A nomogram combining plasma fibrinogen and systemic immune-inflammation index predicts survival in patients with resectable gastric cancer

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Hyperfibrinogenemia and cancer-associated systemic inflammatory response are strongly associated with cancer progression and prognosis. We aimed to develop a novel prognostic score (F-SII score) on the basis of preoperative fibrinogen (F) and systemic immunoinflammatory index (SII), and evaluate its predictive value in patients with resectable gastric cancer (GC). Patients diagnosed with GC between January 2012 and December 2016 were reviewed. The F-SII score was 2 for patients with a high fibrinogen level (≥ 3.37 g/L) and a high SII (≥ 372.8), whereas that for patients with one or neither was 1 or 0, respectively. A high F-SII score was significantly associated with older patient age, a high ASA score, large tumor size, large proportion of perineural invasion, and late TNM stage. Multivariate analysis indicated that the F-SII score, histological grade, and TNM stage were independent factors for overall survival (OS). The Harrell’s concordance index (C-index) of a nomogram based on the F-SII score and several clinicopathological manifestations was 0.72, which showed a better predictive ability for OS than the TNM stage alone (0.68). In conclusion, preoperative F-SII may serve as a useful predictive factor for OS and refine outcome prediction for patients with resectable GC combined with traditional clinicopathological analysis.
Results

Patient characteristics. In the present study, a total of 608 patients were included. The median patient age was 61 years (range 25–86 years). The median follow-up period was 56.0 months (interquartile range, 41–71 months). The 1-yr, 3-yr, and 5-yr OS rates for the present study were 85.9%, 58.3%, and 48.0%, respectively. The baseline characteristics of the patients are summarized in Table 1.

Associations of the plasma fibrinogen level, SII, and F-SII score. The univariate analysis showed that the fibrinogen level and SII were associated with OS. Age, ASA score, tumor location, tumor size, histological grade, perineural invasion, and TNM stage also had a significant effect on OS (Table 2). According to our multivariate analysis, the fibrinogen level and SII were independent factors for prognosis (HR, 1.509; 95% CI, 1.181–1.929; \( P < 0.001 \); HR, 1.452; 95% CI, 1.128–1.868; \( P = 0.004 \), respectively). In addition, well or moderately differentiated tumors and stage I disease were associated with good prognosis in GC (Table 2).

Patients were classified into two independent groups based on the cutoff thresholds of fibrinogen and SII (low < 3.37 g/L or high ≥ 3.37 g/L and low < 372.8 or high ≥ 372.8, respectively) for subsequent analyses. It is showed that decreased plasma fibrinogen and SII were both associated with shorter OS (both \( P < 0.001 \)) (Fig. 1A,B). To further investigate the effect of the plasma fibrinogen level and SII on patient prognosis, we divided the patients into four groups based on the cutoff thresholds of fibrinogen and SII. Kaplan–Meier analysis indicated obvious differences between the four subgroups (\( P < 0.001 \), Fig. 1C). There was no significant difference in subgroups of either plasma fibrinogen ≥ 3.37 g/L or SII ≥ 372.8 (\( P > 0.05 \), Fig. 1C). Therefore, we combined the two subgroups. Patients were divided into three F-SII score subgroups based on the following criteria: score 2, both a high fibrinogen level (≥ 3.37 g/L) and a high SII (≥ 372.8); score 1, either a high fibrinogen level or a high SII; and score 0, both a low fibrinogen level (< 3.37 g/L) and a low SII (< 3.728).

The F-SII score independently predicts OS. The univariate analysis showed that the F-SII score had a significant effect on OS (\( P < 0.001 \)). The results of the multivariate analysis indicated that the F-SII score, histological grade, and TNM stage were independent prognostic factors of OS in GC patients (all \( P < 0.05 \)) (Table 2). Kaplan–Meier analysis showed that a high F-SII score was associated with short OS (\( P < 0.05 \), Fig. 1D). To further analyze the F-SII score's performance in patients with different TNM stages and adjuvant chemotherapy strategies, we conducted a subgroup analysis. When stratified by TNM stage, there was no significant difference in 5-yr OS between the three groups of patients with stage I GC (\( P = 0.144 \); Fig. 2A). However, the prognostic value of the F-SII score was maintained for stages II (\( P = 0.002 \); Fig. 2B), I–II (\( P < 0.001 \); Fig. 2C) and III (\( P < 0.001 \); Fig. 2D). The F-SII also stratified OS irrespective of adjuvant chemotherapy administration (\( P < 0.05 \); Fig. 3A,B).

