

# Evaluation and validation of the prognostic value of nutrition and immunity parameters in gastric cancer after R0 resection

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## Abstract

Precise predictive tools are critical for choosing the individualized treatment protocols and follow-up procedures for patients with gastric cancer (GC). In this study, we aimed to evaluate and validate the prognostic abilities of preoperative nutrition and immunity parameters in GC after curative R0 resection.

We established two nomograms based on 437 patients who underwent curative radical gastrectomy for gastric cancer to predict the postoperative overall survival (OS) and recurrence-free survival (RFS), and then compared the predictive accuracy and discriminative ability of the nomograms with the TNM stage systems for GC. An internal validation cohort of 141 patients and an external validation cohort of 116 patients were used to validate the result.

The independent predictive factors for OS or RFS, including T stage, N stage, differentiated degree, neutrophil monocyte lymphocyte ratio (NMLR) and albumin globulin ratio (AGR) were used to establish the 2 nomograms. The C-index of the OS nomogram was 0.802, which was higher than that of the AGR, the NMLR and the TNM stage. The C-index of the RFS nomogram was 0.850, which was higher than that of the AGR, the NMLR and the TNM stage. Analogously, the areas under the receiver operating characteristics curves (AUROCs, 0.920 for OS and 0.897 for RFS, respectively) of the two nomograms were higher than that of the NMLR, the AGR and the TNM stage. In the internal validation cohort, the C-indexes of the OS and RFS nomograms were 0.812 and 0.826, respectively. In the external validation cohort, the C-indexes of the OS and RFS nomograms were 0.866 and 0.880, respectively.

The proposed nomograms including nutrition and immunity parameters were proved to have excellent predictive ability in survival and recurrence for patients with GC after R0 resection.

**Abbreviations:** AGR = albumin globulin ratio, AUROC = area under the ROC curve, BMI = body mass index, CEA = carcinoembryonic antigen, CI = confidence interval, CONUT = controlling nutritional status, CRP = C-reactive protein, CT = computed tomography, GC = gastric cancer, HR = hazard ratio, MLR = monocyte lymphocyte ratio, NLR = neutrophil lymphocyte ratio, NMLR = neutrophil monocyte lymphocyte ratio, OS = overall survival, PGE2 = prostaglandin E2, PLR = platelet lymphocyte ratio, PMLR = platelet monocyte lymphocyte, PNI = prognostic nutritional index, PNLN = platelet neutrophil lymphocyte, RFS = recurrence-free survival, ROC = receiver operating characteristics, TCM = traditional Chinese medicine, TLRs = toll-like receptors, TNM = tumor-node-metastasis.

**Keywords:** albumin globulin ratio, gastrectomy, gastric cancer, immunity, neutrophil monocyte lymphocyte ratio, nutrition, prognostic

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## 1. Introduction

Gastric cancer (GC), one of the most common malignant tumors, is the fourth most prevalent malignant cancer, as well as the second most frequent cause of cancer death, worldwide.<sup>[1]</sup> Almost two thirds of the cases occur in developing countries and the incidence of GC in Eastern Asia occupies the first in the world.<sup>[1]</sup> Surgical operation remains the major treatment for GC. Despite comprehensive postoperative anti-tumor treatment resulting in prolonged survival for GC patients, long-term survival after surgery remains poor.<sup>[2,3]</sup> Accurate predictive tools are very important for personalized therapy. In general, the tumor-node-metastasis (TNM) stage is used to guide further treatment after surgery, especially chemotherapy. However, Shah et al reported that the TNM stage system was not always in conformity with the survival time.<sup>[4]</sup> Therefore, the development of more accurate predictive tools with novel prognostic factors is urgently required.

The findings of the prognostic factors in GC are becoming increasingly popular and important but were still controversial.<sup>[5,6]</sup> An increasing number of studies showed that immunity and nutritional status were closely associated with malignant tumor progression.<sup>[7,8]</sup> Several nutrition and immunity parameters, such as preoperative body weight loss, body mass index (BMI), prognostic nutritional index (PNI), albumin globulin ratio (AGR), C-reactive protein (CRP), neutrophil lymphocyte ratio (NLR), monocyte lymphocyte ratio (MLR) and platelet lymphocyte ratio (PLR), have been reported frequently to have independent prognostic value in kinds of cancers.<sup>[9–16]</sup> And Liao et al found that neutrophil monocyte lymphocyte ratio (NMLR) had more accurate predictive power than other immunity parameters.<sup>[17]</sup> Based on it, we considered that the combined effect of nutrition and immunity parameters could provide more precise predictive power than any single parameter.

To improve and refine the predictive ability of traditional TNM stage system for GC, several novel predictive tools have been developed.<sup>[18,19]</sup> As we know, there was no specialized nomogram for GC after gastrectomy prognosis, which incorporated both the NMLR and the AGR. Therefore, we conducted this study to assess the association between the NMLR, the AGR and the prognosis for GC after R0 resection, develop reliable nomograms to accurately predict the survival rates, and validate their predictive ability.

## 2. Methods

According to the ethical guidelines of Declaration of Helsinki from 1975, this study was approved by the Ethics Review Committee of Wujin Hospital affiliated with Jiangsu University.

### 2.1. Study population

A total of 967 consecutive gastric cancers proved histologically undergoing radical open gastrectomy, from Wujin Hospital between January 2013 and October 2014, were considered for this retrospective study. The inclusion criteria were as follows:

- (1) had detailed laboratory test data, especially NMLR and AGR;
- (2) did not have preoperative distant metastases diagnosed by imaging tests;
- (3) did not receive any preoperative antitumor treatments;
- (4) conducted R0 resection and lymph node dissection;

- (5) had complete follow-up data, including laboratory and imaging examination.

Finally, 578 patients were taken into the present study, including a primary cohort (January 2013 to May 2014, n=437) to establish the nomograms and an internal validation cohort (June 2014 to October 2014, n=141) to assess the predictive ability. Further, We used another independent cohort as an external validation cohort (May 2012 to October 2015, n=116), which met the strict criteria above, with gastric cancers confirmed by histopathology after surgery selected from the Southern Branch of Wujin Hospital affiliated with Jiangsu University.

