Original Article

Retrospective study on the prognostic prediction of inflammatory markers and the C-reactive protein/albumin ratio in first-line immunotherapy for advanced HER2 negative gastric cancer patients

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Background: Immune checkpoint inhibitors (ICIs) have shown significant clinical benefits in the treatment of advanced human epidermal growth factor receptor 2 (HER2) negative gastric cancer, and are now widely used in combination with chemotherapy for first-line treatment. However, significant individual variability in the treatment response poses challenges in optimizing therapeutic strategies. Systemic inflammatory biomarkers are gaining attention for their ability to reflect tumor-related inflammation and the immune response balance. These markers could be used to predict treatment outcomes and guide personalized therapy. This study aimed to evaluate the prognostic value of peripheral blood inflammatory markers, such as the Systemic Immune Inflammation Index (SII), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and C-reactive protein/albumin ratio (CAR), in patients with HER2 negative advanced gastric cancer undergoing first-line immunotherapy with ICIs.

Methods: The clinical data of advanced gastric cancer patients treated with immunotherapy at Jiangsu Cancer Hospital between January 2018 and December 2023 were retrospectively collected. The patients were categorized into progressive disease (PD) and effective treatment [complete response (CR), partial response (PR), stable disease (SD)] groups based on their response after two cycles of treatment. The changes in the SII, NLR, PLR, and CAR based on the baseline data and post-treatment measurements were evaluated. The optimal cut-off values for these markers were determined using X-tile software based on their distribution characteristics. Kaplan-Meier survival analysis, log-rank tests, and Cox regression models were used to assess the prognostic ability of these markers.

Results: A total of 142 patients with advanced gastric cancer were included in the study, of whom, 22 had PD after first-line immunotherapy, and 120 had SD. No significant differences were observed in the baseline characteristics of the patients between the effective treatment group and the PD group (P>0.05). Using X-tile software, the optimal cut-off values for the SII, NLR, PLR, and CAR were 548.22 [hazard ratio (HR): 2.421; 95% confidence interval (CI): 1.214–3.710], 3.75 (HR: 3.210; 95% CI: 2.030–5.115), 245.65 (HR: 2.137; 95% CI: 1.577–4.240), and 0.56 (HR: 1.846; 95% CI: 1.388–2.245), respectively. After two cycles of immunotherapy, the NLR, PLR, SII, and CAR values of the patients in the effective treatment (CR + PR + SD) group all decreased significantly. The Kaplan-Meier survival curve analysis showed that the patients with high SII, NLR, PLR, and CAR values had a poorer prognosis in terms of progression-free survival (PFS) and overall survival (OS) (P<0.05) than those with low values.

Conclusions: Inflammatory markers (i.e., the SII, NLR, PLR, and CAR) can be used to predict the prognosis of HER2 negative advanced gastric cancer patients undergoing first-line immunotherapy.

Keywords: Gastric cancer; inflammatory markers; C-reactive protein/albumin ratio (CAR); immunotherapy; prognosis

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Introduction

Gastric cancer is one of the most common malignant tumors of the digestive system (1). In 2020, it was the fifth most common cancer and the fourth leading cause of cancer death worldwide with 1,089,103 new cases, and 768,793 deaths (2). Early gastric cancer often presents with no obvious symptoms or only mild symptoms, and many patients are already in the advanced stage at the time of diagnosis (3).

In recent years, immunotherapy, particularly immune checkpoint inhibitor (ICI) therapy, has shown significant efficacy in the treatment of various advanced solid tumors (4). Several phase-III studies, including CheckMate-649 (5) and ATTRACTION-4 (6), have explored the efficacy of ICI therapy combined with chemotherapy in the first-line treatment of advanced gastric cancer, and the findings of these studies have significantly informed treatment guidelines and clinical practice. Currently, immunotherapy combined with chemotherapy is widely used in the treatment of gastric cancer, and some patients have shown favorable treatment responses, extending their progression-free survival (PFS) and overall survival (OS). However, despite advancements in treatment, the prognosis of advanced gastric cancer patients remains poor, and there is significant individual variability in the efficacy of immunotherapy (7). Some patients may be unresponsive to immunotherapy or may experience immune-related adverse events (8). Therefore, identifying biomarkers that can effectively predict the efficacy of immunotherapy and patient prognosis is crucial to providing more precise treatment options.