Associations of the plasma fibrinogen level, SII, and F-SII score with clinicopathological characteristics. The associations of the plasma fibrinogen level and SII with clinicopathological characteristics are shown in Table 3. Elevated plasma fibrinogen levels and a high SII were associated with older age at surgery (\( P = 0.001 \) and \( P = 0.021 \)), a high ASA score (\( P = 0.006 \) and \( P = 0.015 \)), tumor size ≥ 5 cm (both \( P < 0.001 \)), and a late TNM stage (both \( P < 0.001 \)). Moreover, we assessed the association between the F-SII score and clinicopathological factors (Table 3). A high F-SII score was associated with older patient age (\( P < 0.001 \)), a high ASA score (\( P = 0.002 \)), large tumor size (\( P < 0.001 \)), a large proportion of perineural invasion (\( P = 0.033 \)), and late TNM stage (\( P < 0.001 \)) (Table 3).

Predictive nomogram for OS. To evaluate the predictive value of the F-SII score, we constructed a nomogram that integrated the independent prognostic factors consisting of TNM stage, histological grade, and F-SII score (Fig. 4A). In this nomogram, each factor was ascribed a weighted point total that indicated a survival prognosis. For internal validation, the calibration curve suggested that the 3- and 5-yr survival rates predicted by the nomogram were consistent with the actual survival rates (Fig. 4B,C). The Harrell's concordance index (C-index) of the nomogram was 0.72, which showed a better predictive ability for OS than the TNM stage (C-index 0.68) and F-SII (C-index 0.62). The areas under the 3-yr and 5-yr ROC curves of the nomogram were 0.797 and 0.80, respectively (Fig. 5A,B). Therefore, combined with the above results, the nomogram is superior to the TNM staging system in predicting the OS of patients with GC.

Discussion

In this study, we confirmed that the preoperative plasma fibrinogen and SII were independent prognostic factors in patients with resectable GC. Moreover, the F-SII score, a newly proposed cumulative score, remained an independent prognostic factor in the multivariate analysis. In addition, its prognostic significance was maintained in the subgroup analysis of patients diagnosed with TNM stages I–II or stage III, as well as patients who did or did not receive adjuvant chemotherapy. We found that a high F-SII score was also associated with older age at surgery, a high ASA score, a large tumor size, the presence of perineural invasion, and a late TNM stage. Then, we developed a prognostic nomogram that included the TNM stage, histological grade, and F-SII score and predicted OS with an accuracy of 0.72. Thus, the F-SII score as an easy and inexpensive indicator might provide important prognostic information to help clinicians estimate the patient outcome by combining with conventional clinicopathological analysis. To the best of our knowledge, this is the first study to determine the clinical value of the F-SII score in patients with resectable GC.

