (1.97–4.25)	**0.002**

Notes: Adjusted for potential confounding factors, including age, gender, chemotherapy, radiotherapy, surgical type, Pathological type, and histological differentiation. A $p < 0.05$ was considered statistical significance and marked in bold text.
Abbreviations: CI, Confidence interval; HR, hazard ratio.

High NAR Values Were Associated with Decreased Recurrence-Free Survival in Gastric Cancer Patients

Kaplan-Meier analysis was utilized to evaluate recurrence-free survival, demonstrating that gastric cancer patients with high NAR values had significantly shorter recurrence-free survival than those with low NAR values (Figure 3). To determine the factors affecting recurrence-free survival, both univariate and multivariate Cox proportional hazards regression analyses were performed.

Univariate analysis revealed that tumor stage, resection status, chemotherapy, radiotherapy, histological differentiation, and NAR values were significantly associated with recurrence-free survival (Table 4). After adjusting for potential

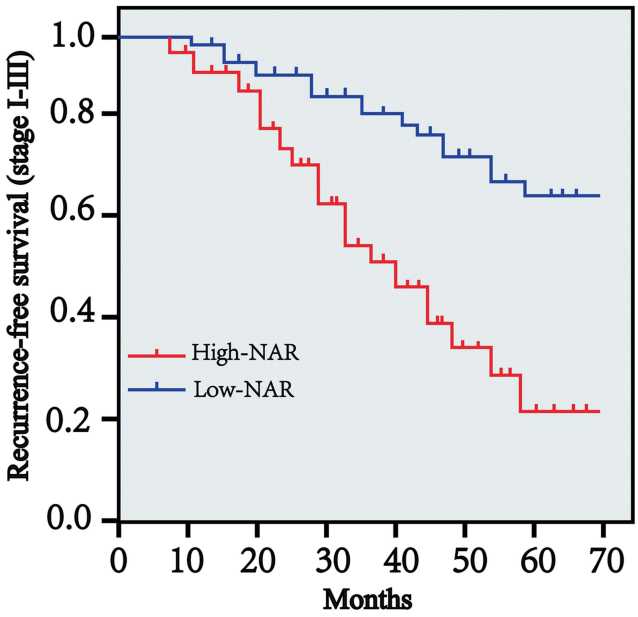

Figure 3 The association between NAR values and recurrence-free survival in gastric cancer patients, with an HR=4.51, 95% CI: 2.28–7.51, and p = 0.007.

confounders such as tumor stage, resection status, chemotherapy, radiotherapy, and histological differentiation, multivariate analysis identified NAR values, tumor stage, histological differentiation, and resection status as independent prognostic factors influencing recurrence-free survival (Table 4).

Table 4 Univariate and Multivariate Cox Proportional Hazards Regression Analyses of Prognostic Factors for Recurrence-Free Survival

Variables	Univariate Analysis HR (95% CI)	p-value	Multivariate Analysis HR (95% CI)	Adjusted p-value
Age (year)				
<60	1.00 (Reference)		1.00 (Reference)	
≥60	0.91 (0.72–1.31)	0.217	1.02 (0.91–1.42)	0.316
Gender				
Male	1.00 (Reference)		1.00 (Reference)	
Female	1.06 (0.92–1.42)	0.442	0.92 (0.73–1.34)	0.351
Tumor stage				
I	1.00 (Reference)		1.00 (Reference)	
II	2.76 (1.19–4.25)	**0.008**	2.23 (1.13–4.52)	**0.001**
III	3.58 (2.71–5.71)	**0.001**	3.15 (1.53–5.28)	**0.002**
Resection status				
R0	1.00 (Reference)		1.00 (Reference)	
R1	3.76 (1.82–6.29)	**0.001**	3.24 (1.38–6.17)	**0.005**
R2	6.15 (3.02–8.34)	**0.003**	4.85 (2.93–7.24)	**0.002**
Chemotherapy				
No	1.00 (Reference)		1.00 (Reference)	
Yes	3.32 (1.56–6.24)	**0.014**	0.98 (0.71–1.82)	0.162
Radiotherapy				
No	1.00 (Reference)		1.00 (Reference)	
Yes	2.76 (1.22–3.68)	**0.017**	1.05 (0.73–1.54)	0.291

(*Continued*)

Table 4 (Continued).