Inflammatory responses play a critical role in the occurrence, development, and metastasis of tumors (9). The Systemic Immune Inflammation Index (SII), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and C-reactive protein/albumin ratio (CAR) are systemic inflammatory biomarkers based on neutrophil, lymphocyte, platelet counts, and C-reactive protein (CRP) levels, respectively.

The SII is a comprehensive inflammatory biomarker calculated as the product of the neutrophil count and platelet count divided by the lymphocyte count. The SII reflects both the inflammatory response and immune status of the body. The NLR is another marker that reflects the balance between tumor-related inflammation and the immune response. Elevated neutrophil levels are closely associated with systemic inflammatory responses, which can promote DNA damage and genomic instability, accelerating somatic mutations and enhancing the proliferation of mutated cells (10,11). The PLR is calculated based on the ratio of the platelet count to the lymphocyte count. Platelets play a critical role in the tumor microenvironment by encapsulating tumor cells within thrombi, protecting them from natural killer-cell-mediated cytolysis. The CAR evaluates the comprehensive effect of inflammation and nutrition, which is closely related to tumor progression (12,13).

These markers are closely related to the immune response of the body, and due to their simplicity, low cost,

Highlight box

Key findings

- This study identifies Systemic Immune Inflammation Index (SII), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and C-reactive protein/albumin ratio (CAR) as prognostic biomarkers in human epidermal growth factor receptor 2 (HER2)-negative advanced gastric cancer patients receiving first-line immunotherapy.

What is known and what is new?

- Inflammatory biomarkers are associated with cancer prognosis, but their predictive value in immune checkpoint inhibitors (ICIs)-treated HER2-negative gastric cancer remains unclear.
- The patients with high SII, NLR, PLR, and CAR values have a poorer prognosis in terms of progression-free survival and overall survival. SII is an independent prognostic factor, reinforcing its potential in guiding patient stratification for immunotherapy.

What is the implication, and what should change now?

- SII, NLR, PLR, and CAR can serve as cost-effective prognostic biomarkers for treatment outcome prediction in gastric cancer patients receiving ICIs. Future prospective studies are needed to validate these findings and explore their clinical utility in personalized treatment strategies.

and widespread applicability, they have gained increasing attention in the diagnosis and prognosis of various malignancies, including lung cancer, liver cancer (14), and breast cancer (15). These markers reflect both the immune status and inflammatory level of the body and are closely associated with changes in the tumor microenvironment, which may influence the efficacy of immunotherapy and patient prognosis. However, research on the application of these inflammatory markers in human epidermal growth factor receptor 2 (HER2) negative advanced gastric cancer patients receiving immunotherapy is limited.

This study aimed to evaluate the prognostic value of the SII, NLR, PLR, and CAR in patients with HER2 negative advanced gastric cancer undergoing first-line immunotherapy with ICIs. The study's objective was to develop more precise prognostic assessment tools and to generate robust scientific evidence supporting personalized treatment strategies for patients with advanced gastric cancer. We present this article in accordance with the REMARK reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-192/rc).

Methods

Study design

This retrospective study collected the clinical data of untreated HER2 negative advanced gastric cancer patients at Jiangsu Cancer Hospital between January 2018 and December 2023. The treatment regimen, including the use of ICIs in combination with systemic chemotherapy, was determined based on clinical practice and guidelines. The selection criteria were guided by the study protocol and the treating physician's judgment at the time of therapy initiation. All patients received two cycles of first-line systemic chemotherapy containing ICIs, and underwent a single computed tomography evaluation post-treatment. The sample size was determined retrospectively based on the availability of existing clinical cases. Despite being limited by the nature of retrospective data collection, the sample size was sufficient to ensure the robustness and reliability of the statistical analyses performed in this study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Nanjing Medical University (No. 2023-184). As this study was a retrospective analysis that only used patients' previous clinical and imaging data, the informed consent of the patients was not required.

