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ORIGINAL RESEARCH

# Gustave Roussy Immune Score (GRImScore) as a Novel Prognostic Index for Stage III Gastric Cancer Patients: A Real-World Retrospective Study

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**Objective:** This study aimed to investigate whether Gustave Roussy immune score (GRImScore) serves as a novel prognostic index for predicting survival in patients with advanced gastric cancer.

**Methods:** GRImScore was based on three objective markers: (1) albumin level (<3.5 g/L = 1 point, ≥3.5 g/L = 0 point); (2) lactate dehydrogenase level (≥250 U/L = 1 point, <250 U/L = 0 point); (3) neutrophil to lymphocyte ratio (NLR) (≥2.70 = 1 point, <2.70 = 0 point). According to GRImScore, these patients were divided into low GRImScore group (0 points) and high GRImScore group (1, 2, or 3 points). Kaplan–Meier method was applied to draw survival curves for disease free survival (DFS) and overall survival (OS), and differences among these groups were analyzed using Log rank tests. Univariate and multivariate Cox proportional hazards models were used to analyze the relationship between the enrolled parameters and OS. Nomograms were developed based on the results of multivariate Cox regression analysis using the consistency index (C-index) and decision curve analyses (DCA) for internal validation.

**Results:** Based on GRImScore, 134 patients were in low GRImScore group and 61 were in high GRImScore group. The median DFS and OS in low GRImScore group were significantly longer than that in high GRImScore group (DFS: 40.52 months vs 22.83 months, $\chi^2$=7.033, *P*=0.0080; OS: 55.07 months vs 31.83 months, $\chi^2$=6.328, *P*=0.0119). According to multivariable Cox analysis, GRImScore was significantly associated with DFS (HR, 2.798; 95% CI: 1.711–11.008, *P* = 0.001) and OS (HR, 2.631; 95% CI: 1.645–10.725, *P* = 0.001). The nomogram constructed by multivariate Cox analysis showed good performance in predicting DFS (C-index: 0.717, 95% CI: 0.595–0.814) and OS (C-index: 0.725, 95% CI: 0.605–0.819).

**Conclusion:** GRImScore, a novel prognostic index, is a prognostic indicator for patients with advanced gastric cancer. Nomograms based on the GRImScore showed good predictive ability.

**Keywords:** advanced gastric cancer, Gustave Roussy immune score, GRImScore, albumin, neutrophil to lymphocyte ratio

## Introduction

Gastric cancer (GC) has the highest incidence rate in Asia, accounting for 75.7% of global gastric cancer cases (968,350 new cases worldwide).[1] GC has the fifth and third highest incidence and mortality rates, respectively, and there are approximately 359,000 new cases of gastric cancer and 260,000 deaths from GC in China.[2] Radical surgical resection and lymph node dissection remain the primary treatments for GC, and adjuvant therapy, including chemotherapy, radiotherapy, and targeted therapy, are also the primary treatment option for GC.[3] Although the global burden of GC has shown an obvious downward trend, GC remains a major global health challenge in certain areas, such as China, Japan, and South Korea.[4] These treatment methods aim to prolong the survival time and improve the quality of life of patients; however, some clinical studies have demonstrated that these treatment methods cannot sufficiently improve the prognosis and survival rate of patients. In recent years, some clinical trials have been conducted to explore new treatment methods or biomarkers for gastric cancer.[5–7]

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Recently, numerous studies have demonstrated a relationship between inflammation, nutrition, immunity, and tumorigenesis.[8–10] Different scoring systems are constructed by combining clinical and laboratory parameters used to guide clinical patient selection and prognosis assessment, and dividing patients into different prognostic risk groups.[11–13] In Mezheyeuski A's study, they generated a signature of immune activation (SIA, ratio of CD8A to C1QA), this score was the independent of conventional parameters and comparable with the state-of-art immune score, and was also associated with patient survival in oesophageal adenocarcinoma, bladder cancer, lung adenocarcinoma and melanoma.[11] In Min-Oo HH's study, they used four commonly biochemical markers to construct a prognostic score for intrahepatic cholangiocarcinoma patients, including serum aspartate aminotransferase, alkaline phosphatase, cystatin C and creatinine-based estimated glomerular filtration rate.[12]

Among the burgeoning biological indicators, Gustave Roussy immune score (GRImScore) was first elaborated based on lactate dehydrogenase (LDH) level, albumin level, total bilirubin level, AST-to-ALT ratio, and neutrophil to lymphocyte ratio (NLR) were used to select patients undergoing treatment with immune-checkpoint therapies (ICTs) during Phase I trials.[14] In Basoglu T's study, they demonstrated that high GRIm score was an independent poor prognostic factor, and GRIm score can be used as a noninvasive, easily applicable, practical prognostic factor in pancreatic cancer patients.[15] Other study also found that GRIm score was useful for predicting postoperative complications in elderly colon cancer patients and might be suitable as a surrogate marker for selecting candidates for surgery or perioperative treatment.[16]

The representativeness of advanced gastric cancer (AGC) patients in the discovery and validation cohorts of these scoring systems is insufficient, especially in stage III gastric cancer. However, the ability of this prognostic score to predict the survival time of advanced gastric cancer patients is still unknown. The objective of the current study was to investigate whether the GRImScore serves as a novel prognostic index for predicting survival in patients with AGC.

# Patients and Methods

## Patients Section

A total of 195 patients with advanced gastric cancer who underwent surgery at the Xingtai People's Hospital between January 2016 and December 2017 were enrolled in this study. Clinical and pathological information was obtained retrospectively from the electronic medical records system. This study was approved by the Ethics Committee of Xingtai People's Hospital (20251412) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all the enrolled patients.

All selected patients were diagnosed with AGC in accordance with histopathological examination. The inclusion criteria were as follows: (1) hematological examinations, including routine blood and biochemical examinations, were performed after admission, (2) detailed information of medical records and follow-up data, (3) all enrolled patients received surgical treatment, and (4) no evidence of organ metastasis. The exclusion criteria were: (1) received antitumor therapy such as preoperative chemotherapy, (2) other malignant tumors or metastatic tumors, and (3) accompanying autoimmune diseases that could not be controlled.

## GRImScore Calculation Method

In this study, the GRImScore was calculated using three objective markers: (1) albumin level (<3.5 g/L = 1 point, ≥3.5 g/L = 0 point); (2) lactate dehydrogenase (LDH) level (≥250 U/L = 1 point, < 250 U/L = 0 point); and (3) neutrophil-to-lymphocyte ratio (NLR) (≥2.70 = 1 point, <2.70 = 0 points). Before surgery, the peripheral neutrophil count was divided by the lymphocyte count to calculate NLR. The best critical value for NLR was determined using ROC analysis with the highest sensitivity and specificity for predicting OS. NLR was 2.70 in the current study. According to GRImScore, these patients were divided into a low GRImScore group (0 points) and a high GRImScore group (1, 2, or 3 points).

## Followed-up

Survival information was obtained via telephone or outpatient follow-up. We defined the duration from surgery to death of the patient for any reason or the date of the last follow-up as overall survival (OS), and the interval from surgery to the occurrence of either local or distant metastasis as disease-free survival (DFS). The last follow-up was conducted on April 10, 2024.

## Data Analysis Statistics

Statistical analysis was conducted using SPSS Statistics software (version 26.0; IBM Corporation) and R statistical computing language version 4.2.2 (http://www.R-project.org/). The clinicopathological characteristics of patients with advanced gastric cancer were analyzed using descriptive statistics. Differences between groups were determined using Fisher's exact test and chi-squared test for numerical variables. The median survival time of OS and DFS were determined using the Kaplan–Meier method, and differences in survival time were determined using the log rank test. The underlying independent variables associated with OS and DFS were determined using the Cox proportional hazard regression model. The constructed models were described using hazard ratios (HR) and 95% confidence intervals (CI). The best critical value for NLR is the receiver operating characteristic (ROC) curve, which has the highest sensitivity and specificity for predicting OS. Nomograms were developed based on the results of multivariate Cox regression analysis using the consistency index (C-index) and decision curve analyses (DCA) for internal validation. Statistical significance was defined as a *P*-value less than 0.05.

# Results

## Association of Prognostic Scores with Survival

According to the best critical value for NLR by ROC, these patients with advanced gastric cancer were divided into a low NLR group (<2.70) and a high NLR group (≥2.70) in this study. There were 143 cases with an NLR score of 0 divided into the low NLR group and 52 cases with an NLR score of 1 divided into the high NLR group. The median DFS and OS in low NLR group were significantly longer than that in high NLR group (DFS: 40.77 months vs 22.00 months, $\chi^2$=8.437, *P*=0.0037; OS: 54.87 months vs 30.12 months, $\chi^2$=7.297, *P*=0.0069) (Figure 1A and B). Based on the GRImScore, 134 cases with GRImScore 0 were divided into the low-score group, and 61 cases with GRImScore from 1 to 3 points were divided into the high-score group. The median DFS and OS in low GRImScore group were significantly longer than that in high GRImScore group (DFS: 40.52 months vs 22.83 months, $\chi^2$=7.033, *P*=0.0080; OS: 55.07 months vs 31.83 months, $\chi^2$=6.328, *P*=0.0119) (Figure 1C and D).

## Baseline Characteristics According to GRImScore

A total of 195 patients with AGC were enrolled in this study between January 2016 and December 2017 at our hospital. The study included 129 men (66.2%) and 66 women (33.8%). The median age of the patients was 60 years (range: 28–83 years). According to the TNM stage system, the 195 stage III cases comprised: 72 (36.9%) IIIA (T2-4aN1-3aM0), 82 (42.1%) IIIB (T3-4bN0-3bM0), and 41 (21.0%) IIIC (T4a-4bN3a-bM0). Of these patients, 156 (80.0%) underwent distal gastrectomy, 9 (4.6%) underwent proximal gastrectomy, and 30 (15.4) underwent total gastrectomy. GRImScore showed a statistically significant association with the type of surgery (*P*=0.026) and postoperative chemotherapy (*P*=0.014) (Table 1).