Variables	Univariate Analysis HR (95% CI)	p-value	Multivariate Analysis HR (95% CI)	Adjusted p-value
Surgical type				
Proximal gastrectomy	1.00 (Reference)		1.00 (Reference)	
Distal gastrectomy	1.23 (0.94–1.57)	0.261	0.93 (0.82–1.34)	0.173
Total gastrectomy	0.87 (0.62–1.14)	0.412	1.05 (0.97–1.45)	0.261
Pathological type				
Papillary adenocarcinoma	1.00 (Reference)		1.00 (Reference)	
Mucinous adenocarcinoma	0.98 (0.88–1.49)	0.282	1.25 (0.85–1.51)	0.432
Tubular adenocarcinoma	0.86 (0.72–1.31)	0.291	0.93 (0.82–1.45)	0.163
Signet ring cell carcinoma	1.03 (0.91–1.33)	0.167	1.26 (0.92–1.47)	0.332
Histological differentiation				
Well	1.00 (Reference)		1.00 (Reference)	
Moderate	2.26 (1.21–3.79)	**0.001**	2.62 (0.93–4.35)	**0.023**
Poor	3.62 (1.42–5.72)	**0.004**	3.44 (1.37–5.87)	**0.002**
NAR values				
Low	1.00 (Reference)		1.00 (Reference)	
High	4.32 (2.15–6.23)	**0.001**	3.51 (1.58–5.26)	**0.003**

Notes: Adjusted for potential confounding factors, including age, gender, chemotherapy, radiotherapy, surgical type, and pathological type. A $p < 0.05$ was considered statistical significance and marked in bold text.
Abbreviations: CI, Confidence interval; HR, hazard ratio.

Overall Survival and Recurrence-Free Survival Stratified by Tumor Stage

These findings confirmed that tumor stage serves as an independent prognostic factor for both overall survival and recurrence-free survival in gastric cancer patients. Kaplan-Meier analyses were performed to further investigate the prognostic significance of NAR within subgroups stratified by tumor stage. The results indicated that patients with high NAR values had significantly worse overall survival in stage II and III disease but not in stage I, compared to those with low NAR values (Figure 4A–C). A similar pattern was also observed for recurrence-free survival (Figure 4D–F).

Discussion

This study revealed a significant association between NAR values and various clinicopathological characteristics of advanced gastric cancer, including tumor stage ($p < 0.0001$), resection status ($p < 0.0001$), chemotherapy ($p < 0.0001$), radiotherapy (($p < 0.0001$), and histological differentiation ($p < 0.0001$) (Table 2). Furthermore, lower NAR values were associated with poorer overall survival and recurrence-free survival, identifying NAR as an independent prognostic factor for adverse survival outcomes (Tables 3 and 4). These findings indicate that NAR could serve as a valuable prognostic biomarker in advanced gastric cancer, aiding in the early identification of high-risk patients and guiding timely therapeutic interventions.

The present findings substantiate the growing body of evidence highlighting the prognostic significance of NAR in various malignancies.[9,12–15,17] Specifically, our results demonstrate that preoperative NAR is a robust and independent predictor of overall survival and recurrence-free survival among patients with advanced gastric cancer undergoing radical gastrectomy (Tables 3 and 4). The biological plausibility of NAR as a prognostic marker resides in its integration of systemic inflammation and nutritional status, both of which are critical components implicated in cancer progression and metastasis.[20–23]

The role of neutrophils in cancer biology is well established; they actively contribute to tumor initiation, growth, invasion, and metastasis via the secretion of growth factors, angiogenic mediators, and matrix metalloproteinases, facilitating extracellular matrix remodeling and tumor cell invasion.[24,25] Additionally, neutrophils promote an immunosuppressive tumor microenvironment by inhibiting cytotoxic T lymphocyte activity, thereby enabling immune escape and