Inclusion and exclusion criteria

To be eligible for inclusion in the study, the patients had to meet the following inclusion criteria: (I) have histologically or pathologically diagnosed gastric adenocarcinoma; (II) have stage IV disease as per the staging system of the American Joint Committee on Cancer (i.e., be unable to undergo curative surgery, or have post-surgical recurrence and distant metastasis); (III) have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2; (IV) have complete clinical data before treatment and imaging data available for effective evaluation; (V) have not undergone antitumor treatment previously; (VI) have HER2 negative expression; and (VII) have undergone at least two cycles of immunotherapy. Patients were excluded from the study if they met any of the following exclusion criteria: (I) had incomplete clinical or follow-up data; (II) had multiple primary tumors or mixed pathological types; (III) had concurrent hematological or immune system diseases; and/or (IV) had severe organ dysfunction.

Data collection and follow-up

The clinical data were collected retrospectively from the hospital's electronic medical records. Clinical, pathological and blood test data were retrospectively collected by two senior oncologists independently. Both oncologists had extensive experience in the diagnosis and treatment of gastric cancer. Any discrepancies in data interpretation were resolved through discussion to reach a consensus. Clinical characteristics, such as age, gender, smoking history, alcohol consumption, ECOG score, tumor location, surgical history, metastasis site/s, and treatment plans were recorded. Baseline and post-two-cycle peripheral blood test data, including the neutrophil count, lymphocyte count, platelet count, CRP, and albumin level, were also documented. Microsatellite instability (MSI) status and combined positive score (CPS) level were not systematically assessed for most patients in this retrospective study; therefore, no specific inclusion or exclusion criteria were applied based on MSI status and CPS level was not included in the analysis. The ratios were calculated as follows:

$$SII = N \times P/L \quad [1]$$

$$NLR = N/L \quad [2]$$

$$PLR = P/L \quad [3]$$

$$CAR = C/A \quad [4]$$

where N represents the neutrophil count, L represents the lymphocyte count, P represents the platelet count, A represents the albumin level, and C represents the CRP.

Treatment efficacy was classified as a complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD) using the Response Evaluation Criteria in Solid Tumors version 1.1 or the Response Evaluation Criteria in Solid Tumors for immune-based therapeutics. The patients were allocated to the effective treatment group (comprising the patients with a CR + PR + SD) and the PD group based on their response after two cycles of immunotherapy.

Statistical methods

SPSS Statistics 26.0 (IBM Corp., Armonk, NY, USA) and Graphpad Prism 9 (GraphPad Software, San Diego, CA, USA) were used for the data analysis. Comparisons between groups were performed using the independent sample *t*-test or an analysis of variance for the continuous variables, and the Chi-squared test for the categorical variables. X-tile software (Yale School of Medicine, New Haven, CT, USA) was used to determine the optimal cut-off values for the NLR, PLR, SII, and CAR. The Wilcoxon test was used to evaluate the relationship between changes in tumor efficacy and inflammatory markers. The survival analysis was conducted using the Kaplan-Meier method and the log-rank test, and Cox regression models were used for the univariate and multivariate analyses.

Results

Patients' baseline data

A total of 185 patients with untreated advanced gastric cancer were initially identified from the database. After the application of the inclusion and exclusion criteria, 43 patients were excluded due to incomplete follow-up data (n=23), a lack of baseline inflammatory marker measurements (n=12), or a misdiagnosis of tumor stage (n=8). Thus, ultimately, 142 patients were included in the final analysis, of whom 22 experienced PD, and 120 maintained SD. The median follow-up time was 35.5 months (range, 3.5–61 months). No significant differences were observed between the patients in the effective treatment and PD groups in terms of the baseline characteristics (P<0.05) (*Table 1*).