## Comparing the Performance of GRImScore Based on Common Hematological Parameters

In the current study, we enrolled patients with common hematological parameters, including ALT, AST, GGT, TBIL, DBIL, IDBIL, TP, ALB, GLOB, A/G, PALB, Urea, CREA, UA, ALP, Glu, CHOL, TRIG, LDH, W, N, L, M, E, B, Hb, R, Hct, P, NLR, INR, FIB, CEA, AFP, CA199, CA724, CA125. The parameters were divided into two groups based on the median hematological parameter values. The GRImScore was significantly associated with ALT (*P*=0.021), ALB (*P*=0.001), PALB (*P*<0.001), CHOL (*P*=0.009), TRIG (*P*=0.022), N (*P*=0.005), L (*P*<0.001), Hb (*P*=0.012), R (*P*=0.046), NLR (*P*<0.001), INR (*P*=0.019), and FIB (*P*<0.001). Detailed information is provided in Table 2.

## Univariate Analysis and Multivariate Cox Analysis

In this study, we used GRImScore, sex, age, BMI, ALT, AST, TBIL, TP, GLOB, A/G, PALB, ALP, CHOL, TRIG, ABO blood type, W, N, L, Hb, R, P, INR, FIB, CEA, AFP, CA199, CA724, CA125, radical resection, type of surgery, primary tumor site, TLN, PLN, tumor size, differentiation, pTNM stage, Lauren type, HER2, CK, and postoperative

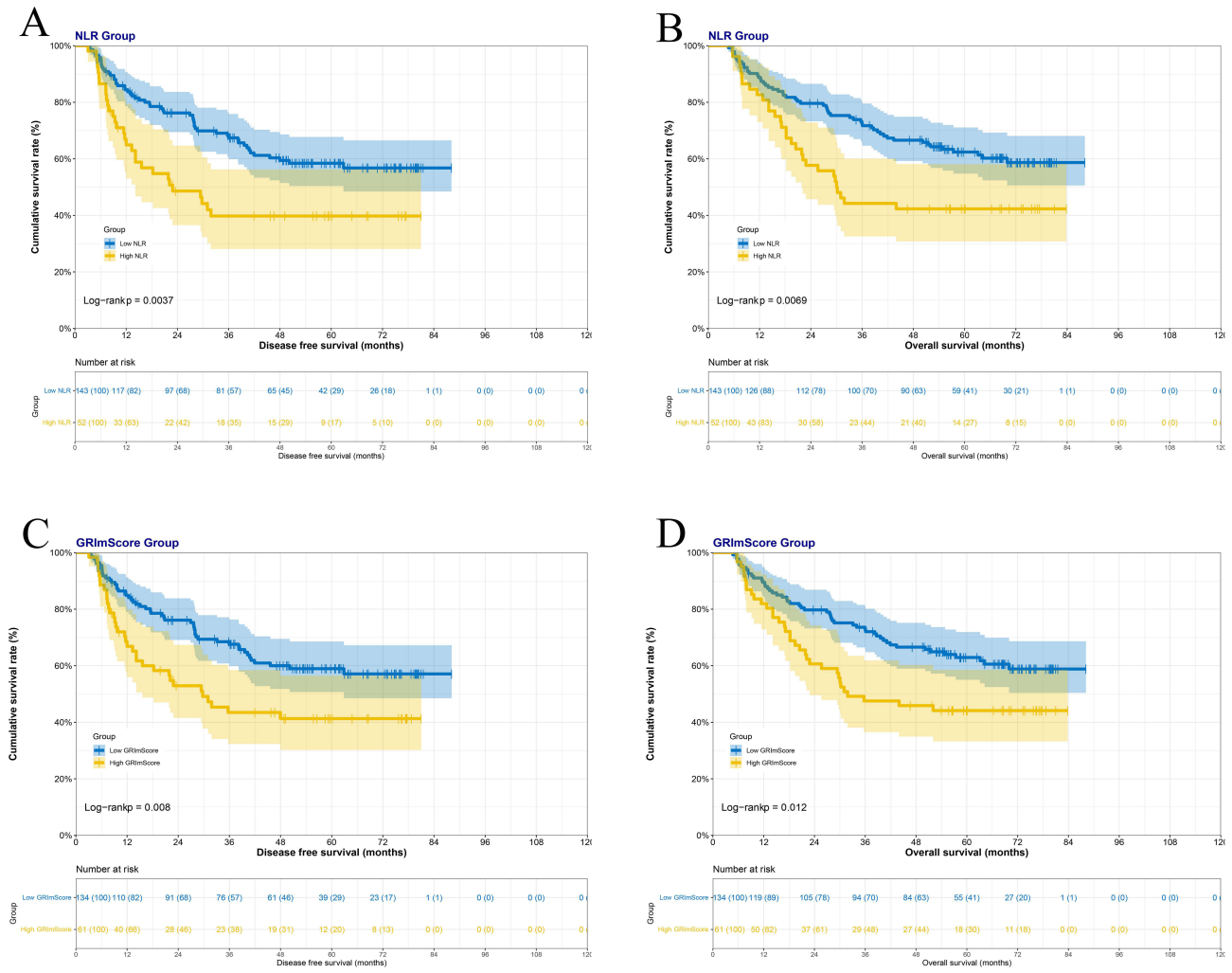


**Figure 1** Kaplan–Meier survival curves of advanced gastric cancer patients for DFS (**A** and **C**) and OS (**B** and **D**) stratified by NLR or GRImScore.

chemotherapy. In the univariate analysis of DFS, GRImScore, PALB, Hb, CA199, type of surgery, TLN, tumor size, pTNM stage, CK, and postoperative chemotherapy were significant factors. Multivariate analysis showed that GRImScore, PALB, Hb, CA199, type of surgery, TLN, tumor size, pTNM stage, and postoperative chemotherapy were potential prognostic factors for DFS (Table 3). In the univariate analysis of OS, GRImScore, GLOB, PALB,

**Table 1** The Clinical Pathological Characteristics According to the GRImScore

| Parameters<br>n | Level | Overall<br>195 | Low GRImScore<br>134 | High GRImScore<br>61 | *P* |
|---|---|---|---|---|---|
| Sex | Male | 129 (66.2) | 89 (66.4) | 40 (65.6) | 1.000 |
| | Female | 66 (33.8) | 45 (33.6) | 21 (34.4) | |
| Age (years) | ≤60 | 94 (48.2) | 71 (53.0) | 23 (37.7) | 0.068 |
| | >60 | 101 (51.8) | 63 (47.0) | 38 (62.3) | |
| Weight (kg) | ≤60 | 85 (43.6) | 58 (43.3) | 27 (44.3) | 1.000 |
| | >60 | 110 (56.4) | 76 (56.7) | 34 (55.7) | |
| Height (cm) | ≤168 | 90 (46.2) | 60 (44.8) | 30 (49.2) | 0.677 |
| | >168 | 105 (53.8) | 74 (55.2) | 31 (50.8) | |

(*Continued*)

**Table 1** (Continued).

| Parameters<br>n | Level | Overall<br>195 | Low GRImScore<br>134 | High GRImScore<br>61 | *P* |
|---|---|---|---|---|---|
| BMI | ≤22.10 | 95 (48.7) | 62 (46.3) | 33 (54.1) | 0.390 |
| | >22.10 | 100 (51.3) | 72 (53.7) | 28 (45.9) | |
| Radical resection | R0 | 159 (81.5) | 114 (85.1) | 45 (73.8) | 0.166 |
| | R1 | 23 (11.8) | 13 (9.7) | 10 (16.4) | |
| | R2 | 13 (6.7) | 7 (5.2) | 6 (9.8) | |
| Type of surgery | Distal gastrectomy | 156 (80.0) | 104 (77.6) | 52 (85.2) | 0.026 |
| | Proximal gastrectomy | 9 (4.6) | 4 (3.0) | 5 (8.2) | |
| | Total gastrectomy | 30 (15.4) | 26 (19.4) | 4 (6.6) | |
| Primary tumor site | Upper 1/3 | 17 (8.7) | 11 (8.2) | 6 (9.8) | 0.312 |
| | Middle 1/3 | 20 (10.3) | 13 (9.7) | 7 (11.5) | |
| | Low 1/3 | 132 (67.7) | 88 (65.7) | 44 (72.1) | |
| | Whole | 26 (13.3) | 22 (16.4) | 4 (6.6) | |
| TLN | ≤30 | 94 (48.2) | 61 (45.5) | 33 (54.1) | 0.339 |
| | >30 | 101 (51.8) | 73 (54.5) | 28 (45.9) | |
| PLN | ≤8 | 97 (49.7) | 67 (50.0) | 30 (49.2) | 1.000 |
| | >8 | 98 (50.3) | 67 (50.0) | 31 (50.8) | |
| Tumor size | ≤20 mm | 31 (15.9) | 25 (18.7) | 6 (9.8) | 0.260 |
| | >20 and >50 mm | 91 (46.7) | 59 (44.0) | 32 (52.5) | |
| | ≥50 mm | 73 (37.4) | 50 (37.3) | 23 (37.7) | |
| Differentiation | Poorly differentiated | 94 (48.2) | 69 (51.5) | 25 (41.0) | 0.359 |
| | Moderately differentiated | 99 (50.8) | 64 (47.8) | 35 (57.4) | |
| | Well differentiated | 2 (1.0) | 1 (0.7) | 1 (1.6) | |
| Pathology | Adenocarcinoma | 69 (35.4) | 51 (38.1) | 18 (29.5) | 0.055 |
| | Mucinous carcinoma | 8 (4.1) | 3 (2.2) | 5 (8.2) | |
| | Signet ring cell carcinoma | 8 (4.1) | 8 (6.0) | 0 (0.0) | |
| | Mixed carcinoma | 109 (55.9) | 71 (53.0) | 38 (62.3) | |
| | Others | 1 (0.5) | 1 (0.7) | 0 (0.0) | |
| pTNM stage | IIIA | 72 (36.9) | 49 (36.6) | 23 (37.7) | 0.850 |
| | IIIB | 82 (42.1) | 58 (43.3) | 24 (39.3) | |
| | IIIC | 41 (21.0) | 27 (20.1) | 14 (23.0) | |
| pT stage | T2 | 2 (1.0) | 1 (0.7) | 1 (1.6) | 0.468 |
| | T3 | 104 (53.3) | 72 (53.7) | 32 (52.5) | |
| | T4a | 69 (35.4) | 50 (37.3) | 19 (31.1) | |
| | T4b | 20 (10.3) | 11 (8.2) | 9 (14.8) | |
| pN stage | N0 | 7 (3.6) | 4 (3.0) | 3 (4.9) | 0.941 |
| | N1 | 21 (10.8) | 15 (11.2) | 6 (9.8) | |
| | N2 | 74 (37.9) | 50 (37.3) | 24 (39.3) | |
| | N3a | 67 (34.4) | 46 (34.3) | 21 (34.4) | |
| | N3b | 26 (13.3) | 19 (14.2) | 7 (11.5) | |
| Lauren type | Intestinal | 85 (43.6) | 57 (42.5) | 28 (45.9) | 0.579 |
| | Diffuse | 51 (26.2) | 38 (28.4) | 13 (21.3) | |
| | Mixed | 59 (30.3) | 39 (29.1) | 20 (32.8) | |
| HER2 | No | 182 (93.3) | 128 (95.5) | 54 (88.5) | 0.132 |
| | Yes | 13 (6.7) | 6 (4.5) | 7 (11.5) | |
| CK | No | 24 (12.3) | 21 (15.7) | 3 (4.9) | 0.060 |
| | Yes | 171 (87.7) | 113 (84.3) | 58 (95.1) | |
| Postoperative chemotherapy | No | 91 (46.7) | 71 (53.0) | 20 (32.8) | 0.014 |
| | Yes | 104 (53.3) | 63 (47.0) | 41 (67.2) | |