### 2.2. Data collection

Clinicopathological data were collected, such as age, gender, operative features, tumor location, tumor size, pathologic type, tumor differentiation, infiltrating level, number of metastasis lymph nodes, TNM stage and survival time. Laboratory tests included neutrophil, lymphocyte, monocyte, platelets, albumin, globulin, D-dimer and carcinoembryonic antigen (CEA). The definitions of NLR, MLR, PLR, NMLR, platelet neutrophil lymphocyte ratio (PNLR), platelet monocyte lymphocyte ratio (PMLR) and AGR were shown in file S1, <http://links.lww.com/MD/D830>. The TNM stage system in the present study was designed by the American Joint Committee on Cancer (AJCC, 8th ed., 2018).

### 2.3. Follow-up

After surgery, during the first year, patients returned to examine once a month; during the second year, patients returned to examine once a quarter; during the third year, patients returned to examine twice a year; and then patients returned to examine annually. The examination items at each visit included thoracic and abdominal computed tomography (CT), blood routine, hepatic and renal function, D-dimer and CEA. The definitions of overall survival (OS) and recurrence-free survival (RFS) were shown in file S1, <http://links.lww.com/MD/D830>.

### 2.4. Statistical analysis

The receiver operating characteristics (ROC) curve was used to calculate the optimal cutoff values (by Youden index) of nutrition and immunity parameters and the areas under the ROC curve (AUROC) with MedCalc 18.2.1 for Windows (MedCalc Software Inc., Ostend, Belgium). AUROC was used to assess the discrimination abilities of immunity parameters and compare the predictive ability of the nomograms with conventional clinical TNM staging systems.

For continuous variables, the differences between groups were analyzed by one-factor analysis of variance (One-Way ANOVA). For categorical variables, the differences between groups were analyzed by the chi-square test. Survival analysis was conducted by log-rank tests. Survival rates, actually cumulative survival rates, were calculated using Kaplan-Meier method. Survival curves were also drawn by the Kaplan-Meier method. Univariate analysis was used to pick out significant factors and estimate the OS and RFS. The parameters in nomograms were selected by multivariate analysis using the multivariable Cox proportional hazard regression model. The above mentioned statistical analyses were performed with SPSS 20.0 for Windows (SPSS Inc., Chicago, IL).

The nomograms were established by the package of rms in R version 3.6.0 (<http://www.r-project.org/>). Discrimination between predictive model and actual data was quantified according to the concordance index (C-index). The value of the C-index ranges from 0.5 to 1.0, with the higher value indicating a higher accuracy. Calibration plots for 3-, 5-year overall survival and 3-, 5-year recurrence-free survival were generated to assess the performance characteristics of the constructed nomograms. Bootstraps with 1000 resample were used for validation of the nomograms and C-index. For all statistical tests,  $P < .05$  considered significant.

### 3. Results

#### 3.1. Clinicopathologic characteristics

A total of 694 patients with gastric cancer were taken into the present study, 437 in the primary cohort, 141 in the internal validation cohort, and 116 in the external validation cohort (Table 1). The median follow-up time was 63, 57 and 57 months; the mean age was  $65.6 \pm 8.9$ ,  $65.8 \pm 8.3$ , and  $67.2 \pm 10.3$  years, the mean tumor size was  $4.3 \pm 2.4$ ,  $4.4 \pm 2.5$ , and  $3.9 \pm 2.3$  cm in the primary, internal validation and external validation cohort, respectively. The laboratory findings were roughly similar among these 3 cohorts, except in monocyte ( $P = .001$ ), albumin ( $P < .001$ ) and globulin ( $P = .001$ ). The vast majority of patients with stage II and stage III gastric cancer underwent adjuvant chemotherapy after surgery, except few patients with advanced age, or poor physical condition. There was no significant difference of postoperative complications among the three cohorts, as described in Table 1.

#### 3.2. Overall survival and recurrence-free survival

In the primary cohort, the 1-, 3-, and 5-year OS rate was 95.4%, 70.9%, and 54.7%, respectively. The 1-, 3- and 5-year RFS rate was 92.4%, 48.1% and 32.7%, respectively. In the internal validation cohort, the 1-, 3- and 5-year OS rate was 97.2%, 70.9%, and 57.4%, respectively. The 1-, 3- and 5-year RFS rate was 96.5%, 54.6% and 34.0%, respectively. In the external validation cohort, the 1-, 3- and 5-year OS rate was 97.4%, 71.6% and 59.3%, respectively. The 1-, 3- and 5-year RFS rate was 97.4%, 50.9% and 40.2%, respectively.