It was reported that plasma fibrinogen is synthesized as an acute-phase reactant glycoprotein by hepatocytes. Several studies have reported the mechanisms of hyperfibrinogenemia in various tumors. In patients with lung cancer, interleukin-6 produced by tumor cells stimulates the secretion of fibrinogen.
| Characteristics          | No | %  |
|-------------------------|----|-----|
| Age (years)             |    |     |
| ≥ 60                    | 354| 58.2|
| < 60                    | 254| 41.8|
| Sex                     |    |     |
| Male                    | 461| 75.8|
| Female                  | 147| 24.2|
| BMI (kg/m²)             |    |     |
| ≥ 24                    | 160| 26.3|
| < 24                    | 448| 73.7|
| ASA score               |    |     |
| 1                       | 40 | 6.6 |
| 2                       | 446| 73.4|
| 3                       | 122| 20.1|
| Tumor location          |    |     |
| Upper                   | 207| 34.0|
| Middle                  | 124| 20.4|
| Lower                   | 277| 45.6|
| Tumor size (cm)         |    |     |
| ≥ 5                     | 267| 43.9|
| < 5                     | 341| 56.1|
| Histological grade      |    |     |
| Well or moderately       | 202| 33.2|
| differentiated           |    |     |
| Poorly or not            | 406| 66.8|
| differentiated           |    |     |
| Vascular invasion       |    |     |
| Yes                     | 68 | 11.2|
| No                      | 540| 88.8|
| Perineural invasion     |    |     |
| Yes                     | 217| 35.7|
| No                      | 391| 64.3|
| Lymphatic invasion      |    |     |
| Yes                     | 65 | 10.7|
| No                      | 543| 89.3|
| Pathological tumor stage|    |     |
| T1                      | 98 | 16.1|
| T2                      | 36 | 5.9 |
| T3                      | 47 | 7.7 |
| T4                      | 427| 70.2|
| Pathological lymph node stage |    |     |
| N0                      | 225| 37  |
| N1                      | 105| 17.3|
| N2                      | 117| 19.2|
| N3                      | 161| 26.5|
| TNM stage               |    |     |
| I                       | 115| 18.9|
| II                      | 141| 23.2|
| III                     | 352| 57.9|
| Adjuvant chemotherapy   |    |     |
| Yes                     | 325| 53.5|
| No                      | 283| 46.5|
| Fibrinogen level (g/L)  |    |     |
| ≥ 3.37                  | 258| 42.4|
| < 3.37                  | 350| 57.6|
| SII                     |    |     |
| ≥ 372.8                 | 328| 53.9|
| < 372.8                 | 280| 46.1|
| F-SII score             |    |     |
| Continued               |    |     |
fibrinogen, which is synthesized by cancer cells, promotes the proliferation of fibroblast growth factor-2 [26]. Finally, plasma fibrinogen promotes tumor cell growth and angiogenesis by interacting with fibroblast growth factor-2 and vascular endothelial growth factor [16,17]. On the other hand, since Virchow originally made a link between cancer and inflammation in the nineteenth century, a growing body of evidence [3,18] has suggested that the levels of inflammatory markers play a vital role in tumor progression and metastasis. Hu et al. [7] reported that a high SII was related to liver cirrhosis, a large tumor size, low tumor differentiation, early recurrence, high circulating tumor cell levels, and a poor prognosis in patients with hepatocellular carcinoma. Moreover, Wang et al. [10] found that high SII was associated with old age at surgery, poor Borrmann classification, a large tumor size, advanced tumor invasion, lymph node metastasis, distant metastasis, advanced TNM stage, a high CEA level, and a poor outcome in patients with gastric cancer. It was reported that a high SII was also connected with sex, the hemoglobin level, and a poor prognosis in patients with small-cell lung cancer [19]. In the present study, we showed that the plasma fibrinogen level and SII are independent prognostic factors of OS in GC patients. Therefore, we created the F-SII score consisting of the plasma fibrinogen level and SII.

Table 1. Patient and tumor characteristics. BMI Body Mass Index, ASA score American Society of Anesthesiologists score, SII Systemic immune-inflammation index, F-SII Fibrinogen and systemic immune-inflammation index.

| Characteristics | BMI | ASA score | SII | F-SII |
|-----------------|-----|-----------|-----|-------|
|                 | 0   | 208       | 34.2|       |
|                 | 1   | 214       | 35.2|       |
|                 | 2   | 186       | 30.6|       |

Table 2. Univariate and multivariate Cox regression analyses for overall survival in patients with gastric cancer. BMI Body Mass Index, ASA score American Society of Anesthesiologists score, SII Systemic immune-inflammation index, F-SII Fibrinogen and systemic immune-inflammation index score.