Changes in the SII, NLR, PLR, and CAR values after two cycles of immunotherapy

After two cycles of treatment, the patients in the effective group (CR + PR + SD) showed a significant decrease in the markers of SII, NLR, PLR, and CAR, while those in the PD group showed an increase in the markers, especially in their PLR and CAR values (*Figure 1*).

Survival analysis

Using X-tile software, the optimal cut-off values for the SII, NLR, PLR, and CAR were 548.22 [hazard ratio (HR): 2.421; 95% confidence interval (CI): 1.214–3.710], 3.75 (HR: 3.210; 95% CI: 2.030–5.115), 245.65 (HR: 2.137; 95% CI: 1.577–4.240), and 0.56 (HR: 1.846; 95% CI: 1.388–2.245), respectively. The Kaplan-Meier survival curves indicated that patients with high SII, NLR, PLR, and CAR values had a poorer prognosis in terms of PFS and OS than those with low values (P<0.05) (*Figure 2*).

Cox regression analysis

The univariate analysis showed that the ECOG score, differentiation, the SII, and the NLR were associated with OS (P<0.05). The multivariate analysis showed that the SII was an independent predictor of OS (P<0.05) (*Table 2*).

Discussion

Immunotherapy has been widely applied in the treatment of cancer. The ORIENT-16 study, conducted in the Chinese population, evaluated the efficacy of first-line sintilimab combined with the XELOX regimen (16), and found that the combination therapy significantly prolonged the OS of the entire population (15.2 *vs.* 12.3 months; HR: 0.766; 95% CI: 0.626–0.936; P=0.009). However, a phase-III Asian study, ATTRACTION-4, showed that nivolumab combined with chemotherapy (either XELOX or SOX) significantly extended the median PFS (10.5 *vs.* 8.3 months; HR: 0.68; 95% CI: 0.51–0.90; P=0.0007), with objective response rate (ORR) of 57% and 48%, respectively; however, the combination therapy did not produce any OS benefit (17.5 *vs.* 17.2 months; HR: 0.90; 95% CI: 0.75–1.08; P=0.26). This result is inconsistent with the OS outcome of the CheckMate-649 study; however, this may be due to differences in the patients' baseline characteristics,

Table 1 Patients' baseline data

Variables	PD group (n=22)	CR + PR + SD group (n=120)	χ^2	P value
Gender			0.229	0.63
Male	12 (54.5)	72 (60.0)		
Female	10 (45.5)	48 (40.0)		
Age (years)			0.352	0.55
<65	8 (36.4)	36 (30.0)		
≥65	14 (63.6)	84 (70.0)		
Surgical history			0.168	0.68
No	16 (72.7)	82 (68.3)		
Yes	6 (27.3)	38 (31.7)		
Smoking history			0.012	0.91
No	18 (81.8)	97 (80.8)		
Yes	4 (18.2)	23 (19.2)		
Drinking history			3.176	0.08
No	15 (68.2)	101 (84.2)		
Yes	7 (31.8)	19 (15.8)		
ECOG score			0.373	0.54
0–1	18 (81.8)	91 (75.8)		
2	4 (18.2)	29 (24.2)		
Primary tumor location			1.857	0.17
GEJ	2 (9.1)	26 (21.7)		
Non-GEJ	20 (90.9)	94 (78.3)		
Primary tumor size (cm)			1.265	0.26
<5	5 (22.7)	42 (35.0)		
≥5	17 (77.3)	78 (65.0)		
Differentiation			1.19	0.27
Poor	9 (40.9)	35 (29.2)		
Well or moderate	13 (59.1)	85 (70.8)		
Lung metastasis			0.068	0.79
No	3 (13.6)	14 (11.7)		
Yes	19 (86.4)	106 (88.3)		
Liver metastasis			2.772	0.10
No	7 (31.8)	20 (16.7)		
Yes	15 (68.2)	100 (83.3)		
Bone metastasis			0.939	0.33
No	6 (27.3)	22 (18.3)		
Yes	16 (72.7)	98 (81.7)		

Data are presented as n (%). CR, complete response; ECOG, Eastern Cooperative Oncology Group; GEJ, gastroesophageal junction adenocarcinoma; PD, progressive disease; PR, partial response; SD, stable disease.