**Abbreviations**: BMI, Body mass index; TLN, Total lymph node; PLN, Positive lymph node; HER2, Human epidermal growth factor receptor 2; CK, Cytokeratin.


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**Table 2** The Common Hematological Parameters Characteristics According to the GRImScore

| Parameters<br>n | Level | Overall<br>195 | Low GRImScore<br>134 | High GRImScore<br>61 | *P* |
|---|---|---|---|---|---|
| ALT | ≤18.50 | 96 (49.2) | 58 (43.3) | 38 (62.3) | 0.021 |
| | >18.50 | 99 (50.8) | 76 (56.7) | 23 (37.7) | |
| AST | ≤21.70 | 88 (45.1) | 56 (41.8) | 32 (52.5) | 0.218 |
| | >21.70 | 107 (54.9) | 78 (58.2) | 29 (47.5) | |
| GGT | ≤14.20 | 95 (48.7) | 61 (45.5) | 34 (55.7) | 0.243 |
| | >14.20 | 100 (51.3) | 73 (54.5) | 27 (44.3) | |
| TBIL | ≤10.13 | 98 (50.3) | 63 (47.0) | 35 (57.4) | 0.235 |
| | >10.13 | 97 (49.7) | 71 (53.0) | 26 (42.6) | |
| DBIL | ≤3.86 | 97 (49.7) | 65 (48.5) | 32 (52.5) | 0.721 |
| | >3.86 | 98 (50.3) | 69 (51.5) | 29 (47.5) | |
| IDBIL | ≤6.60 | 98 (50.3) | 61 (45.5) | 37 (60.7) | 0.071 |
| | >6.60 | 97 (49.7) | 73 (54.5) | 24 (39.3) | |
| TP | ≤70.00 | 97 (49.7) | 61 (45.5) | 36 (59.0) | 0.111 |
| | >70.00 | 98 (50.3) | 73 (54.5) | 25 (41.0) | |
| ALB | ≤35.00 | 88 (45.1) | 49 (36.6) | 39 (63.9) | 0.001 |
| | >35.00 | 107 (54.9) | 85 (63.4) | 22 (36.1) | |
| GLOB | ≤26.50 | 85 (43.6) | 58 (43.3) | 27 (44.3) | 1.000 |
| | >26.50 | 110 (56.4) | 76 (56.7) | 34 (55.7) | |
| A/G | ≤1.60 | 93 (47.7) | 59 (44.0) | 34 (55.7) | 0.173 |
| | >1.60 | 102 (52.3) | 75 (56.0) | 27 (44.3) | |
| PALB | ≤235.0 | 97 (49.7) | 53 (39.6) | 44 (72.1) | <0.001 |
| | >235.0 | 98 (50.3) | 81 (60.4) | 17 (27.9) | |
| Urea | ≤5.50 | 92 (47.2) | 64 (47.8) | 28 (45.9) | 0.931 |
| | >5.50 | 103 (52.8) | 70 (52.2) | 33 (54.1) | |
| CREA | ≤80.50 | 97 (49.7) | 66 (49.3) | 31 (50.8) | 0.961 |
| | >80.50 | 98 (50.3) | 68 (50.7) | 30 (49.2) | |
| UA | ≤290.0 | 100 (51.3) | 62 (46.3) | 38 (62.3) | 0.055 |
| | >290.0 | 95 (48.7) | 72 (53.7) | 23 (37.7) | |
| ALP | ≤75.00 | 95 (48.7) | 67 (50.0) | 28 (45.9) | 0.707 |
| | >75.00 | 100 (51.3) | 67 (50.0) | 33 (54.1) | |
| Glu | ≤5.25 | 92 (47.2) | 65 (48.5) | 27 (44.3) | 0.692 |
| | >5.25 | 103 (52.8) | 69 (51.5) | 34 (55.7) | |
| CHOL | ≤4.20 | 96 (49.2) | 57 (42.5) | 39 (63.9) | 0.009 |
| | >4.20 | 99 (50.8) | 77 (57.5) | 22 (36.1) | |
| TRIG | ≤1.21 | 93 (47.7) | 56 (41.8) | 37 (60.7) | 0.022 |
| | >1.21 | 102 (52.3) | 78 (58.2) | 24 (39.3) | |
| LDH | ≤180 | 95 (48.7) | 66 (49.3) | 29 (47.5) | 0.946 |
| | >180 | 100 (51.3) | 68 (50.7) | 32 (52.5) | |
| W | ≤6.70 | 97 (49.7) | 68 (50.7) | 29 (47.5) | 0.794 |
| | >6.70 | 98 (50.3) | 66 (49.3) | 32 (52.5) | |
| N | ≤3.75 | 98 (50.3) | 77 (57.5) | 21 (34.4) | 0.005 |
| | >3.75 | 97 (49.7) | 57 (42.5) | 40 (65.6) | |
| L | ≤1.95 | 95 (48.7) | 43 (32.1) | 52 (85.2) | <0.001 |
| | >1.95 | 100 (51.3) | 91 (67.9) | 9 (14.8) | |
| M | ≤0.49 | 97 (49.7) | 66 (49.3) | 31 (50.8) | 0.961 |
| | >0.49 | 98 (50.3) | 68 (50.7) | 30 (49.2) | |
| E | ≤0.15 | 95 (48.7) | 60 (44.8) | 35 (57.4) | 0.139 |
| | >0.15 | 100 (51.3) | 74 (55.2) | 26 (42.6) | |

(*Continued*)

**Table 2** (Continued).

| Parameters n | Level | Overall 195 | Low GRImScore 134 | High GRImScore 61 | *P* |
|---|---|---|---|---|---|
| B | ≤0.04 | 88 (45.1) | 63 (47.0) | 25 (41.0) | 0.529 |
| | >0.04 | 107 (54.9) | 71 (53.0) | 36 (59.0) | |
| Hb | ≤127.50 | 97 (49.7) | 58 (43.3) | 39 (63.9) | 0.012 |
| | >127.50 | 98 (50.3) | 76 (56.7) | 22 (36.1) | |
| R | ≤4.35 | 96 (49.2) | 59 (44.0) | 37 (60.7) | 0.046 |
| | >4.35 | 99 (50.8) | 75 (56.0) | 24 (39.3) | |
| Hct | ≤38.67 | 97 (49.7) | 61 (45.5) | 36 (59.0) | 0.111 |
| | >38.67 | 98 (50.3) | 73 (54.5) | 25 (41.0) | |
| P | ≤265.0 | 98 (50.3) | 70 (52.2) | 28 (45.9) | 0.505 |
| | >265.0 | 97 (49.7) | 64 (47.8) | 33 (54.1) | |
| NLR | Low | 143 (73.3) | 134 (100.0) | 9 (14.8) | <0.001 |
| | High | 52 (26.7) | 0 (0.0) | 52 (85.2) | |
| INR | ≤1.06 | 93 (47.7) | 72 (53.7) | 21 (34.4) | 0.019 |
| | >1.06 | 102 (52.3) | 62 (46.3) | 40 (65.6) | |
| FIB | ≤3.15 | 98 (50.3) | 80 (59.7) | 18 (29.5) | <0.001 |
| | >3.15 | 97 (49.7) | 54 (40.3) | 43 (70.5) | |
| CEA | ≤2.15 | 95 (48.7) | 70 (52.2) | 25 (41.0) | 0.192 |
| | >2.15 | 100 (51.3) | 64 (47.8) | 36 (59.0) | |
| AFP | ≤2.89 | 96 (49.2) | 68 (50.7) | 28 (45.9) | 0.636 |
| | >2.89 | 99 (50.8) | 66 (49.3) | 33 (54.1) | |
| CA199 | ≤14.10 | 97 (49.7) | 71 (53.0) | 26 (42.6) | 0.235 |
| | >14.10 | 98 (50.3) | 63 (47.0) | 35 (57.4) | |
| CA724 | ≤2.52 | 99 (50.8) | 69 (51.5) | 30 (49.2) | 0.885 |
| | >2.52 | 96 (49.2) | 65 (48.5) | 31 (50.8) | |
| CA125 | ≤10.82 | 98 (50.3) | 69 (51.5) | 29 (47.5) | 0.721 |
| | >10.82 | 97 (49.7) | 65 (48.5) | 32 (52.5) | |

**Abbreviations**: ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; GGT, γ-glutamyl transpeptidase; TBIL, Total bilirubin; DBIL, Direct bilirubin; IBIL, Indirect bilirubin; TP, Total protein; ALB, Albumin; GLOB, Globularproteins; A/G, Albumin/Globularproteins; PALB, Prealbumin; CREA, Creatinine; UA, Uric acid; ALP, Alkaline phosphatase; Glu, Glucose; CHOL, Cholesterol; TRIG, Triglyceride; LDH, Lactate dehydrogenase; W, White blood cell; N, Neutrophils; L, Lymphocyte; M, Monocyte; E, eosinophil; B, Basophil; Hb, Hemoglobin; R, Red blood cell; Hct, Hematocrit; P, Platelet; NLR, Neutrophil-to-lymphocyte ratio; FIB, Fibrinogen; CEA, Carcinoembryonic antigen; AFP, Alpha-fetoprotein; CA199, Cancer antigen 199; CA724, Cancer antigen 724; CA125, Cancer antigen 125.