| Characteristics | Univariate analysis | Multivariate analysis<sup>a</sup> | Multivariate analysis<sup>b</sup> |
|-----------------|--------------------|-----------------------------------|-----------------------------------|
|                 | HR (95%CI)         | P-values                          | HR (95%CI)                        | P-values |
| Age (≥60 vs. <60 years) | 1.269 (1.006–1.602) | 0.045                             | 1.052 (0.821–1.348)               | 0.689 |
| Sex (Female vs. Male) | 0.815 (0.615–1.073) | 0.145                             |                                   |       |
| BMI (≥24 vs. <24 kg/m2) | 0.895 (0.689–1.162) | 0.405                             |                                   |       |
| ASA score | 0.009 | 0.272 | 0.282 |
| 2 vs. 1 | 1.118 (0.690–1.813) | 0.650 | 0.993 (0.668–1.623) | 0.979 | 0.992 (0.607–1.620) | 0.973 |
| 3 vs. 1 | 1.663 (0.992–2.786) | 0.054 | 1.240 (0.728–2.114) | 0.428 | 1.235 (0.725–2.106) | 0.437 |
| Tumor location | | | |
| Middle vs. upper | 0.825 (0.606–1.124) | 0.224 | 0.984 (0.713–1.358) | 0.923 | 0.986 (0.714–1.362) | 0.933 |
| Lower vs. upper | 0.651 (0.505–0.840) | 0.001 | 0.810 (0.624–1.051) | 0.112 | 0.809 (0.624–1.050) | 0.112 |
| Tumor size (≥5 vs. <5 cm) | 2.187 (1.737–2.753) | <0.001 | 1.251 (0.983–1.591) | 0.069 | 1.253 (0.985–1.594) | 0.066 |
| Histological grade: Well or moderately differentiated vs. Poorly or not differentiated | 0.498 (0.382–0.651) | <0.001 | 0.721 (0.546–0.952) | 0.021 | 0.721 (0.546–0.952) | 0.021 |
| Vascular invasion (Yes vs. No) | 1.309 (0.938–1.828) | 0.113 | 1.034 (0.815–1.312) | 0.781 | 1.033 (0.813–1.311) | 0.792 |
| Perineural invasion (Yes vs. No) | 1.714 (1.362–2.157) | <0.001 | 1.034 (0.815–1.312) | 0.781 | 1.033 (0.813–1.311) | 0.792 |
| Lymphatic invasion (Yes vs. No) | 1.159 (0.817–1.643) | 0.408 | 1.034 (0.815–1.312) | 0.781 | 1.033 (0.813–1.311) | 0.792 |
| TNM stage | | | |
| II vs. I | 4.254 (2.212–8.183) | <0.001 | 3.125 (1.602–6.094) | 0.001 | 3.119 (1.599–6.084) | 0.001 |
| III vs. I | 11.485 (6.267–21.048) | <0.001 | 7.619 (4.050–14.332) | <0.001 | 7.614 (4.047–14.322) | <0.001 |
| Adjuvant chemotherapy (Yes vs. No) | 1.033 (0.823–1.297) | 0.780 | 1.033 (0.823–1.297) | 0.780 | 1.033 (0.823–1.297) | 0.780 |
| Fibrinogen level (≥3.37 vs. <3.37 g/L) | 2.097 (1.668–2.636) | <0.001 | 1.509 (1.181–1.929) | 0.001 | 1.509 (1.181–1.929) | 0.001 |
| SII (≥372.8 vs. <372.8) | 2.013 (1.584–2.558) | <0.001 | 1.452 (1.128–1.868) | 0.004 | 1.452 (1.128–1.868) | 0.004 |
| F-SII score | | | |
| 1 vs. 0 | 1.493 (1.094–2.036) | 0.012 | 1.505 (1.097–2.066) | 0.011 | 1.505 (1.097–2.066) | 0.011 |
| 2 vs. 0 | 2.656 (1.979–3.564) | <0.001 | 2.201 (1.612–3.004) | <0.001 | 2.201 (1.612–3.004) | <0.001 |
In agreement with previous findings, we demonstrated that both a high fibrinogen level and a high SII (F-SII score 2) are related to advanced tumor stage and a poor prognosis. In contrast, decreased levels of both (F-SII score 0) are related to early tumor stage and a favorable prognosis. Furthermore, a high F-SII score was associated with aggressive tumor biological phenotypes, such as large tumor size, the presence of perineural invasion, and advanced tumor stage. Combined with the above results, the complex interaction between an elevated systemic inflammatory response and tumor progression was partially revealed. Of note, its prognostic significance was still maintained in the subgroup analysis of patients diagnosed with TNM stages I–II or stage III, as well as patients who did or did not receive adjuvant chemotherapy, suggesting that the F-SII score might provide additional prognostic information as a complement to the complete clinicopathological predictive models. As a result, the F-SII score could be an accurate prognostic indicator.

At present, the nomogram fulfills a necessary role in personalisation of oncological treatments by integrating diverse prognostic and determinant variables to generate the probability of a clinical event20. In our study, we developed a nomogram that includes the preoperative TNM stage, histological grade, and F-SII score to improve outcome prediction in GC patients after surgery. We found that the nomogram showed more accurate predictive
ability than the TNM stage alone. In addition, the F-SII score can be considered a supplement to physical examinations, such as cross-sectional imaging, endoscopic ultrasonography, and endoscopy, to refine risk stratification in patients with gastric cancer before and after treatment.