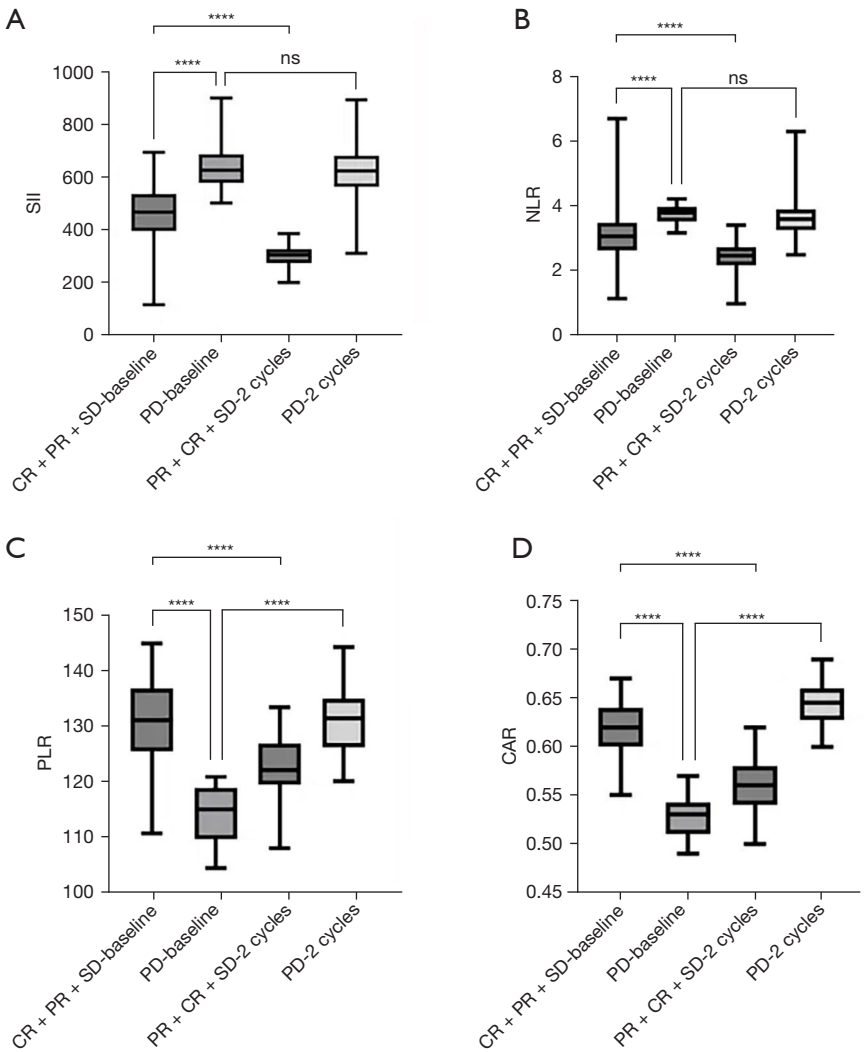

Figure 1 Changes in biomarkers after two cycles of treatment: patients in the effective treatment (CR + PR + SD) group showed a significant decrease in these markers, while those in the PD showed an increase in these markers, particularly in the PLR and CAR values. (A) Changes in the SII; (B) changes in the NLR; (C) changes in the PLR; (D) changes in the CAR. ****, indicates P<0.001; ns indicates no statistically significant difference (P>0.05). CAR, C-reactive protein/albumin ratio; CR, complete response; NLR, neutrophil-to-lymphocyte ratio; PD, progressive disease; PLR, platelet-to-lymphocyte ratio; PR, partial response; SD, stable disease; SII, Systemic Immune Inflammation Index.

ethnicity, and subsequent treatment regimens. Thus, there is still a lack of ideal biomarkers for evaluating treatment efficacy and predicting the outcomes of patients undergoing immunotherapy (17).