**Table 3** Univariate and Multivariate Analysis for DFS in Advanced Gastric Cancer Patients

| Parameters | Group | DFS | Univariate | | | Multivariate | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *P* | HR | 95% CI | | *P* | HR | 95% CI | |
| | | | | Low | High | | | Low | High |
| GRImScore | Low | 0.009 | 1 (Ref.) | | | 0.001 | 1 (Ref.) | | |
| | High | | 1.786 | 1.156 | 2.759 | | 2.798 | 1.711 | 11.008 |
| Sex | Male | 0.403 | 1 (Ref.) | | | | | | |
| | Female | | 1.373 | 0.653 | 2.885 | | | | |
| Age | ≤60 | 0.636 | 1 (Ref.) | | | | | | |
| | >60 | | 1.192 | 0.577 | 2.462 | | | | |
| BMI | ≤22.10 | 0.960 | 1 (Ref.) | | | | | | |
| | >22.10 | | 0.982 | 0.482 | 2.000 | | | | |
| ALT | ≤18.50 | 0.362 | 1 (Ref.) | | | | | | |
| | >18.50 | | 0.731 | 0.372 | 1.435 | | | | |

(*Continued*)

**Table 3** (Continued).

| Parameters | Group | DFS | Univariate | | | Multivariate | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *P* | HR | 95% CI | | *P* | HR | 95% CI | |
| | | | | Low | High | | | Low | High |
| AST | ≤21.70 | 0.414 | 1 (Ref.) | | | | | | |
| | >21.70 | | 0.739 | 0.358 | 1.526 | | | | |
| TBIL | ≤10.13 | 0.103 | 1 (Ref.) | | | | | | |
| | >10.13 | | 0.622 | 0.351 | 1.100 | | | | |
| TP | ≤70.00 | 0.972 | 1 (Ref.) | | | | | | |
| | >70.00 | | 1.017 | 0.401 | 2.579 | | | | |
| GLOB | ≤26.50 | 0.083 | 1 (Ref.) | | | | | | |
| | >26.50 | | 0.467 | 0.197 | 1.106 | | | | |
| A/G | ≤1.60 | 0.101 | 1 (Ref.) | | | | | | |
| | >1.60 | | 0.506 | 0.224 | 1.143 | | | | |
| PALB | ≤235.0 | 0.000 | 1 (Ref.) | | | 0.001 | 1 (Ref.) | | |
| | >235.0 | | 0.207 | 0.096 | 0.443 | | 0.416 | 0.254 | 0.682 |
| ALP | ≤75.00 | 0.195 | 1 (Ref.) | | | | | | |
| | >75.00 | | 0.674 | 0.372 | 1.224 | | | | |
| CHOL | ≤4.20 | 0.561 | 1 (Ref.) | | | | | | |
| | >4.20 | | 1.216 | 0.629 | 2.351 | | | | |
| TRIG | ≤1.21 | 0.169 | 1 (Ref.) | | | | | | |
| | >1.21 | | 1.622 | 0.815 | 3.230 | | | | |
| ABO blood type | A | 0.076 | 1 (Ref.) | | | | | | |
| | B | 0.462 | 1.364 | 0.596 | 3.120 | | | | |
| | O | 0.153 | 1.867 | 0.792 | 4.403 | | | | |
| | AB | 0.016 | 4.590 | 1.329 | 15.858 | | | | |
| W | ≤6.70 | 0.560 | 1 (Ref.) | | | | | | |
| | >6.70 | | 0.767 | 0.314 | 1.873 | | | | |
| N | ≤3.75 | 0.103 | 1 (Ref.) | | | | | | |
| | >3.75 | | 2.184 | 0.855 | 5.577 | | | | |
| L | ≤1.95 | 0.694 | 1 (Ref.) | | | | | | |
| | >1.95 | | 1.170 | 0.535 | 2.559 | | | | |
| Hb | ≤127.50 | 0.030 | 1 (Ref.) | | | 0.002 | 1 (Ref.) | | |
| | >127.50 | | 2.582 | 1.094 | 6.094 | | 2.150 | 1.319 | 3.504 |
| R | ≤4.35 | 0.245 | 1 (Ref.) | | | | | | |
| | >4.35 | | 1.542 | 0.743 | 3.199 | | | | |
| P | ≤265.0 | 0.391 | 1 (Ref.) | | | | | | |
| | >265.0 | | 0.754 | 0.396 | 1.438 | | | | |
| INR | ≤1.06 | 0.853 | 1 (Ref.) | | | | | | |
| | >1.06 | | 0.943 | 0.504 | 1.762 | | | | |
| FIB | ≤3.15 | 0.203 | 1 (Ref.) | | | | | | |
| | >3.15 | | 1.553 | 0.789 | 3.055 | | | | |
| CEA | ≤2.15 | 0.609 | 1 (Ref.) | | | | | | |
| | >2.15 | | 0.860 | 0.483 | 1.532 | | | | |
| AFP | ≤2.89 | 0.367 | 1 (Ref.) | | | | | | |
| | >2.89 | | 0.770 | 0.437 | 1.358 | | | | |
| CA199 | ≤14.10 | 0.011 | 1 (Ref.) | | | 0.004 | 1 (Ref.) | | |
| | >14.10 | | 2.256 | 1.208 | 4.213 | | 3.102 | 1.429 | 6.734 |
| CA724 | ≤2.52 | 0.921 | 1 (Ref.) | | | | | | |
| | >2.52 | | 0.970 | 0.534 | 1.765 | | | | |
| CA125 | ≤10.82 | 0.192 | 1 (Ref.) | | | | | | |
| | >10.82 | | 0.676 | 0.376 | 1.217 | | | | |

(*Continued*)

**Table 3** (Continued).

| Parameters | Group | DFS | Univariate | | | Multivariate | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *P* | HR | 95% CI | | *P* | HR | 95% CI | |
| | | | | Low | High | | | Low | High |
| Radical resection | R0 | 0.495 | 1 (Ref.) | | | | | | |
| | R1 | 0.800 | 1.139 | 0.415 | 3.131 | | | | |
| | R2 | 0.238 | 2.274 | 0.581 | 8.907 | | | | |
| Type of surgery | Distal gastrectomy | 0.017 | 1 (Ref.) | | | 0.011 | 1 (Ref.) | | |
| | Proximal gastrectomy | 0.059 | 7.447 | 0.929 | 59.716 | 0.210 | 4.351 | 0.436 | 43.386 |
| | Total gastrectomy | 0.007 | 4.376 | 1.484 | 12.905 | 0.003 | 7.241 | 1.978 | 26.512 |
| Primary tumor site | Upper 1/3 | 0.098 | 1 (Ref.) | | | | | | |
| | Middle 1/3 | 0.190 | 3.364 | 0.549 | 20.614 | | | | |
| | Low 1/3 | 0.027 | 7.809 | 1.264 | 48.257 | | | | |
| | Whole | 0.029 | 6.720 | 1.214 | 37.183 | | | | |
| TLN | ≤30 | 0.004 | 1 (Ref.) | | | 0.010 | 1 (Ref.) | | |
| | >30 | | 1.954 | 1.234 | 3.096 | | 1.831 | 1.152 | 2.908 |
| PLN | ≤8 | 0.649 | 1 (Ref.) | | | | | | |
| | >8 | | 1.191 | 0.561 | 2.525 | | | | |
| Tumor size | ≤20 mm | 0.005 | 1 (Ref.) | | | 0.003 | 1 (Ref.) | | |
| | >20 and <50 mm | 0.005 | 3.785 | 1.494 | 9.590 | 0.011 | 3.431 | 1.327 | 8.871 |
| | ≥50 mm | 0.001 | 4.729 | 1.857 | 12.045 | 0.001 | 5.082 | 1.950 | 13.248 |
| Differentiation | Poorly differentiated | 0.235 | 1 (Ref.) | | | | | | |
| | Moderately differentiated | 0.180 | 1.685 | 0.786 | 3.614 | | | | |
| | Well differentiated | 0.181 | 7.117 | 0.402 | 126.109 | | | | |
| pTNM stage | IIIA | 0.010 | 1 (Ref.) | | | 0.026 | 1 (Ref.) | | |
| | IIIB | 0.003 | 2.188 | 1.309 | 3.657 | 0.008 | 2.032 | 1.208 | 3.418 |
| | IIIC | 0.243 | 1.456 | 0.775 | 2.737 | 0.079 | 1.783 | 0.935 | 3.400 |
| Lauren type | Intestinal | 0.093 | 1 (Ref.) | | | | | | |
| | Diffuse | 0.030 | 2.465 | 1.091 | 5.570 | | | | |
| | Mixed | 0.576 | 1.238 | 0.586 | 2.616 | | | | |
| HER2 | No | 0.180 | 1 (Ref.) | | | | | | |
| | Yes | | 0.448 | 0.138 | 1.450 | | | | |
| CK | No | 0.032 | 1 (Ref.) | | | | | | |
| | Yes | | 0.365 | 0.145 | 0.918 | | | | |
| Postoperative chemotherapy | No | 0.025 | 1 (Ref.) | | | 0.031 | 1 (Ref.) | | |
| | Yes | | 0.590 | 0.373 | 0.935 | | 0.601 | 0.379 | 0.954 |

**Abbreviations**: BMI, Body mass index; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; TBIL, Total bilirubin; TP, Total protein; GLOB, Globularproteins; A/G, Albumin/Globularproteins; PALB, Prealbumin; ALP, Alkaline phosphatase; CHOL, Cholesterol; TRIG, Triglyceride; W, White blood cell; N, Neutrophils; L, Lymphocyte; Hb, Hemoglobin; R, Red blood cell; P, Platelet; INR, International normalized ratio; FIB, Fibrinogen; CEA, Carcinoembryonic antigen; AFP, Alpha-fetoprotein; CA199, Cancer antigen 199; CA724, Cancer antigen 724; CA125, Cancer antigen 125; TLN, Total lymph node; PLN, Positive lymph node; HER2, Human epidermal growth factor receptor 2; CK, Cytokeratin.