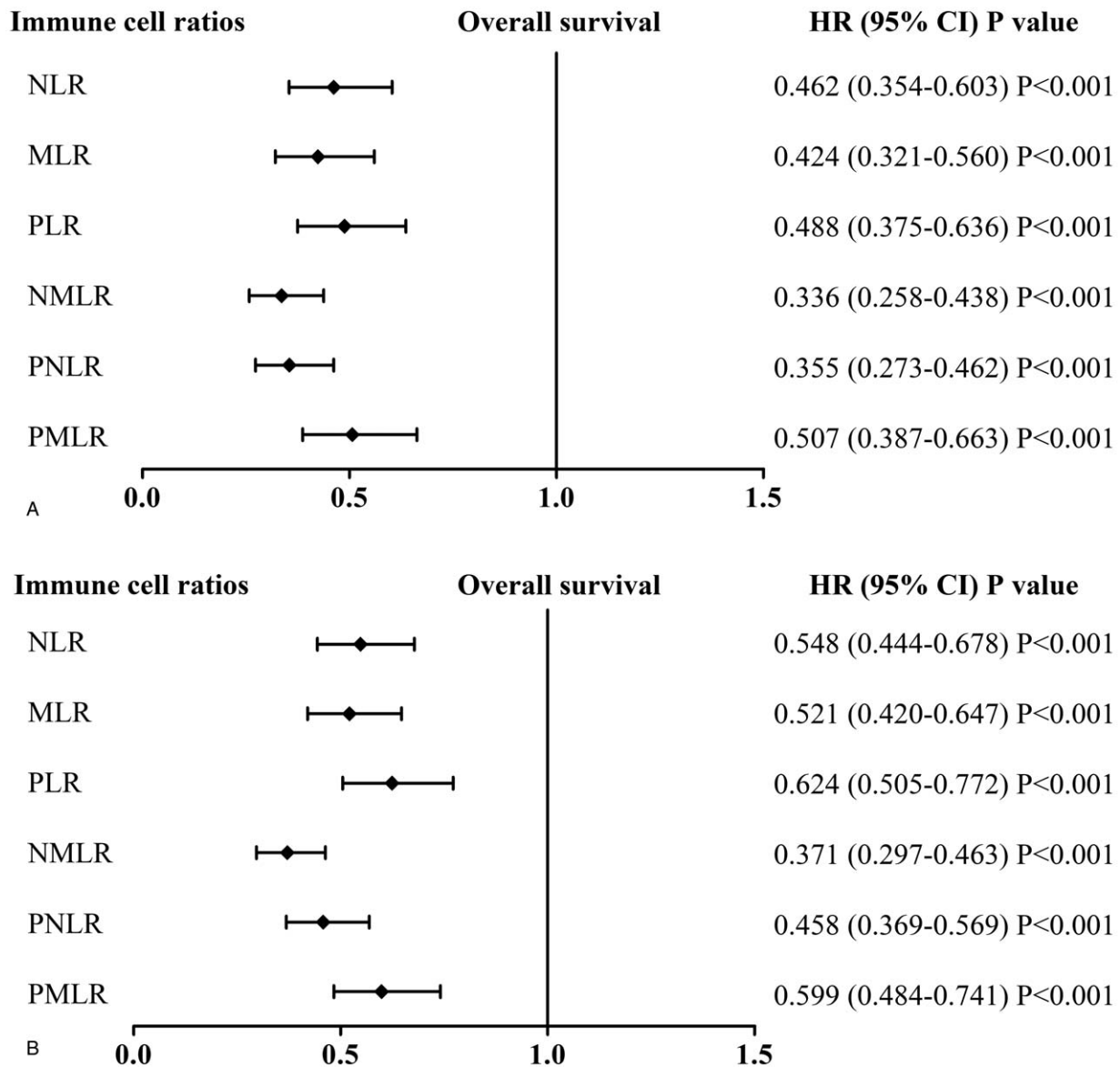
#### 3.3. Predictive value of the nutrition and immunity parameters in the primary cohort

The optimal cutoff values of nutrition and immunity parameters were estimated from the ROC curves when the Youden index was maximal (The ROC curves of AGR, MLR, NLR, NMLR, PLR, PMLR and PNLR were shown in S2-S15 Figures, <http://links.lww.com/MD/D831>). For OS, the optimal cutoff level for NLR, MLR, PLR, NMLR, PMLR, PNLR and AGR was 2.78, 0.22, 152.81, 1.20, 61.01, 462.00 and 1.62, respectively. For RFS, the optimal cutoff level for NLR, MLR, PLR, NMLR, PMLR, PNLR and AGR was 2.61, 0.23, 144.29, 1.13, 63.89, 636.07 and 1.60, respectively. In conclusion, the final cutoff level for NLR, MLR, PLR, NMLR, PMLR, PNLR and AFR were set to 2.70, 0.23, 148, 1.17, 62, 550, and 1.61, respectively. The association between each systemic immune parameter and the OS or RFS was analyzed using log-rank tests. As show in Figure 1, NLR (both  $P < .001$ ), MLR (both  $P < .001$ ), PLR (both  $P < .001$ ), NMLR (both  $P < .001$ ), PMLR (both  $P < .001$ ), and PNLR (both

**Table 1**  
Characteristics of patients in the primary and validation cohorts.

Characteristics	Primary cohort (n=437)	Internal validation cohort (n=141)	External validation cohort (n=116)	P value
Age, years	65.6±8.9	65.8±8.3	67.2±10.3	.227
Gender (male/female)	314/123	98/43	87/29	.621
Neutrophil, 10 <sup>9</sup> /L	4.2±1.7	4.2±1.9	4.4±2.0	.750
Monocyte, 10 <sup>9</sup> /L	0.4±0.2	0.4±0.2	0.5±0.2	.001
Lymphocyte, 10 <sup>9</sup> /L	1.5±0.5	1.6±0.5	1.6±0.7	.399
Erythrocyte, 10 <sup>9</sup> /L	4.1±0.7	4.2±0.6	4.2±0.7	.995
Platelet, 10 <sup>9</sup> /L	218.9±67.9	216.5±90.1	229.2±75.9	.333
Albumin, g/L	39.8±4.9	39.2±4.5	41.8±5.7	<.001
Globulin, g/L	26.1±4.4	25.2±4.1	24.5±4.1	.001
D-dimer, mg/L	0.7±2.5	0.6±0.8	1.2±3.0	.087
CEA, ng/ml	10.0±42.6	9.5±25.2	5.8±19.0	.541
Tumor size, cm	4.3±2.4	4.4±2.5	3.9±2.3	.370
Tumor differentiation (I/II/III/IV)	10/79/220/128	3/35/77/26	0/17/72/27	.028
TNM stage (I/II/III)	118/121/198	39/39/63	29/28/59	.857
T stage (T1/T2/T3/T4)	97/45/221/74	36/13/68/24	20/15/49/32	.123
N stage (N0/N1/N2/N3)	167/75/71/124	48/28/35/30	44/12/28/32	.062
Location (Upper/Mid/Lower/Diffuse)	201/93/136/7	55/33/52/1	45/33/35/3	.356
Adjuvant chemotherapy	304	92	72	.255
Total complications	104	35	33	.588
Infection	48	14	13	.930
Chylous ascites	3	1	2	.609
Delayed gastric emptying	25	8	6	.974
Bleeding	10	4	3	.932
Anastomotic leak	9	4	4	.667
Duodenal leak	2	1	1	.864
Occlusion	4	2	2	.740
Pancreatic fistula	3	1	2	.609

CEA=carcinoembryonic antigen, Tumor differentiation: I=well differentiated, II=moderately differentiated, III=poorly differentiated, IV=signet ring cell or mucinous.