MSI (18), programmed death-ligand 1 (PD-L1) (19), the tumor mutational burden (TMB) (20), and Epstein-Barr virus infection (20) are currently recognized as potential biomarkers for assessing the efficacy of immunotherapy in gastric cancer (21). However, many challenges arise in efficacy assessments of these biomarkers; for example, PD-L1 expression can vary depending on multiple factors, such as the choice of detection antibody, the diagnostic platform employed, the anatomical tumor site, and spatiotemporal heterogeneity. The optimal PD-L1 cut-off value for different treatment regimens remains unclear. At the same time, patients with a high-TMB generally exhibit better responses to immunotherapy. This association is particularly evident in tumors such as melanoma, lung cancer, and bladder cancer, where the neoantigen load is positively correlated with $CD8^+$ T cell infiltration. In

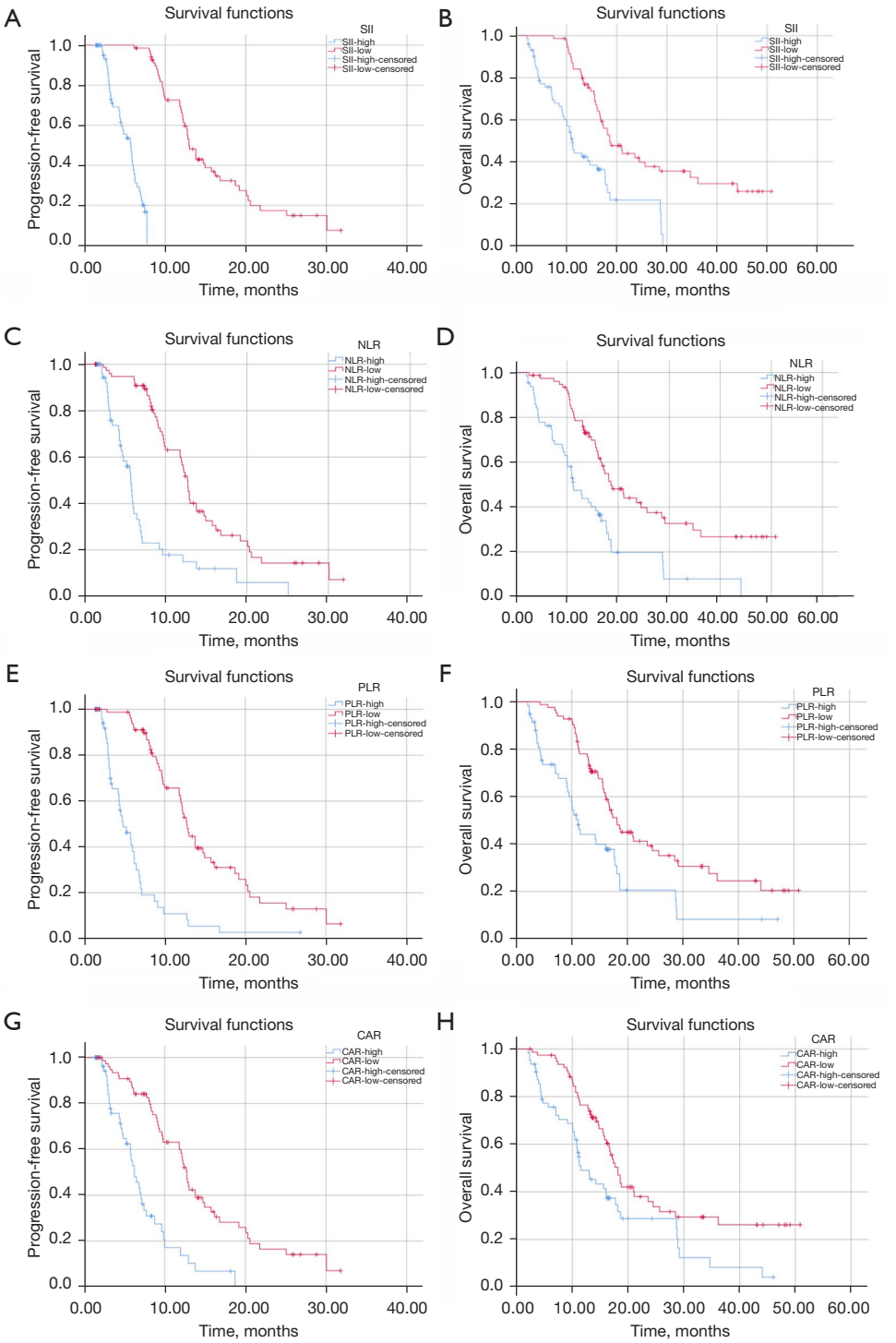

Figure 2 Kaplan-Meier survival curves for patients with high and low SII, NLR, PLR, and CAR values: patients with higher values for these biomarkers had poorer PFS and OS than those with lower values (P<0.05). (A,B) The PFS and OS curves for high and low SII values, respectively; (C,D) the PFS and OS curves for high and low NLR values, respectively; (E,F) the PFS and OS curves for high and low PLR values, respectively; (G,H) the PFS and OS for high and low CAR values, respectively. CAR, C-reactive protein/albumin ratio; NLR, neutrophil-to-lymphocyte ratio; OS, overall survival; PFS, progression-free survival; PLR, platelet-to-lymphocyte ratio; SII, Systemic Immune Inflammation Index.

Table 2 Cox regression analysis

Factors	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (≥65/<65 years)	1.180 (0.730–1.860)	0.55		
Gender (male/female)	0.740 (0.410–1.330)	0.29		
ECOG status (0–1/2)	1.640 (0.810–3.305)	<0.001	1.175 (0.625–2.209)	0.48
Differentiation (poor/well-moderate)	1.876 (1.095–3.221)	<0.001	1.051 (0.568–1.937)	0.94
Previous surgery (no/yes)	0.635 (0.450–1.315)	0.052		
Primary tumor size (≥5/<5 cm)	1.670 (1.012–2.804)	0.07		
SII (≥548.22/<548.22)	2.421 (1.214–3.710)	<0.001	2.495 (1.231–5.508)	0.01
NLR (≥3.75/<3.75)	3.210 (2.030–5.115)	<0.001	1.032 (0.568–1.847)	0.82
PLR (≥245.65/<245.65)	2.137 (1.577–4.240)	0.71		
CAR (≥0.56/<0.56)	1.846 (1.388–2.245)	0.67		

CAR, C-reactive protein/albumin ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; HR, hazard ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SII, Systemic Immune Inflammation Index.