CA199, type of surgery, TLN, tumor size, and pTNM stage were significant factors. Multivariate analysis showed that GRImScore, PALB, CA199, type of surgery, TLN, tumor size, and pTNM stage were potential prognostic factors for OS (Table 4). According to the multivariable Cox analysis, the GRImScore was significantly associated with DFS (HR, 2.798; 95% CI: 1.711–11.008, $P = 0.001$) and OS (HR, 2.631; 95% CI: 1.645–10.725, $P = 0.001$).

**Table 4** Univariate and Multivariate Analysis for OS in Advanced Gastric Cancer Patients

| Parameters | Group | OS | Univariate | | | Multivariate | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *P* | HR | 95% CI | | *P* | HR | 95% CI | |
| | | | | Low | High | | | Low | High |
| GRImScore | Low | 0.013 | 1 (Ref.) | | | 0.001 | 1 (Ref.) | | |
| | High | | 1.736 | 1.124 | 2.681 | | 2.631 | 1.645 | 10.725 |
| Sex | Male | 0.758 | 1 (Ref.) | | | | | | |
| | Female | | 1.127 | 0.526 | 2.417 | | | | |
| Age | ≤60 | 0.284 | 1 (Ref.) | | | | | | |
| | >60 | | 1.474 | 0.725 | 2.996 | | | | |
| BMI | ≤22.10 | 0.820 | 1 (Ref.) | | | | | | |
| | >22.10 | | 0.921 | 0.454 | 1.868 | | | | |
| ALT | ≤18.50 | 0.397 | 1 (Ref.) | | | | | | |
| | >18.50 | | 0.748 | 0.383 | 1.464 | | | | |
| AST | ≤21.70 | 0.388 | 1 (Ref.) | | | | | | |
| | >21.70 | | 0.738 | 0.370 | 1.472 | | | | |
| TBIL | ≤10.13 | 0.094 | 1 (Ref.) | | | | | | |
| | >10.13 | | 0.619 | 0.352 | 1.086 | | | | |
| TP | ≤70.00 | 0.980 | 1 (Ref.) | | | | | | |
| | >70.00 | | 0.989 | 0.408 | 2.399 | | | | |
| GLOB | ≤26.50 | 0.034 | 1 (Ref.) | | | | | | |
| | >26.50 | | 0.383 | 0.157 | 0.931 | | | | |
| A/G | ≤1.60 | 0.062 | 1 (Ref.) | | | | | | |
| | >1.60 | | 0.461 | 0.204 | 1.041 | | | | |
| PALB | ≤235.0 | 0.000 | 1 (Ref.) | | | 0.000 | 1 (Ref.) | | |
| | >235.0 | | 0.209 | 0.097 | 0.448 | | 0.322 | 0.189 | 0.549 |
| ALP | ≤75.00 | 0.430 | 1 (Ref.) | | | | | | |
| | >75.00 | | 0.795 | 0.450 | 1.405 | | | | |
| CHOL | ≤4.20 | 0.855 | 1 (Ref.) | | | | | | |
| | >4.20 | | 1.065 | 0.541 | 2.096 | | | | |
| TRIG | ≤1.21 | 0.074 | 1 (Ref.) | | | | | | |
| | >1.21 | | 1.929 | 0.939 | 3.965 | | | | |
| ABO blood type | A | 0.112 | 1 (Ref.) | | | | | | |
| | B | 0.659 | 1.213 | 0.515 | 2.857 | | | | |
| | O | 0.288 | 1.643 | 0.657 | 4.105 | | | | |
| | AB | 0.018 | 4.411 | 1.288 | 15.106 | | | | |
| W | ≤6.70 | 0.463 | 1 (Ref.) | | | | | | |
| | >6.70 | | 0.721 | 0.301 | 1.729 | | | | |
| N | ≤3.75 | 0.384 | 1 (Ref.) | | | | | | |
| | >3.75 | | 1.496 | 0.604 | 3.710 | | | | |
| L | ≤1.95 | 0.310 | 1 (Ref.) | | | | | | |
| | >1.95 | | 1.509 | 0.682 | 3.341 | | | | |
| Hb | ≤127.50 | 0.207 | 1 (Ref.) | | | 0.005 | 1 (Ref.) | | |
| | >127.50 | | 1.776 | 0.727 | 4.338 | | 1.970 | 1.225 | 3.170 |
| R | ≤4.35 | 0.098 | 1 (Ref.) | | | | | | |
| | >4.35 | | 1.896 | 0.888 | 4.046 | | | | |
| P | ≤265.0 | 0.574 | 1 (Ref.) | | | | | | |
| | >265.0 | | 0.827 | 0.426 | 1.605 | | | | |
| INR | ≤1.06 | 0.871 | 1 (Ref.) | | | | | | |
| | >1.06 | | 1.054 | 0.559 | 1.988 | | | | |
| FIB | ≤3.15 | 0.104 | 1 (Ref.) | | | | | | |
| | >3.15 | | 1.737 | 0.892 | 3.380 | | | | |

(*Continued*)

**Table 4** (Continued).

| Parameters | Group | OS | Univariate | | | Multivariate | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | *P* | HR | 95% CI | | *P* | HR | 95% CI | |
| | | | | Low | High | | | Low | High |
| CEA | ≤2.15 | 0.373 | 1 (Ref.) | | | | | | |
| | >2.15 | | 0.769 | 0.432 | 1.369 | | | | |
| AFP | ≤2.89 | 0.116 | 1 (Ref.) | | | | | | |
| | >2.89 | | 0.628 | 0.352 | 1.121 | | | | |
| CA199 | ≤14.10 | 0.008 | 1 (Ref.) | | | 0.029 | 1 (Ref.) | | |
| | >14.10 | | 2.336 | 1.244 | 4.386 | | 1.667 | 1.053 | 2.638 |
| CA724 | ≤2.52 | 0.912 | 1 (Ref.) | | | | | | |
| | >2.52 | | 1.034 | 0.572 | 1.869 | | | | |
| CA125 | ≤10.82 | 0.690 | 1 (Ref.) | | | | | | |
| | >10.82 | | 0.888 | 0.495 | 1.592 | | | | |
| Radical resection | R0 | 0.445 | 1 (Ref.) | | | | | | |
| | R1 | 0.491 | 1.397 | 0.539 | 3.621 | | | | |
| | R2 | 0.218 | 2.540 | 0.577 | 11.187 | | | | |
| Type of surgery | Distal gastrectomy | 0.011 | 1 (Ref.) | | | 0.011 | 1 (Ref.) | | |
| | Proximal gastrectomy | 0.111 | 6.136 | 0.657 | 57.260 | 0.042 | 2.534 | 1.034 | 6.206 |
| | Total gastrectomy | 0.004 | 4.988 | 1.666 | 14.939 | 0.018 | 2.012 | 1.127 | 3.594 |
| Primary tumor site | Upper 1/3 | 0.392 | 1 (Ref.) | | | | | | |
| | Middle 1/3 | 0.146 | 3.883 | 0.622 | 24.237 | | | | |
| | Low 1/3 | 0.101 | 4.507 | 0.745 | 27.253 | | | | |
| | Whole | 0.093 | 4.375 | 0.780 | 24.549 | | | | |
| TLN | ≤30 | 0.045 | 1 (Ref.) | | | 0.000 | 1 (Ref.) | | |
| | >30 | | 1.989 | 1.016 | 3.893 | | 2.480 | 1.545 | 3.980 |
| PLN | ≤8 | 0.804 | 1 (Ref.) | | | | | | |
| | >8 | | 1.098 | 0.527 | 2.288 | | | | |
| Tumor size | ≤20 mm | 0.009 | 1 (Ref.) | | | 0.013 | 1 (Ref.) | | |
| | >20 and >50mm | 0.041 | 2.674 | 1.043 | 6.860 | 0.097 | 2.253 | 0.863 | 5.880 |
| | ≥50 mm | 0.004 | 4.023 | 1.572 | 10.297 | 0.009 | 3.626 | 1.379 | 9.532 |
| Differentiation | Poorly differentiated | 0.060 | 1 (Ref.) | | | | | | |
| | Moderately differentiated | 0.044 | 2.186 | 1.022 | 4.676 | | | | |
| | Well differentiated | 0.069 | 16.517 | 0.807 | 338.112 | | | | |
| pTNM stage | IIIA | 0.023 | 1 (Ref.) | | | 0.036 | 1 (Ref.) | | |
| | IIIB | 0.006 | 2.061 | 1.230 | 3.455 | 0.010 | 1.982 | 1.174 | 3.344 |
| | IIIC | 0.139 | 1.627 | 0.854 | 3.101 | 0.109 | 1.726 | 0.885 | 3.367 |
| Lauren type | Intestinal | 0.118 | 1 (Ref.) | | | | | | |
| | Diffuse | 0.045 | 2.299 | 1.019 | 5.183 | | | | |
| | Mixed | 0.796 | 1.109 | 0.507 | 2.424 | | | | |
| HER2 | No | 0.210 | 1 (Ref.) | | | | | | |
| | Yes | | 0.461 | 0.137 | 1.548 | | | | |
| CK | No | 0.318 | 1 (Ref.) | | | | | | |
| | Yes | | 0.631 | 0.256 | 1.557 | | | | |
| Postoperative chemotherapy | No | 0.697 | 1 (Ref.) | | | | | | |
| | Yes | | 1.139 | 0.592 | 2.194 | | | | |

**Abbreviations**: BMI, Body mass index; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; TBIL, Total bilirubin; TP, Total protein; GLOB, Globularproteins; A/G, Albumin/Globularproteins; PALB, Prealbumin; ALP, Alkaline phosphatase; CHOL, Cholesterol; TRIG, Triglyceride; W, White blood cell; N, Neutrophils; L, Lymphocyte; Hb, Hemoglobin; R, Red blood cell; P, Platelet; INR, International normalized ratio; FIB, Fibrinogen; CEA, Carcinoembryonic antigen; AFP, Alpha-fetoprotein; CA199, Cancer antigen 199; CA724, Cancer antigen 724; CA125, Cancer antigen 125; TLN, Total lymph node; PLN, Positive lymph node; HER2, Human epidermal growth factor receptor 2; CK, Cytokeratin.