**Figure 1.** The hazard ratios (HRs) and confidence intervals (CIs) of OS (A) and RFS (B) rates were analyzed using Log-rank method for the immune parameters.

$P < .001$ ) were associated with OS and RFS. The discrimination abilities of immune parameters were compared using ROC curves, as shown in Figure 2. Among all immunity parameters, the NMLR had the highest AUROC value (0.691 for OS and 0.655 for RFS, respectively). As shown in Figure 3, patients with a low NMLR or a high AGR had significantly better OS and RFS.

### 3.4. Prognosticators submitted by univariate and multivariate analyses in the primary cohort

In the primary cohort, univariate analyses were performed to screen out the potential prognosticators first. Subsequently, multivariate analyses were performed to identify the significant prognosticators. The results showed that the differentiated degree ( $P = .022$  for OS,  $P < .001$  for RFS), the T stage (both  $P < .001$ ), the N stage (both  $P < .001$ ), the NMLR (both  $P < .001$ ) and the

AGR (both  $P < .001$ ) were independent prognosticators for OS and RFS, as shown in Table 2.

### 3.5. Development and evaluation of the OS and RFS nomograms

The OS (Fig. 4A) and RFS (Fig. 4B) nomograms were developed with the independent prognosticators obtained in the multivariate analyses. The C-index of the OS nomogram was 0.802 (95% CI: 0.770–0.834), which was higher than that of the AGR (0.607, 95% CI: 0.578–0.636), the NMLR (0.636, 95% CI: 0.605–0.667) and the TNM stage (0.671, 95% CI: 0.642–0.700). The C-index of the RFS nomogram was 0.850 (95% CI: 0.826–0.874), which was higher than that of the AGR (0.626, 95% CI: 0.602–0.651), the NMLR (0.630, 95% CI: 0.605–0.655) and the TNM stage (0.699, 95% CI: 0.675–0.723). Analogously, the OS and RFS nomograms showed the largest AUROC value (0.920

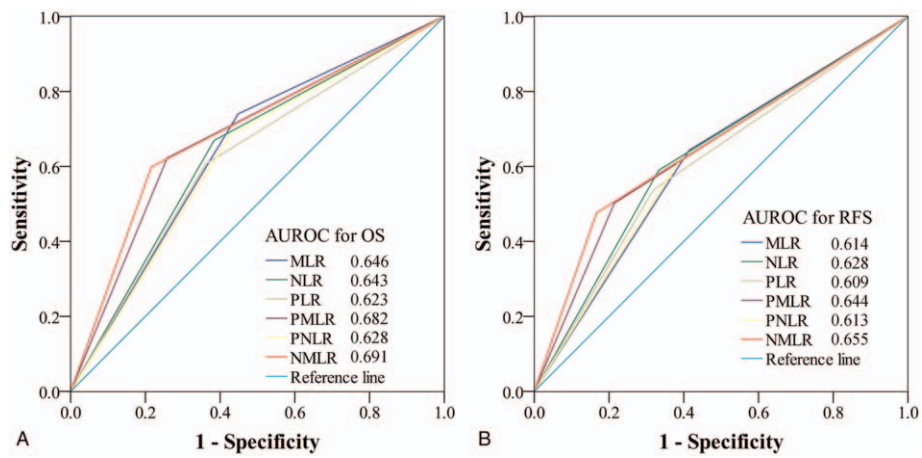


Figure 2. The AUROCs were used to compare the discrimination abilities of the immune parameters for OS (A) and RFS (B).