The strength of our study is that F-SII score measurements were based on standard laboratory tests of plasma fibrinogen and platelet, neutrophil, and lymphocyte counts, which are routinely used in clinical practice. Nevertheless, our study has certain limitations. First, due to the retrospective nature of the study and the lack of external validation, the prognostic significance of the F-SII score in GC patients remains to be examined prospectively in other populations and larger studies in the future. Second, hematological cell counts may be affected by several factors, though we limited some of the possible confounders. Third, we lacked follow-up information for disease-free survival (DFS), and the application of other survival outcomes may strengthen our findings.

Figure 2. Kaplan–Meier analysis of OS of GC patients at each TNM stage according to the F-SII score. (A) Association of the F-SII score with the OS of patients with stage I GC. (B) Association of the F-SII score with the OS of patients with stage II GC. (C) Association of the F-SII score with the OS of patients with stage I-II GC. (D) Association of the F-SII score with the OS of patients with stage III GC.
Conclusion
In conclusion, we created a novel and convenient prognostic score named the F-SII score, which was revealed an independent predictor of survival in patients with resectable GC. The F-SII score may be a useful clinical biomarker for identifying patients at high prognostic risk and planning individualized treatment strategies for GC patients.

Methods
Patient characteristics. We collected data from 608 consecutive patients with resectable gastric adenocarcinoma who were treated between January 2012 and December 2016 at the Department of General Surgery, The First Affiliated Hospital of Xi'an Jiaotong University. All patients provided informed consent prior to study participation. This study was approved by the Institutional Review Board of the First Affiliated Hospital of Xi'an Jiaotong University and conducted in compliance with the principles of the Declaration of Helsinki for medical research involving humans. The inclusion criteria of this study were as follows: (1) gastric adenocarcinoma confirmed histopathologically, (2) complete medical records, and (3) underwent radical gastrectomy. The exclusion criteria of this study were as follows: (1) other malignancies, (2) neoadjuvant chemotherapy, (3) metastatic disease, (4) autoimmune or other inflammatory diseases, (5) perioperative mortality, (6) hematological disease, (7) intravenous or arterial embolization within 3 months and (8) continuous anticoagulant therapy. We gathered the following clinical, pathologic, and laboratory data of the patients: age, sex, BMI, American Society of Anesthesiologists (ASA) score, tumor location, tumor size, histological grade, vascular invasion, perineural invasion, lymphatic invasion, TNM stage, adjuvant chemotherapy, fibrinogen, and SII. In our hospital, 5-fluorouracil-based adjuvant chemotherapy is routinely delivered to patients with advanced GC.

The SII and F-SII score. Preoperative plasma fibrinogen, lymphocyte, neutrophil, and platelet count levels were examined in samples obtained before breakfast within 7 days prior to surgery. As defined previously, the SII was defined as follows: SII = platelet count × neutrophil count/lymphocyte count. The optimal cut-off values for plasma fibrinogen (low < 3.37; high ≥ 3.37 g/L) and SII (low < 372.8; high ≥ 372.8) were obtained through ROC curves. The F-SII score was established based on the combination of different plasma fibrinogen levels and SII values.

Follow-up. Enrolled patients were prospectively followed-up until June 2019. Patients were routinely followed up every 3 months for the first 2 years after treatment and every 6 months thereafter. Patients evaluations included laboratory tests, a physical examination, multislice computed tomography, and other examinations. OS was defined as the time from the date of surgery to death from any cause or the last follow-up.
### Table 3. Associations of Fibrinogen, SII, and F-SII score with clinicopathological characteristics. **BMI** Body Mass Index, **ASA score** American Society of Anesthesiologists score, **SII** Systemic immune-inflammatory index, **F-SII** Fibrinogen and systemic immune-inflammatory index.