## Nomograms Established and Validated

According to the multivariate analyses to establish a nomogram for DFS (Figure 2A), the C-index for the nomogram model predicting DFS was 0.717 (95% CI: 0.699–0.903). Based on multivariate analyses to establish a nomogram for OS

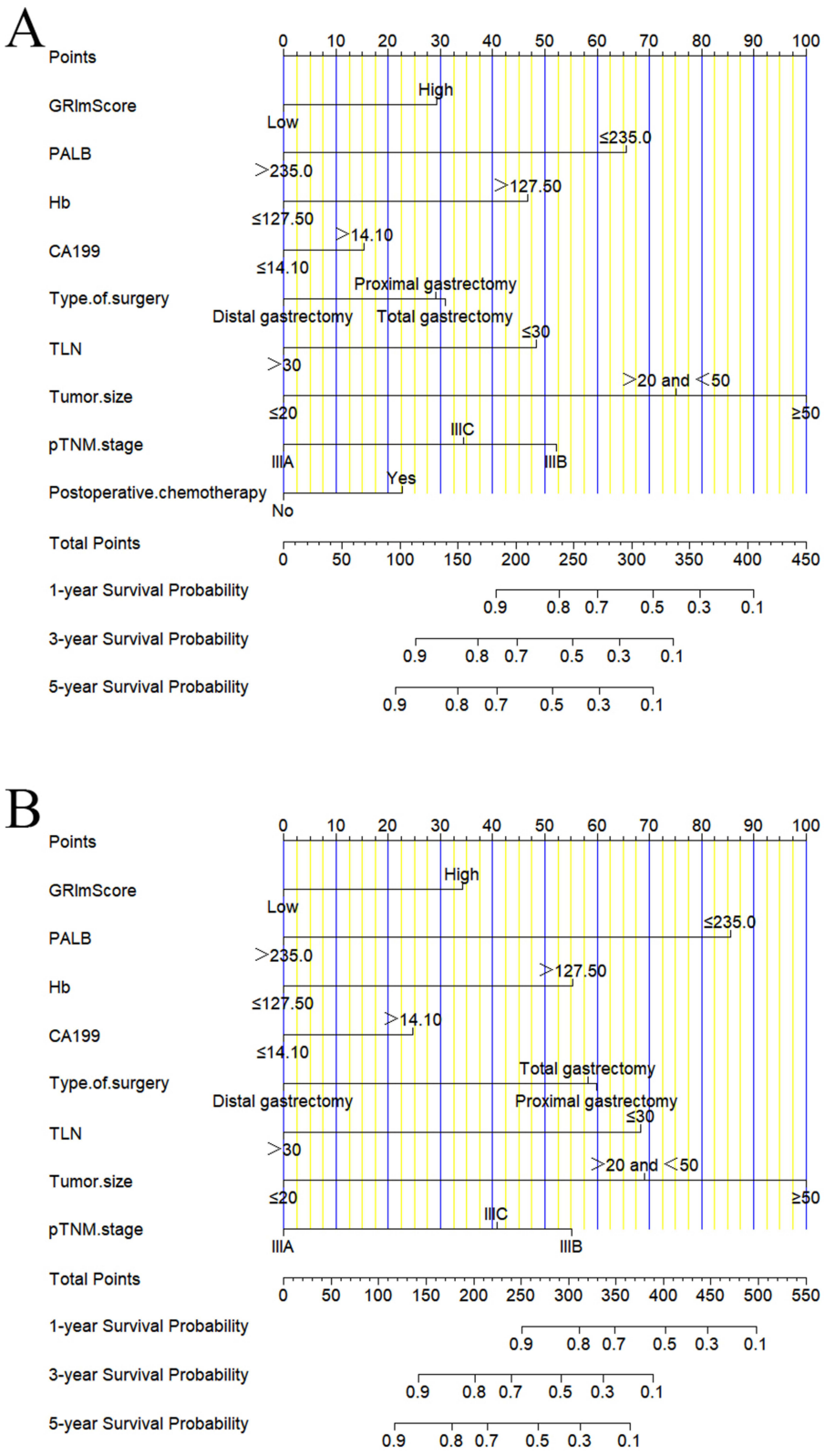


**Figure 2** Nomograms to predict the DFS (**A**) and OS (**B**) of advanced gastric cancer patients.

(Figure 2B), the C-index for the nomogram model predicting OS was 0.807 (95% CI: 0.684–0.890). A calibration curve was used to verify the nomograms, and the results indicated that the curves that predicted DFS at 1-, 3-, and 5-year intervals exhibited a significant correlation between the predictions and actual observations for patients with advanced gastric cancer patients (Figure 3A–C). Calibration curves applied to predict OS at 1-, 3-, and 5-year intervals showed a significant correlation between the predictions and actual observations in advanced gastric cancer patients (Figure 3D and F). Decision curve analysis was used to assess the clinical application of the nomogram model. The results indicated that the nomogram model predicted 3- and 5-year DFS (Figure 4A and B) and OS (Figure 4C and D) in clinical applications better than the GRImScore. Moreover, the nomogram model predicted the 3- and 5-year DFS (Figure 5A and B) and OS (Figure 5C and D) in clinical applications, as well as the NLR.

## Subgroup Analysis

According to the multivariate analysis, type of surgery was the potential prognostic factor for DFS and OS. We analyzed the difference of type of surgery, including the survival curve (DFS: P=0.150, OS: P=0.035) (Figure 6A and B). Patients received Distal gastrectomy had survived longer than those received Proximal gastrectomy and Total gastrectomy.

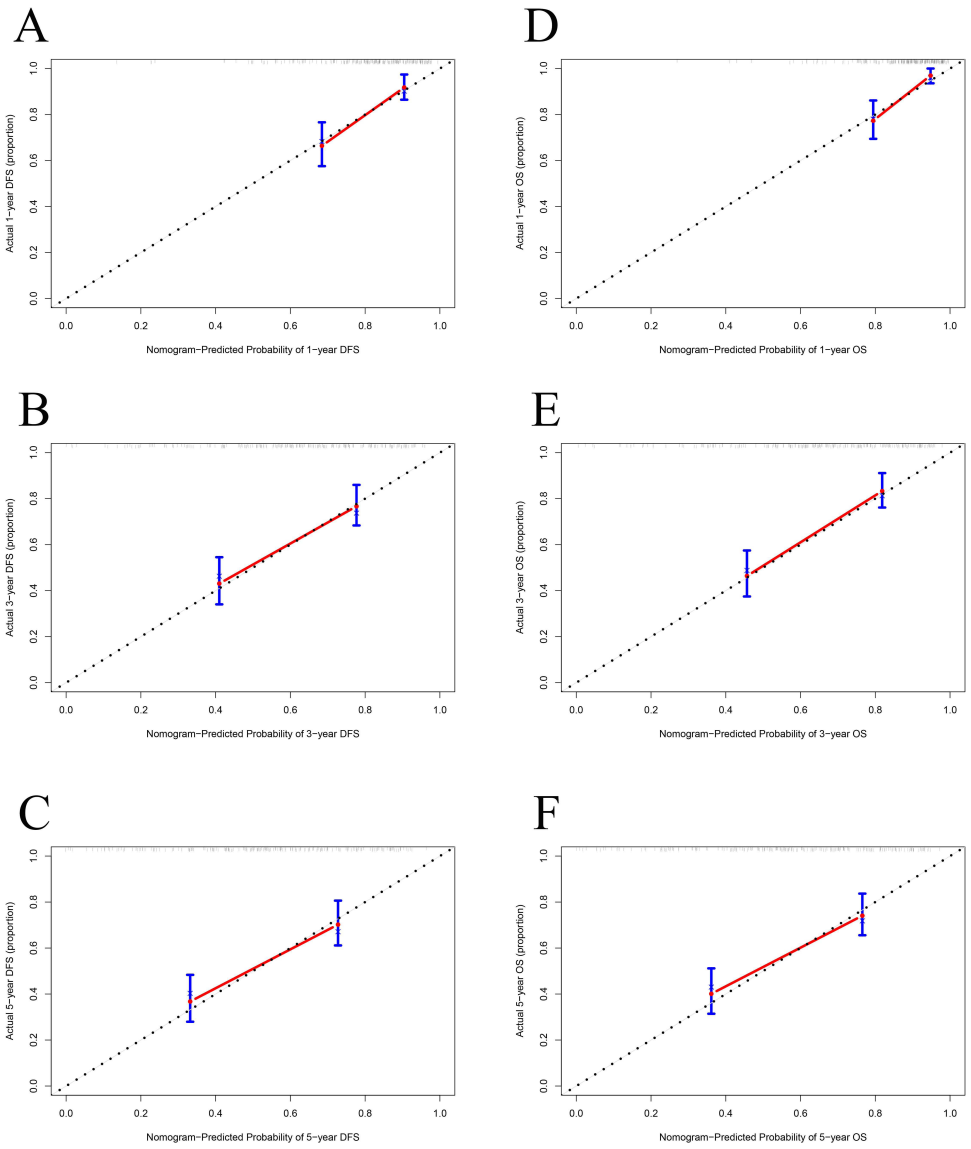


**Figure 3** Calibration curves for assessing 1-, 3-, and 5-year DFS (**A**–**C**) and OS (**D**–**F**) shown good correlation between prediction and observation.