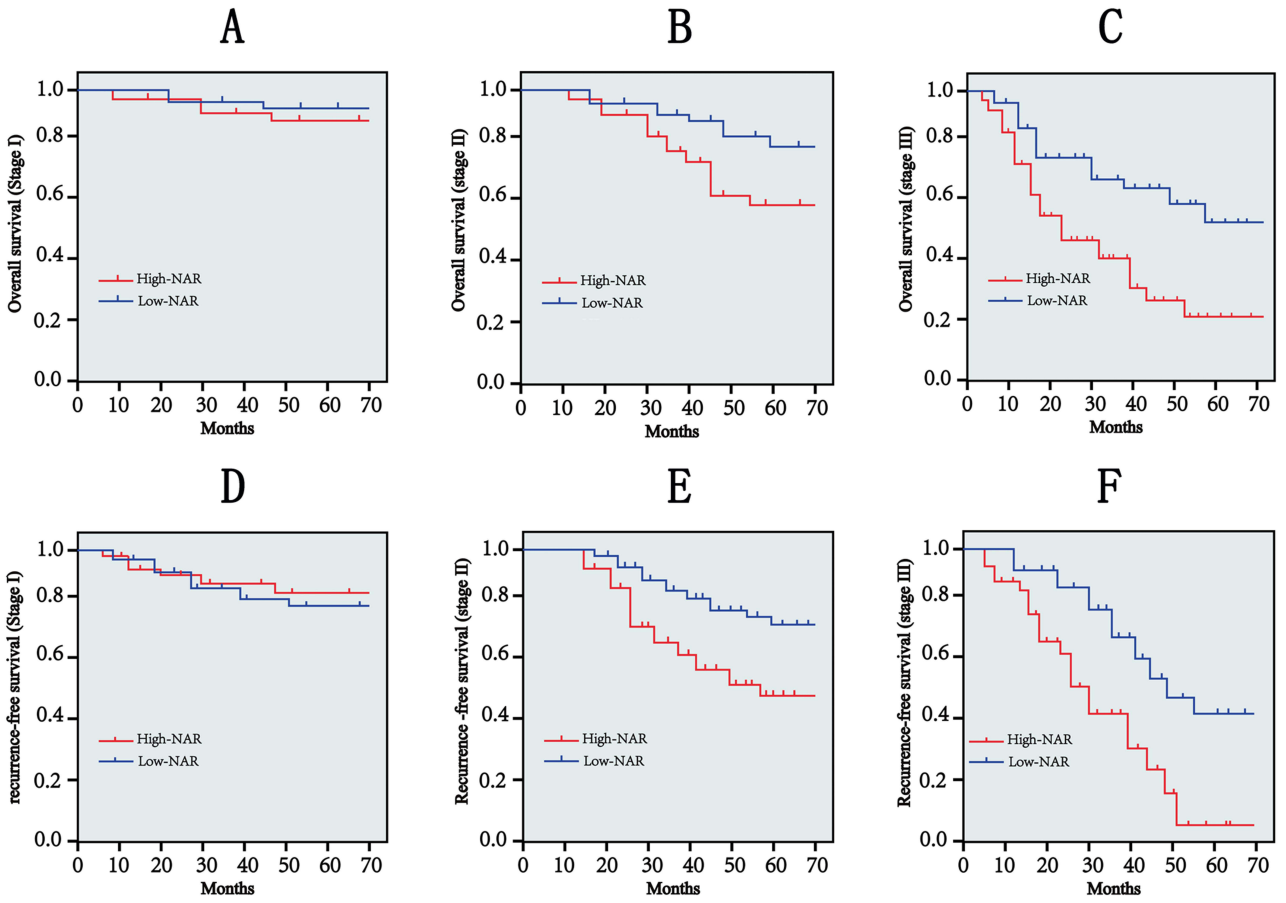

Figure 4 Overall survival and recurrence-free survival stratified by tumor stages. (**A**) the overall survival in stage I disease, HR=0.97, 95% CI:0.63–1.02, and p = 0.317; (**B**) the overall survival in stage II disease, HR=2.03, 95% CI:1.62–4.12, and p = 0.002; (**C**) the overall survival in stage III disease, HR=3.45, 95% CI:2.25–6.84, and p = 0.005; (**D**) the recurrence-free survival in stage I disease, HR=1.04, 95% CI:0.83–1.27, and p = 0.132; (**E**) the recurrence-free survival in stage II disease, HR=2.25, 95% CI:1.31–4.43, and p = 0.003; (**F**) the recurrence-free survival in stage III disease, HR=4.15, 95% CI:2.04–6.42, and p = 0.003.

subsequent tumor progression.[26,27] Elevated neutrophil counts have consistently been correlated with poor prognosis across a wide spectrum of malignancies, including gastrointestinal cancers.[28,29]

Albumin, on the other hand, reflects nutritional reserves and systemic inflammatory status in patients. Hypoalbuminemia, frequently observed in cancer patients, arises from systemic inflammation-induced hepatic suppression, nutritional impairment, and increased catabolic demands associated with tumor metabolism.[30,31] Moreover, reduced serum albumin levels have been correlated with compromised immune responses and poorer prognosis across diverse malignancies, including gastric cancer.[32] Thus, albumin serves as an insightful nutritional marker, indicative of patients' systemic condition, nutritional reserves, and immune competence which are crucial for effective postoperative recovery and response to subsequent therapies.