such cases, high-TMB patients show significantly higher ORR than low-TMB patients. Conversely, for tumors that are not associated with these markers (e.g., breast cancer, prostate cancer, and gliomas), high TMB patients exhibit a significantly lower ORR than low TMB patients. Compared to current biomarkers, such as PD-L1, MSI, and TMB, serum inflammatory markers offer the advantages of convenience, repeatability, and cost-effectiveness (22). Therefore, their predictive and prognostic value has been analyzed in various cancers, such as non-small cell lung cancer (23) and renal cancer (24).

This study analyzed baseline inflammatory markers (the SII, NLR, PLR, and CAR) and their dynamic changes in advanced first-line HER2 negative gastric cancer patients who underwent immunotherapy. We found that these inflammatory markers were closely related to treatment outcomes. Our Kaplan-Meier survival curve analysis showed that higher SII, NLR, PLR, and CAR values are associated with a poorer survival prognosis, which suggests that these markers may have potential predictive value during immunotherapy in advanced gastric cancer patients. This result is consistent with previous findings (25,26) that suggest that inflammation, as a crucial component of the tumor microenvironment, affects the immune evasion and resistance mechanisms of tumors. Lymphocytes are a key component of the immune system and play a crucial role in recognizing and eliminating tumor cells. In patients with malignancies, inflammatory responses within the tumor microenvironment can lead to immunosuppression, including increased neutrophil activity. This immunosuppressive state may weaken the body's ability to mount an effective antitumor response, allowing tumor cells to evade immune surveillance and progress to advanced disease. Additionally, platelet activation can suppress immune cell function by releasing pro-inflammatory cytokines, thereby reducing the host's antitumor immunity, facilitating immune evasion, and promoting tumor progression (27). These mechanisms contribute to the prognostic value of systemic inflammatory biomarkers, such as SII, which integrates the effects of neutrophils, platelets, and lymphocytes, providing a more comprehensive measure of the host immune-inflammatory status. Therefore, the detection of inflammatory markers can not only help assess the patient's immune response status but can also serve as a basis for individualized treatment, predicting treatment efficacy and patient survival.