https://doi.org/10.2147/IJGM.S515795

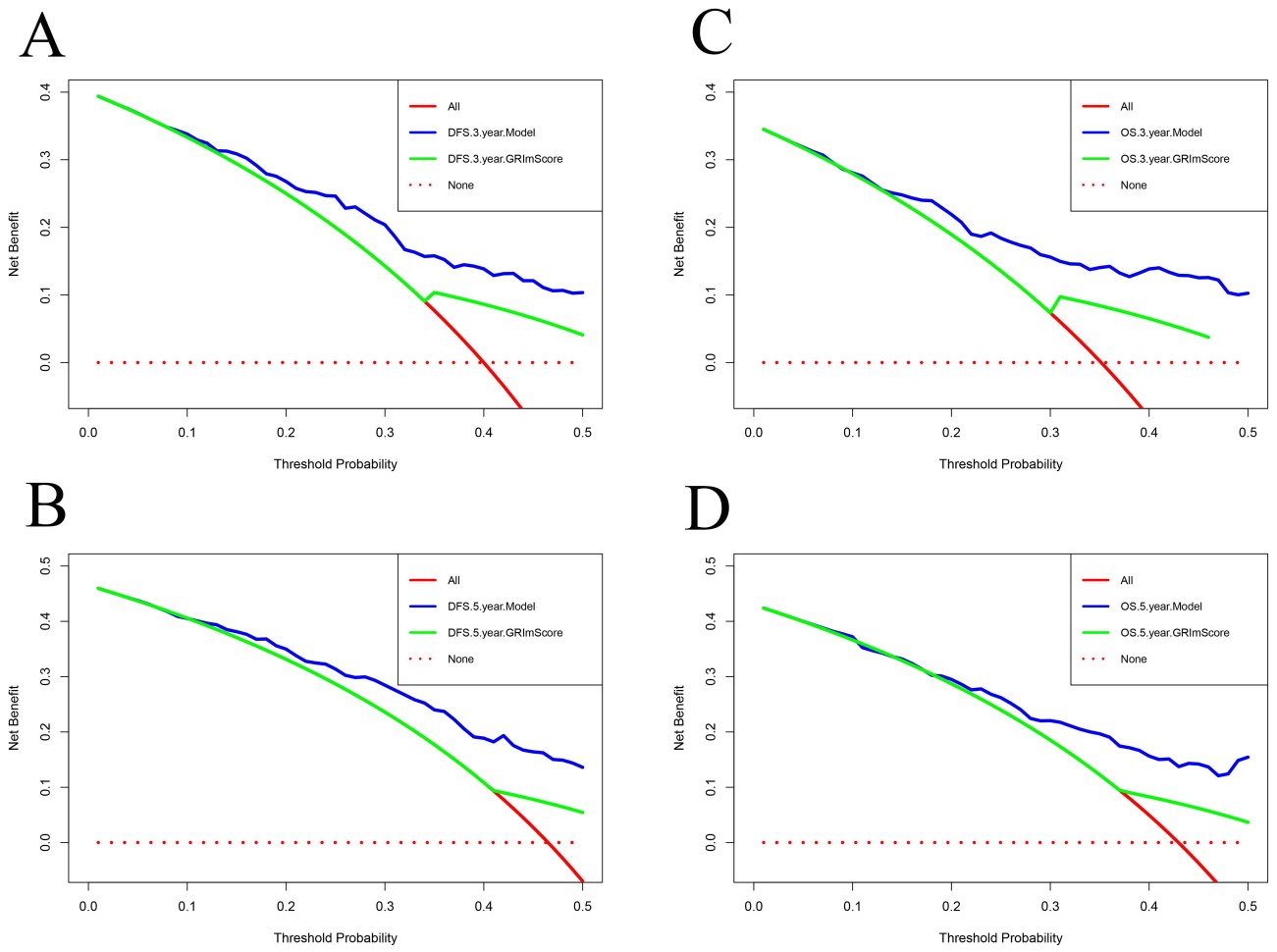


**Figure 4** Decision curve analyses (DCA) for the prognostic models of the nomograms and GRImScore in predicting 3- and 5-year DFS (**A** and **B**) and OS (**C** and **D**) rates.

Moreover, we also analyzed the difference of patients received distal gastrectomy by GRImScore, including the survival curve (DFS: P=0.016, OS: P=0.022) (Figure 6C and D). The median DFS and OS in low GRImScore group were significantly longer than that in high GRImScore group.

## Discussion

GC remains a significant global health challenge, with considerable hurdles in advanced gastric cancer the treatment and prognosis.[17] Although early detection approaches, including screening schemes, help improve outcomes through early intervention, the effective treatment of advanced gastric cancer remains challenging.[18] Stomach carcinogenesis is a prime illustration that the evolution of tumors depends not only on the presence of many key mutations, but also on the intimate interaction between mutant cells and their tumor microenvironment (TME).[19] The role and mechanism of TME in stomach carcinogenesis and prognosis have been well-investigated.[20] In addition, inflammation within the TME is considered an indicator of cancer, which is conducive to cancer cell proliferation, tumor angiogenesis, and immune escape.[21] Numerous clinical and pathological scoring systems have been developed and verified. Among the emerging biological indicators, GRImScore substantiates a multitudinous prognostic value associated with the survival of cancer patients.[22] The prognostic relevance of GRImScore has been studied in some cancer types such as urothelial carcinoma,[23] lung cancer,[24] and esophageal cancer.[25] In Tanabe K's study, they found that GRIm-score is an independent prognostic marker of both OS and PFS (hazard ratio, 1.65 and 1.82, respectively; both $p < 0.001$) for survival outcomes in platinum-refractory metastatic urothelial carcinoma treated with pembrolizumab.[23] In Lenci E's study, they demonatrated that GRImT1 and GRImΔ were more reliable peripheral blood biomarkers of outcome compared to GRImT0 in advanced

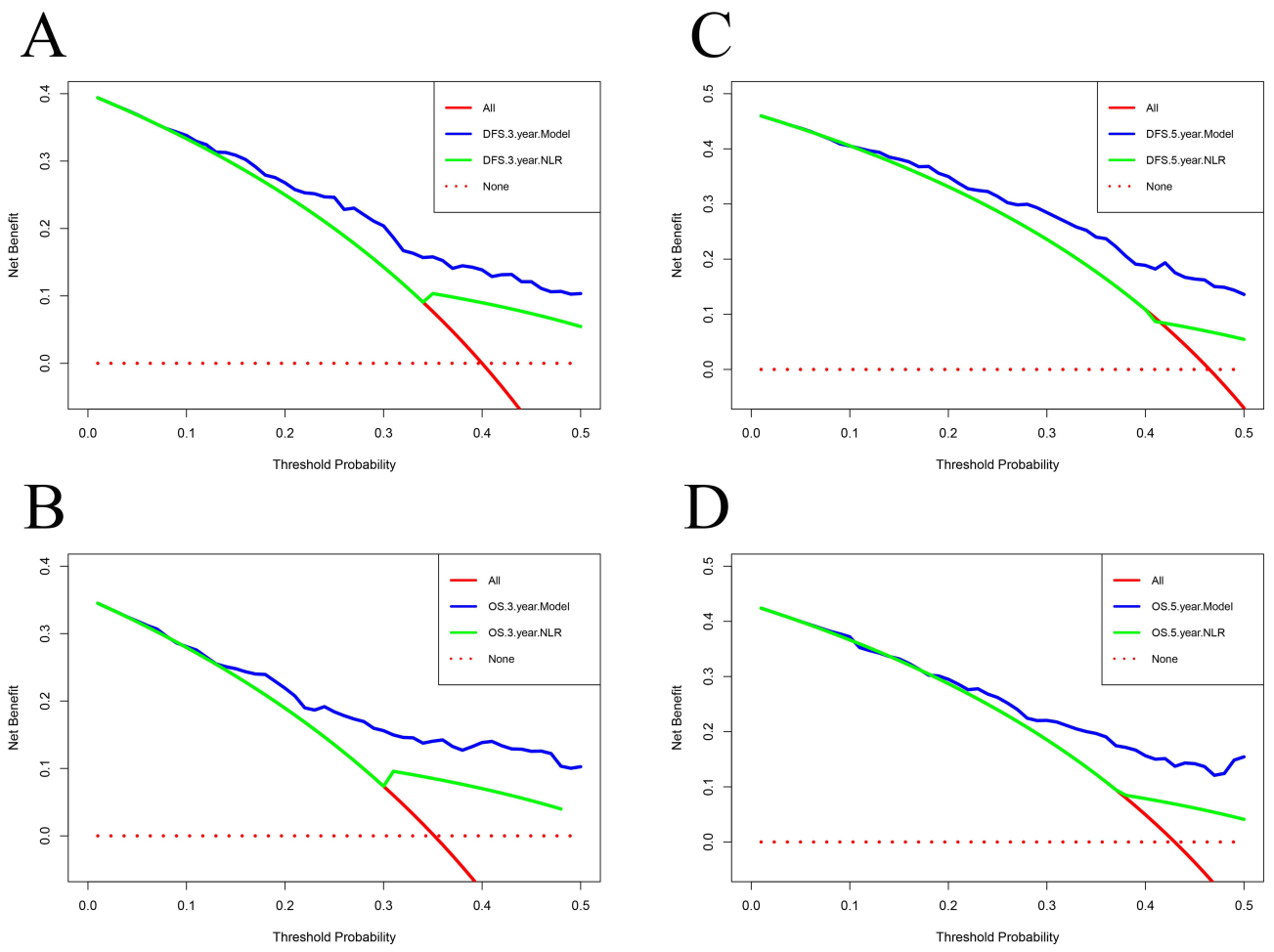


**Figure 5** Decision curve analyses (DCA) for the prognostic models of the nomograms and NLR in predicting 3- and 5-year DFS (**A** and **C**) and OS (**B** and **D**) rates.

non-small cell lung cancer patients treated with pembrolizumab and might represent useful biomarkers to drive clinical decisions in this setting.[24] Another study also shown that the modified GRIm (mGRIm) was significantly associated with metastasis or recurrence before radiotherapy ($\chi^2$ = 6.25), and higher mGRIm score (HR 1.7 95% CI 1.1–2.6) was an independent risk factor of overall survival.[25] GRImScore-based inflammation biomarkers can help to evaluate the prognosis of patients with tumors and identify individuals who are more likely to benefit from a better prognosis. Despite the potential utility of the GRImScore, few studies have investigated its predictive value in advanced gastric cancer.