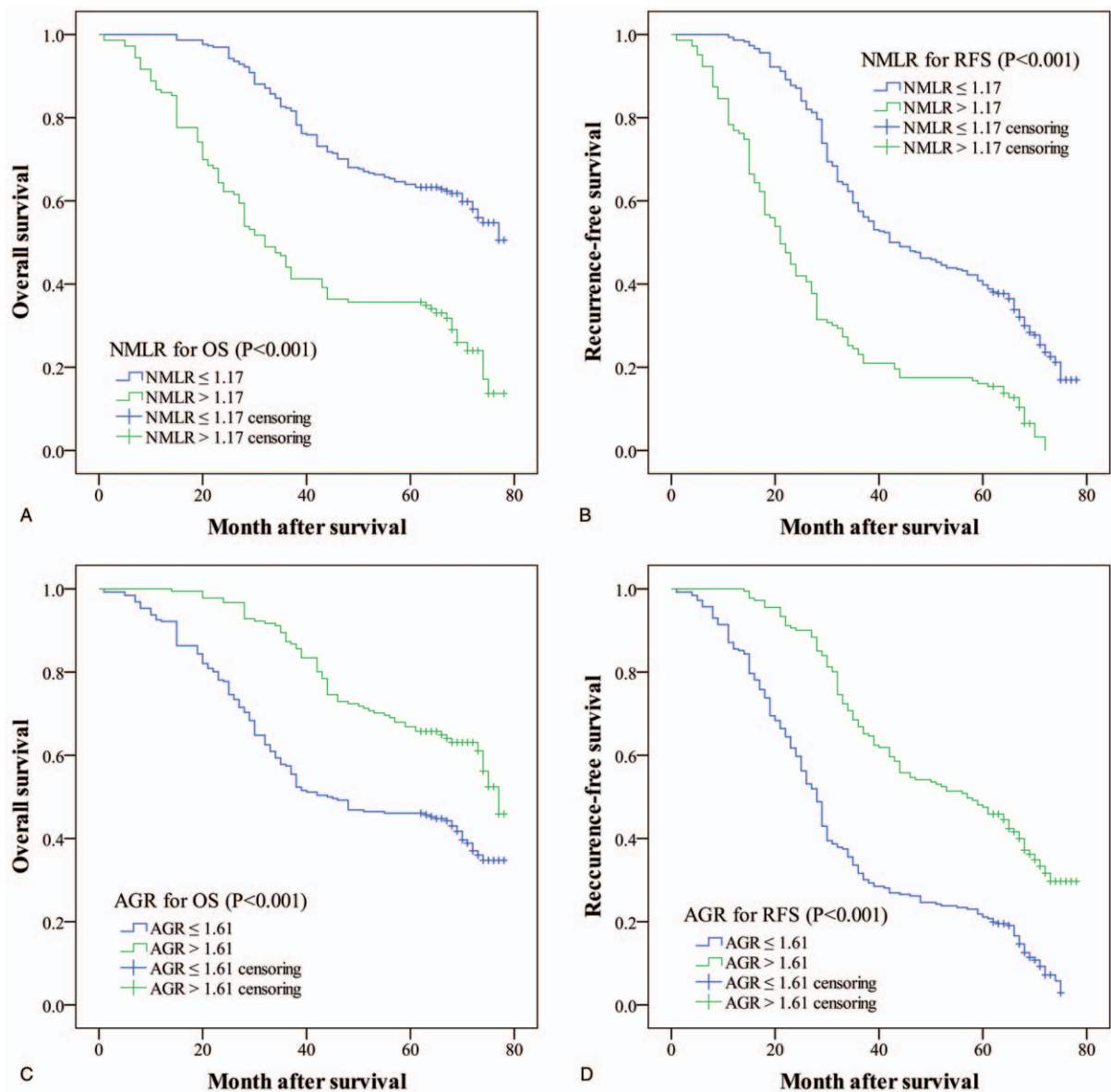


Figure 3. The Kaplan-Meier survival curves of OS according to NMLR (A). The Kaplan-Meier survival curves of RFS according to NMLR (B). The Kaplan-Meier survival curves of OS according to AGR (C). The Kaplan-Meier survival curves of RFS according to AGR (D).

**Table 2**  
Univariate and multivariate analysis of overall survival and recurrence-free survival of gastric cancer in primary cohort.

Prognostic variables	OS				DFS			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR (95%CI)	P value	HR (95%CI)	P value	HR (95%CI)	P value	HR (95%CI)	P value
Tumor size (≤4 cm vs >4cm)	0.514 (0.395–0.669)	<.001	1.183 (0.862–1.624)	.298	0.448 (0.361–0.555)	<.001	1.050 (0.804–1.372)	.720
Differentiated degree	–	<.001	–	.022	–	<.001	–	<.001
T stage	–	<.001	–	<.001	–	<.001	–	<.001
N stage	–	<.001	–	<.001	–	<.001	–	<.001
NMLR (≤1.17 vs >1.17)	0.336 (0.258–0.438)	<.001	0.236 (0.177–0.316)	<.001	0.371 (0.297–0.463)	<.001	0.152 (0.116–0.200)	<.001
AGR (≤1.61 vs >1.61)	2.080 (1.567–2.761)	<.001	2.639 (1.947–3.576)	<.001	2.435 (1.942–3.054)	<.001	4.613 (3.516–6.051)	<.001
D-dimer (≤0.2mg/L, >0.2mg/L)	0.741 (0.551–0.996)	.047	1.078 (0.786–1.480)	.640	0.780 (0.618–0.985)	.037	1.265 (0.980–1.633)	.071
CEA (≤5ng/ml, >5ng/ml)	0.726 (0.534–0.987)	.041	0.806 (0.581–1.118)	.197	0.726 (0.564–0.935)	.013	0.990 (0.756–1.298)	.945

HR=hazard ratio, OS=overall survival, RFS=recurrence-free survival.