Recent studies have highlighted similar prognostic implications of NAR in other cancer types.[9,12–15,17] For example, a study reported that NAR was significantly associated with survival outcomes across various malignancies, reinforcing its utility as a broadly applicable prognostic biomarker.[9] Additionally, studies conducted in nasopharyngeal carcinoma, gastrointestinal stromal tumors, and oral squamous cell carcinoma have consistently demonstrated that elevated preoperative NAR negatively correlates with survival outcomes, thereby underscoring its extensive clinical applicability.[10,11,17]

Our findings align with these studies, further emphasizing the utility of preoperative NAR as an accessible, economical, and reliable prognostic biomarker in clinical practice. The simplicity of calculating NAR facilitates its routine integration into clinical workflows, enabling individualized risk stratification and informed therapeutic decision-

making. Clinicians may therefore identify patients at higher risk for poor outcomes, facilitating earlier intervention and personalized treatment approaches to reduce postoperative morbidity and improve long-term prognosis.

While exploring the prognostic relevance of NAR, it is important to recognize that the inflammatory-nutritional interplay in cancer biology remains complex. This interplay involves numerous inflammatory and immune mediators and is influenced by various factors, including host immune status, intrinsic biological aggressiveness of cancers, and perioperative conditions such as surgical stress and postoperative complications.[33,34] Indeed, a previous study demonstrated that inflammatory biomarkers, such as neutrophil-to-lymphocyte ratio (NLR), retained independent prognostic significance even after accounting for postoperative complications in gastric cancer, highlighting the robustness of inflammatory indices as prognostic indicators in cancer surgery.[35]

Despite these strengths, several limitations must be acknowledged. First, this was a retrospective, single-center study, potentially restricting the generalizability of the findings. Therefore, prospective, multicenter validation studies are necessary to further substantiate the prognostic value of NAR. Additionally, although stringent inclusion and exclusion criteria were applied, residual confounding inherent in retrospective analyses might have influenced the results. Although NAR was identified as an independent prognostic factor in this study, the AUC value of 0.672 indicates only moderate discriminative ability. This limitation suggests that its predictive performance could potentially be improved by combining it with other clinical or inflammatory markers.

Future studies integrating NAR with additional biomarkers or clinical variables into comprehensive nomograms could potentially enhance prognostic precision. Such combined prognostic models have demonstrated value in predicting survival outcomes in other cancers. For instance, a study developed a predictive nomogram incorporating NAR, achieving improved prognostic accuracy for nasopharyngeal carcinoma.[17] Similarly, developing and validating a tailored prognostic nomogram specifically for gastric cancer could be particularly beneficial, facilitating personalized risk assessment and informed clinical decision-making.

Conclusion

In conclusion, our study demonstrates that the preoperative neutrophil-to-albumin ratio (NAR) is an independent and reliable prognostic biomarker for overall survival and recurrence-free survival in patients with advanced gastric cancer undergoing radical gastrectomy. Due to its accessibility, low cost, and robust prognostic performance, NAR can effectively assist clinicians in identifying patients with high-risk profiles, thereby guiding clinical decision-making and facilitating personalized therapeutic approaches. Future prospective multicenter studies are warranted to validate these findings and to further investigate the incorporation of NAR into comprehensive prognostic models, ultimately aiming to improve clinical outcomes for patients with advanced gastric cancer.

Abbreviations

FPAR, fibrinogen-to-prealbumin ratio; NAR, neutrophil-to-albumin ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

Ethics Approval

Informed consent was obtained from the study participants before the commencement of the study, and the study complies with the Declaration of Helsinki. This study was approved by the Ethics Committee of The First Affiliated Hospital of Chengdu Medical College (No. 23526424).

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Disclosure

The authors declare no conflicts of interest in this work.

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