In the current study, the GRImScore, based on ALB level, LDH level, and NLR, was a better prognostic indicator for gastric cancer patients undergoing surgical resection. We demonstrated that the GRImScore had prognostic value in advanced gastric cancer, and patients with a low GRImScore had longer survival than those patients with a high GRImScore (DFS: $P$=0.0080; OS: $P$=0.0119). Multivariate analyses showed that GRImScore was a potential prognostic factor for DFS (HR, 2.798; 95% CI: 1.711–11.008, $P$ = 0.001) and OS (HR: 2.631, 95% CI: 1.645–10.725, $P$ = 0.001) in patients with advanced gastric cancer.

It is generally known the NLR, LDH, and ALB are common laboratory biomarkers in clinical practice. In recent years, numerous studies have demonstrated that inflammation is related to poor prognosis in malignant tumors, with NLR as a susceptible inflammatory indicator in a number of cancers, including advanced colorectal,[26] invasive bladder,[27] early breast,[28] and cervical[29] cancers. Chen et al found that the NLR could serve as a useful prognostic indicator in gastric cancer patients undergoing SOX or XELOX neoadjuvant chemotherapy, thereby optimizing the therapeutic efficacy for gastric cancer.[30] For patients with cancer, a high LDH level has a worse prognosis; however, the mechanisms underlying


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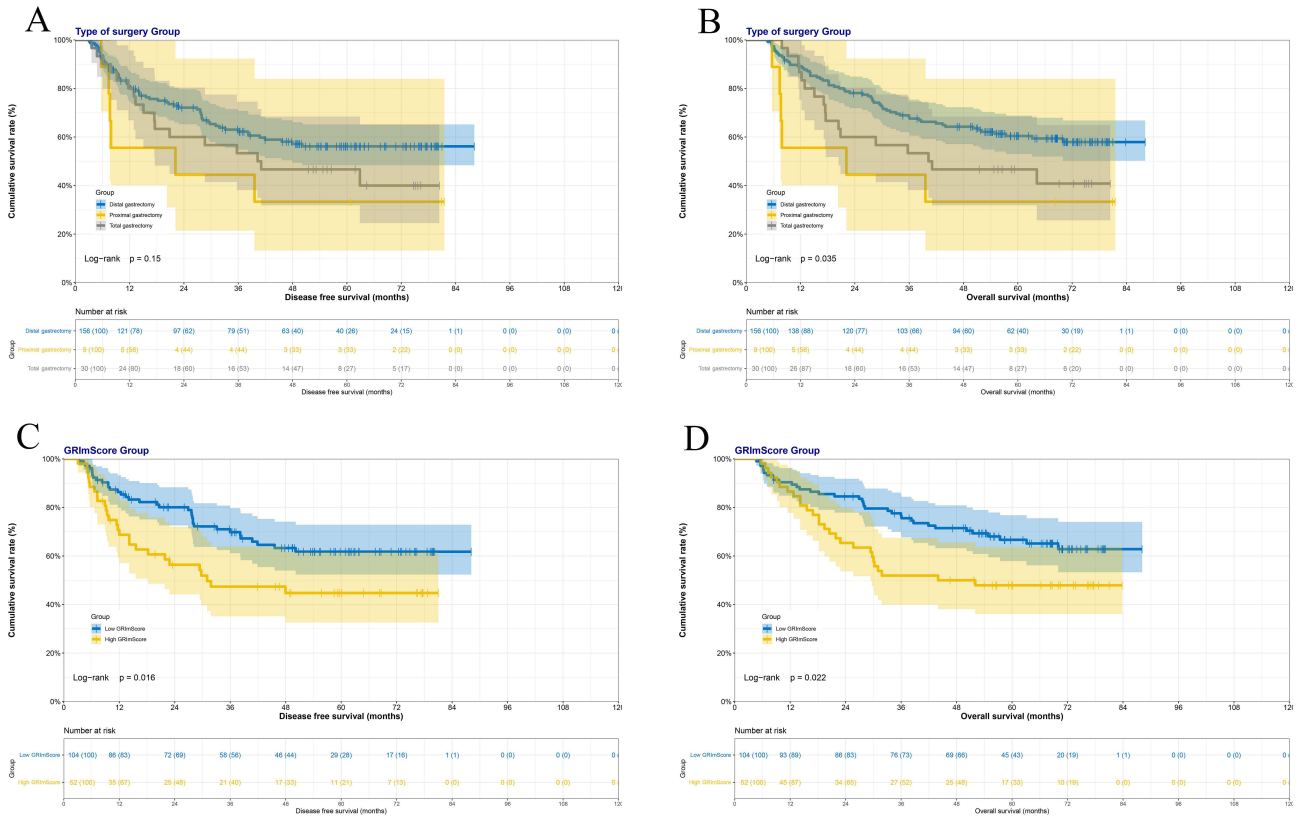


**Figure 6** Kaplan–Meier survival curves of advanced gastric cancer patients for DFS (**A** and **C**) and OS (**B** and **D**) stratified by type of surgery or GRImScore.

gastric cancer remain controversial.[31,32] LDH can reflect inflammatory responses and has a bearing on the invasiveness and immunogenicity of many tumors.[33,34] Gu et al found that higher LDH levels were related to adverse prognosis in patients with bladder cancer, and LDH levels could be regarded as a novel predictive indicator for bladder cancer.[35] A systematic review and meta-analysis demonstrated that a high LDH level was correlated with worse OS and DFS and was also a remarkable predictor of OS.[36] Blood ALB level, a widely common nutritional indicator, has been associated with nutritional status and liver function in multiple cancers.[37] A study indicated that serum ALB concentration was a prognostic indicator of unfavorable overall survival with endometrial cancer patients, and patients with low serum ALB levels exhibited a remarkably worse overall survival ($P$<0.05). Saito found that ALB levels in advanced gastric cancer patients was significantly lower than those with early gastric cancer ($P$<0.05), and ALB level was a useful predictive indicator for the prognosis of older gastric cancer patients ($P$<0.05).

In this study, it is worth noting the NLR based on neutrophils and lymphocytes and common laboratory biomarkers in ordinary clinical practice may be influenced by diverse conditions. Patients with a low NLR had a longer survival than those with a high NLR (DFS, $P$=0.0037; OS, $P$=0.0069). As a result of the GRImScore combined with NLR, ALB, and LDH, multivariate Cox analyses did not include these parameters. Hence, GRImScore is a combined biomarker that can provide comprehensive prognostic value.

Some biological mechanisms can be elaborated, and it is rational to apply GRImScore to evaluate cancer patient survival. In the tumor immune microenvironment, tumor-infiltrating neutrophils influence angiogenesis and immune evasion.[38] However, tumor-infiltrating lymphocytes can also improve the antitumor ability and enhance the clinical response to immunotherapy and chemotherapy.[39] In other words, a higher lymphocyte count indicates a stronger immune response, whereas an increased neutrophil count indicates a higher risk of inflammation. Moreover, a high ALB level represents a better nutritional status, and a high LDH level is associated with tumor invasion and immunogenicity.[40,41]

Above all, our findings demonstrate that the GRImScore has certain prospects as a prognostic tool for advanced gastric cancer patients. Although its prospects are limited, it provides a reference for the prognosis of cancer patients.

Nevertheless, some limitations must be acknowledged when cautiously interpreting our results. First, our study relied on retrospective information from a single-center institution, which may have led to selection bias and limited the universal applicability of our findings. Second, the number of enrolled patients was comparatively small, and further studies with larger and multicenter patients were performed to validate our findings and confirm the practicality of the GRImScore in gastric cancer. Third, although we evaluated various clinicopathological indicators, our analysis did not fully consider other potential confounding factors such as treatment compliance and metastasis. These factors may affect the clinical outcomes of gastric cancer patients. Fourth, the current study mainly examined GRImScore and its relationship with the clinical outcomes of gastric cancer. However, GRImScore did not explore relevant immune biomarkers or features that may influence prognosis. Further studies, combined with the GRImScore and immune-related indicators, may improve the predictive clinical utility.

## Conclusions

In conclusion, our findings indicate that GRImScore, as a novel prognostic index, is a prognostic indicator for advanced gastric cancer patients and has prognostic value in patients with advanced gastric cancer. Our findings also demonstrate that patients with high GRImScore exhibit markedly worse survival outcomes, identifying a subgroup that may benefit from intensified adjuvant therapies, such as chemotherapy. Nomograms based on the GRImScore showed a good predictive ability for OS and DFS rates in patients with gastric cancer. This tool may help gastrointestinal surgeons evaluate the prognosis and therapeutic decisions for patients with gastric cancer.

## Data Sharing Statement

The material supporting the conclusion of this article has been included within the article.

## Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Xingtai People's Hospital. Written informed consent was obtained from all participants.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Disclosure

The authors have declared that no competing interest in this work.

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