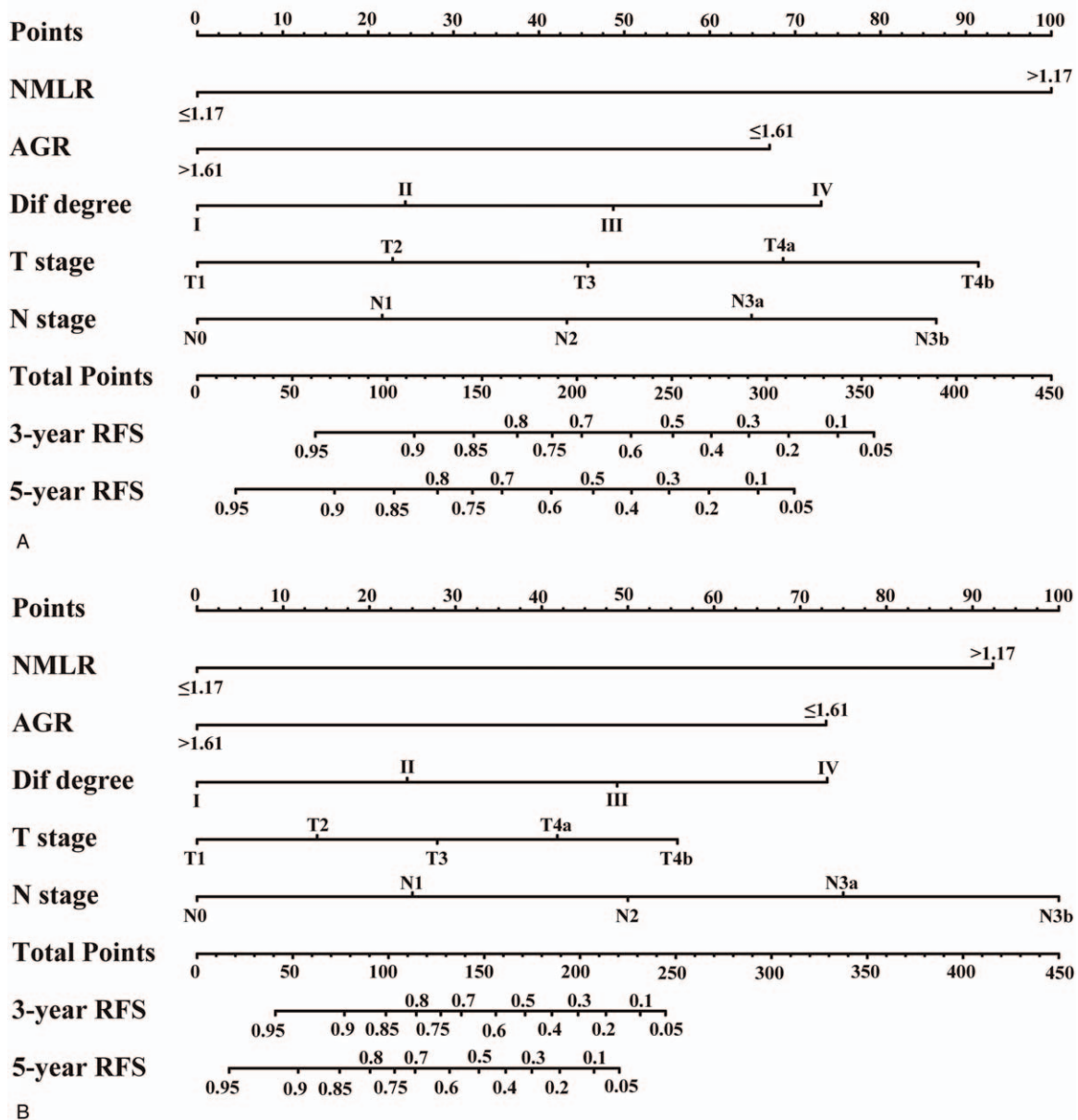


Figure 4. The 3- and 5-year OS (A) and the 3- and 5-year RFS (B) nomograms in primary cohort.

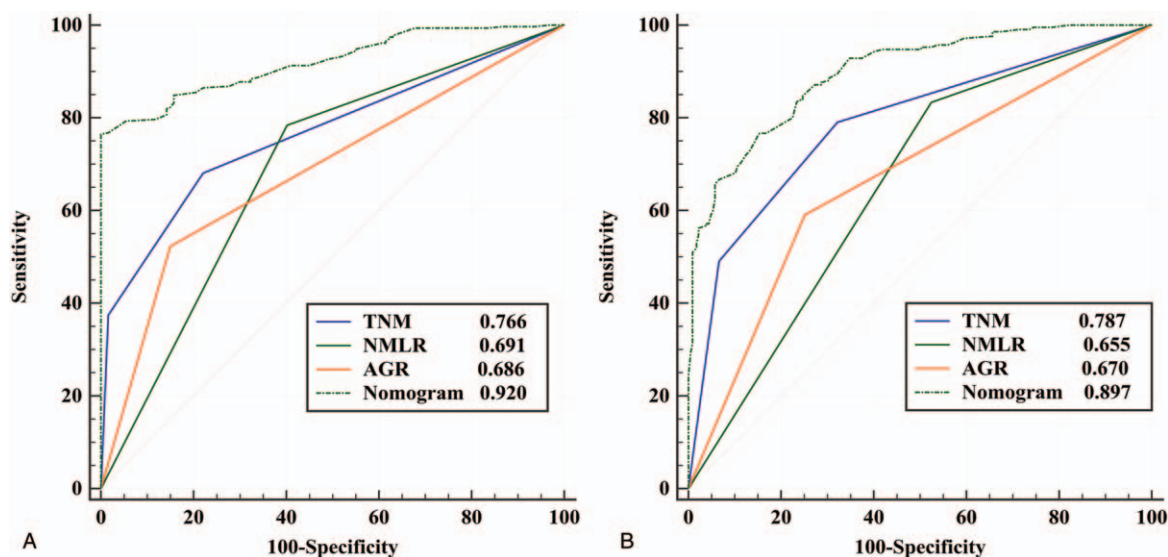


Figure 5. The AUROCs were used to compare the predictive accuracy of each prediction system for OS (A) and RFS (B).

for OS and 0.897 for RFS, respectively) compared with NMLR (0.691 for OS and 0.655 for RFS, respectively), AGR (0.686 for OS and 0.670 for RFS, respectively) and TNM stage (0.766 for OS and 0.787 for RFS, respectively), as shown in Figure 5. In the internal validation cohort, the C-indexes of the OS and RFS nomograms were 0.812 (95% CI: 0.756–0.868) and 0.826 (95% CI: 0.779–0.873), respectively. In the external validation cohort, the C-indexes of the OS and RFS nomograms were 0.866 (95% CI: 0.814–0.918) and 0.880 (95% CI: 0.839–0.92), respectively. The calibration plots of the two nomograms had a good coherence between the predictions and actual values in the probability of 3- and 5-year overall survival and recurrence-free survival, for most of the nomogram-predicted survivals were contained in the actual survivals and 95% confidence intervals, as shown in Figures 6 and 7.