This study also explored the relationship between changes in inflammatory markers (the SII, NLR, PLR, and CAR) after two cycles of immunotherapy and the treatment outcomes. The results showed that in the effective treatment (CR + PR + SD) group, the levels of the NLR, PLR, SII, and CAR significantly decreased, indicating that the immunotherapy effectively improved the patients' immune response and reduced systemic inflammation. Conversely, in the PD group, the NLR, PLR, SII, and CAR values increased, suggesting that the immune suppression status of

these patients was not effectively relieved, and inflammation may intensify with tumor progression. Several meta-analyses have highlighted the prognostic significance of inflammatory markers in advanced gastric cancer treated with ICIs. Tan *et al.* demonstrated that elevated NLR and PLR were associated with poorer OS and PFS, whereas high LMR correlated with improved survival (28). Similarly, Hu *et al.* reported that high baseline PLR was linked to shorter 1-year OS and 6-month PFS in stage IV GC patients, suggesting its potential involvement in tumor progression (29). These findings support the role of dynamic changes in inflammatory markers as predictive factors of the immunotherapy response. Monitoring these markers can provide real-time treatment efficacy information for clinicians that can be used to adjust treatment plans, and improve patients' quality of life and prognosis.

Unexpectedly, a higher proportion of patients with liver metastases was observed in the Effective group compared to the PD group, despite liver metastases being reported as a negative predictive factor for checkpoint inhibitors. This finding could be attributed to the impact of combination therapy, favorable prognostic factors in the Effective group, or the heterogeneity of liver metastases. Given the complex interplay between systemic inflammation and treatment response, we further explored the prognostic value of inflammatory biomarkers. Among the markers analyzed, SII was the only one that remained an independent prognostic factor in the multivariate analysis, suggesting its stronger predictive power compared to NLR, PLR, and CAR. Unlike NLR and PLR, which only reflect the balance between two immune components, SII incorporates neutrophils, platelets, and lymphocytes, providing a more comprehensive measure of systemic inflammation and immune response. Additionally, CAR, which is influenced by CRP and albumin levels, may be affected by factors unrelated to tumor progression, such as nutritional status. These findings support the use of SII as a robust prognostic biomarker in advanced gastric cancer treated with immunotherapy. Further studies are warranted to validate its predictive value in larger cohorts.

Conclusions

Currently, immunotherapy represents an important direction in the treatment of advanced gastric cancer, but evaluating the efficacy of immunotherapy and predicting patient prognosis remains a clinical challenge. This study provides strong evidence supporting the use of inflammatory markers as predictive tools for immunotherapy in clinical practice, especially in patients with advanced gastric cancer. The sample size of 142 patients was limited by the retrospective nature of this study; however, it was sufficient for the multivariate analysis of the SII and other markers. The findings provide a robust basis for further research in larger prospective cohorts. Future research could seek to explore the mechanisms of these markers in combination with immunotherapy, particularly in different immunotherapy regimens. Additionally, combining inflammatory markers with other molecular markers (e.g., PD-L1 expression and the TMB) may provide more information for precision therapy. Moreover, investigating how these markers can predict the occurrence of treatment resistance and exploring their role in individualized therapy will be an important direction for future research.

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None.

Footnote

Reporting Checklist: The authors have completed the REMARK reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-192/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-192/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-192/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). The study was approved by the Ethics Committee of Nanjing Medical University (No. 2023-184). As this study was a retrospective analysis that only used patients' previous clinical and imaging data, the informed consent of the patients was not required.

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