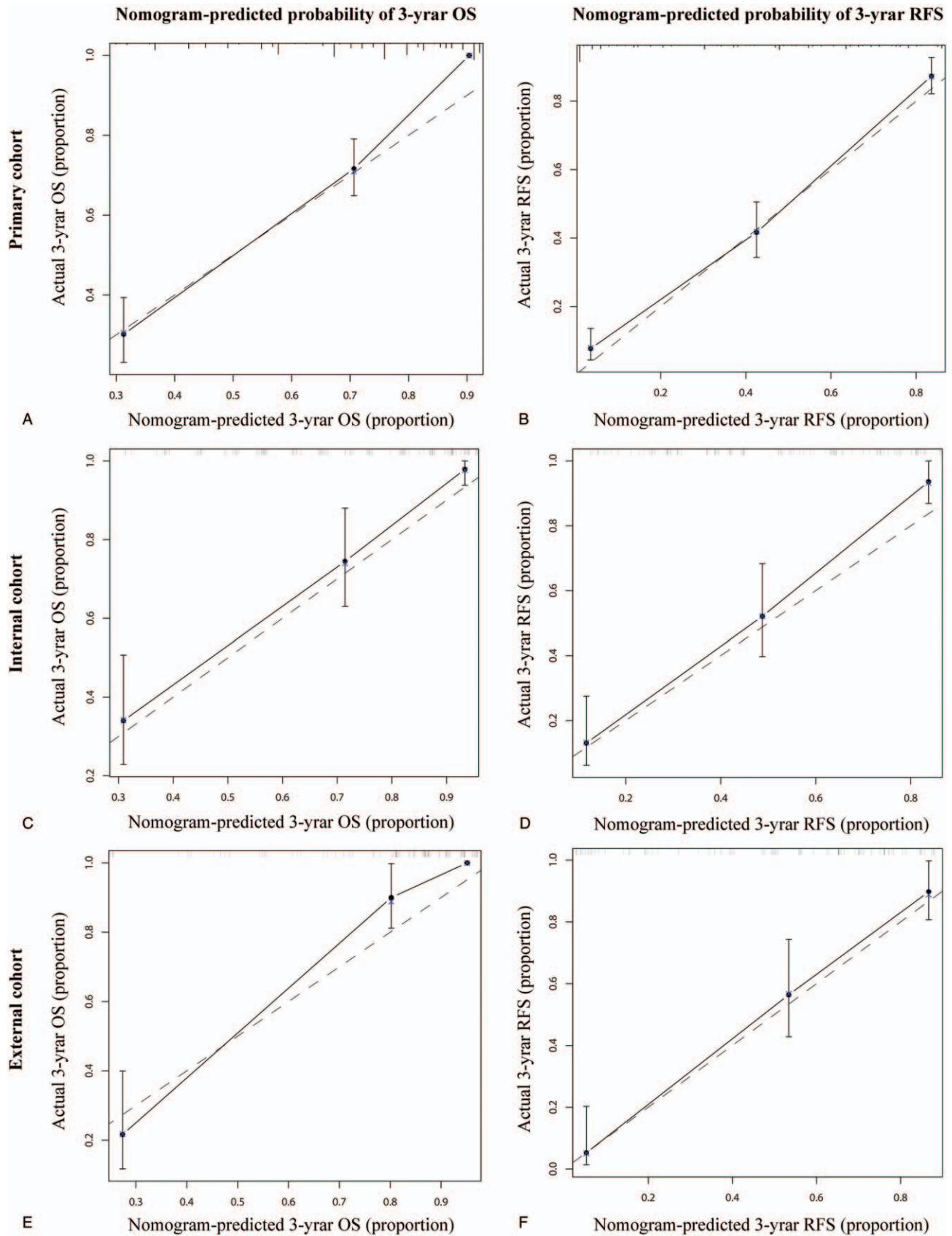
#### 4. Discussion

In the development of GC, the persistent inflammation reactions and immunity responses played an important role, which were considered an independent risk factor for prognosis.<sup>[20,21]</sup> *Helicobacter pylori*, which is associated with GC, stimulates Toll-like receptors (TLRs), induce “infection-associated inflammation” and generate the inflammatory microenvironment by activating innate immunity. The lipoprotein HP1454 of it was proved to regulate T-cell response by shaping T-cell receptor signaling.<sup>[22]</sup> Immune cells, particularly regulatory T cells, have been considered the major component, which were involved in inflammation, immunity and tumorigenesis.<sup>[23]</sup> The inflammatory and immune responses result in neutrophilia, lymphopenia and thrombocytosis. Studies revealed that the absolute counts and ratios of systemic immune cells could predict the prognosis of GC after R0 resection.<sup>[9–12,24,25]</sup> In the present study, it demonstrated that the NMLR was independently associated with both OS and RFS. The development of GC is complicated and changeable, and it is the joint effect of various inflammatory cells, immune cells and tumor cells. It is not enough to predict OS and RFS for GC

with a single inflammatory or immune cell count. Even the NLR, the PLR or the MLR is not the best.<sup>[17]</sup> Therefore, we applied NMLR as a predictive factor to assess the outcomes of GC. The NMLR, which reflects the balance in immune state, had a greater prognostic value in GC than any other immune parameters.

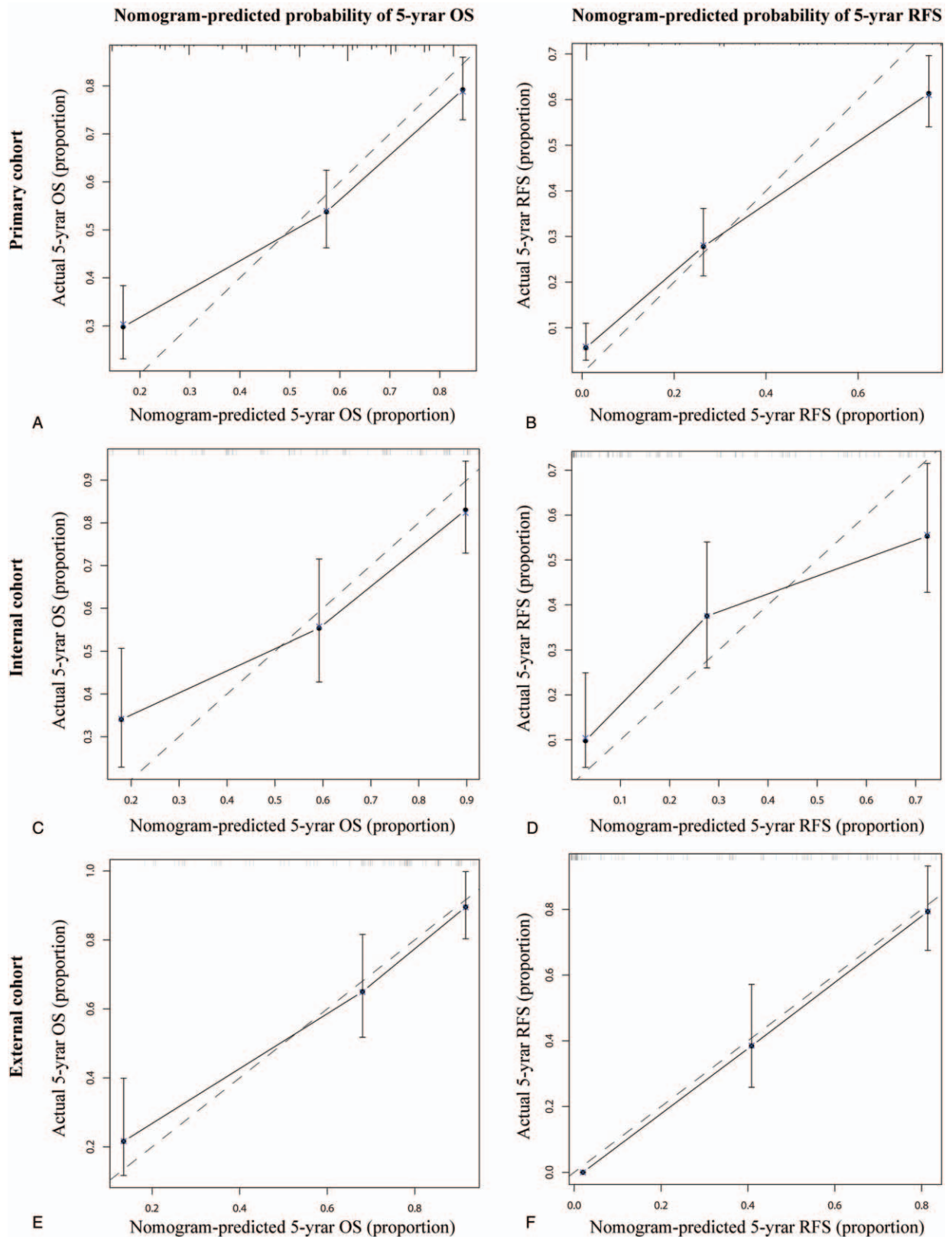
In recent years, the AGR has been identified to be associated with the mortality of many solid tumors, such as nasopharyngeal carcinoma, colorectal cancer, lung cancer, breast cancer and gastric cancer.<sup>[26–29]</sup> Malnutrition, which is reflected by low albumin among patients with GC, can weaken a certain defense system of human including cellular and humoral immunity, and so on, thus decreasing the recognition and cytotoxicity of tumor.<sup>[30]</sup> The previous studies demonstrated that some nutritional indexes, such as preoperative body weight, prognostic nutritional index (PNI) and controlling Nutritional Status (CONUT), were closely associated with the prognosis for gastric cancer.<sup>[31–33]</sup> Albumin plays not only the most common role as nutritional index, but also an important role against cancer. It could restrain the growth and induce the differentiation and apoptosis of tumor cells directly.<sup>[34]</sup> Globulin, contrary to albumin, is a pro-inflammatory protein and has various components, which could induce the cascade reaction of inflammation that can accelerate tumor progression in GC, such as immunoglobulins, acute-phase proteins, and other serum proteins.<sup>[35,36]</sup> In the meantime, there is interaction between inflammation level and nutritional condition. Hypoalbuminemia and hyperglobulinemia, meaning malnutrition and inflammatory activity, may result in poor prognosis.<sup>[37]</sup> Therefore, the AGR could ensure a better forecast accuracy by combining the predictive ability of albumin and globulin.

It was not solely the analysis of predictive ability. Here, for the first time, we insert NMLR and AGR into nomograms for GC after R0 resection based on multivariate analysis. The present nomograms are of predicting ability with better accuracy than the NMLR, the AGR and the TNM stage system. They are applicable to the patients with gastric cancer after R0 resection. They are also useful tools that utilize the common clinical information to provide the relatively accurate prognostic information for



**Figure 6.** The calibration curves for predicting the 3-year OS (A, C, and E) and RFS (B, D, and F) rates by nomogram prediction and actual observation in patients with GC in the primary cohort (A and B), internal validation cohort (C and D), and external validation cohort (E and F). The x-axis represents the nomogram-predicted survival, and the y-axis represents actual survival. The dotted line represents the ideal relationship between predicted and actual survival.





**Figure 7.** The calibration curves for predicting the 5-year OS (A, C, and E) and RFS (B, D, and F) rates by nomogram prediction and actual observation in patients with GC in the primary cohort (A and B), internal validation cohort (C and D), and external validation cohort (E and F). The x-axis represents the nomogram-predicted survival, and the y-axis represents actual survival. The dotted line represents the ideal relationship between predicted and actual survival.

doctors and patients. Not only that, they can be used as a guide to help doctors develop further treatment plan. When the patients were considered to have a bad prognosis via the nomograms, they were strongly advised comprehensive antineoplastic therapies and close follow-up. All the predictors in the 2 nomograms were previously reported to be associated with the prognosis of GC patients after gastrectomy.<sup>[29,38,39]</sup> Although some risk factors, age, sex, D-dimer and CEA, were also considered to correlate with the prognosis of GC patients in some other studies,<sup>[40–43]</sup> they were not applicable in the present study.

The present nomograms have several specific characteristics that are superior to the previous nomograms. First, the parameters included in the present nomograms are much easier to get from routine clinical data, such as NMLR, AGR and TNM stage. Furthermore, the present nomograms did not only include the severity of GC, but the patient's immune and nutritional conditions were also considered. In addition, the NMLR was determining as a factor in nomograms by a comparison of a series of immunity parameters. Finally, internal and external validations were used to confirm the accuracy of the present nomograms.

There are several limitations in the present study. First, the present study was limited by its single center and retrospective essence. Furthermore, because of the differences in ethnicity/race and epidemic between Eastern and Western countries, the nomograms could not completely apply to westerners. In addition, since a few cases were followed up for less than five years, the 5-year overall survival rate and 5-year recurrence-free survival rate were not sufficiently accurate. As another limitation, dynamic changes of nutritional and immune parameters of patients were not evaluated. Moreover, without a universally accepted standard of the cut-off values of NMLR and AGR, we have to create them using ROC curves. Finally, comorbidities, such as hypertension and diabetes, were not reflected in the present nomograms. We assume that comorbidity may affect the prognosis to some extent.

In conclusion, the proposed nomograms including nutrition and immunity parameters could be used to the predict prognosis of GC patients after R0 resection with high sensitivity and accuracy. Patients with high risk of poor prognosis could be screened out using the present nomograms and be advised close follow-up and personalized comprehensive anti-tumor therapy. However, a multi-center and large-scale collaborative study is required to validate whether the present nomograms are accurate enough, and whether there any other predictors should be considered in the prediction system.

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