| Characteristics                  | <3.37 | ≥3.37 | P-values | <372.8 | ≥372.8 | P-values | 0   | 1   | 2   | P-values |
|----------------------------------|-------|-------|----------|--------|--------|----------|-----|-----|-----|----------|
| **Age (years)**                  |       |       |          |        |        |          |     |     |     |          |
| >60                              | 179   | 175   | <0.001   | 149    | 205    | 0.021    |     |     |     | <0.001   |
| <60                              | 171   | 83    |          | 131    | 123    |          | 107 | 88  | 59  |          |
| **Sex**                          |       |       |          |        |        |          |     |     |     |          |
| Male                             | 273   | 188   | 0.144    | 205    | 256    | 0.165    | 159 | 160 | 142 | 0.904    |
| Female                           | 77    | 70    |          | 75     | 72     |          | 49  | 54  | 44  |          |
| **BMI (kg/m²)**                  |       |       |          |        |        |          |     |     |     |          |
| >24                              | 102   | 58    | 0.065    | 82     | 78     | 0.124    | 64  | 56  | 40  | 0.114    |
| <24                              | 248   | 200   |          | 198    | 250    |          | 144 | 158 | 146 |          |
| **ASA score**                    |       |       |          |        |        |          |     |     |     |          |
| 1                                | 22    | 18    | 0.006    | 19     | 21     | 0.015    | 14  | 13  | 13  | 0.002    |
| 2                                | 273   | 173   |          | 219    | 227    |          | 171 | 150 | 125 |          |
| 3                                | 55    | 67    |          | 42     | 80     |          | 23  | 31  | 48  |          |
| **Tumor location**               |       |       |          |        |        |          |     |     |     |          |
| Upper                            | 115   | 92    | 0.559    | 96     | 111    | 0.792    | 67  | 77  | 63  | 0.707    |
| Middle                           | 69    | 55    |          | 60     | 64     |          | 46  | 37  | 41  |          |
| Lower                            | 166   | 111   |          | 124    | 153    |          | 95  | 100 | 82  |          |
| **Tumor size (cm)**              |       |       |          |        |        |          |     |     |     |          |
| ≥5                               | 117   | 150   | <0.001   | 97     | 170    | <0.001   | 60  | 94  | 113 | <0.001   |
| <5                               | 233   | 108   |          | 183    | 158    |          | 148 | 120 | 73  |          |
| **Histological grade**           |       |       |          |        |        |          |     |     |     |          |
| Well or moderately different     | 124   | 78    | 0.179    | 101    | 101    | 0.168    | 81  | 63  | 58  | 0.091    |
| Poorly or not differentiated      | 226   | 180   |          | 179    | 227    |          | 127 | 151 | 128 |          |
| **Vascular invasion**            |       |       |          |        |        |          |     |     |     |          |
| Yes                              | 35    | 33    | 0.281    | 29     | 39     | 0.55     | 20  | 24  | 24  | 0.586    |
| No                               | 315   | 225   |          | 251    | 289    |          | 188 | 190 | 162 |          |
| **Perineural invasion**          |       |       |          |        |        |          |     |     |     |          |
| Yes                              | 118   | 99    | 0.236    | 89     | 128    | 0.063    | 60  | 87  | 70  | 0.033    |
| No                               | 232   | 159   |          | 191    | 200    |          | 148 | 127 | 116 |          |
| **Lymphatic invasion**           |       |       |          |        |        |          |     |     |     |          |
| Yes                              | 36    | 29    | 0.707    | 28     | 37     | 0.611    | 19  | 26  | 20  | 0.605    |
| No                               | 314   | 229   |          | 252    | 291    |          | 189 | 188 | 166 |          |
| **TNM stage**                    |       |       |          |        |        |          |     |     |     |          |
| I                                | 89    | 26    | <0.001   | 78     | 37     | <0.001   | 68  | 31  | 16  | <0.001   |
| II                               | 80    | 61    |          | 60     | 81     |          | 42  | 56  | 43  |          |
| III                              | 181   | 171   |          | 142    | 210    |          | 98  | 127 | 127 |          |
| **Adjuvant chemotherapy**        |       |       |          |        |        |          |     |     |     |          |
| Yes                              | 189   | 136   | 0.753    | 149    | 176    | 0.913    | 107 | 124 | 94  | 0.258    |
| No                               | 161   | 122   |          | 131    | 152    |          | 101 | 90  | 92  |          |

Statistical analysis. Statistical analyses were performed using SPSS software (version 25.0; SPSS Inc., Chicago, IL, USA) and R version 3.6.1 software (http://www.r-project.org/). Extension packages, including "survival", "rms", "foreign", and "survivalROC" were also used. Chi-square tests were performed to analyze categorical variables. Kaplan–Meier survival curves were generated, and the log-rank test was performed to compare survival rates. The best cutoff points of plasma fibrinogen and SII were determined using the Youden index and
ROC curves. Multivariate analysis using a Cox proportional hazards regression model was used based on variables with a P-value of < 0.05 from the univariate analysis. The nomogram was plotted based on the results of the multivariate analysis. The model’s predictive accuracy was estimated by the C-index²⁶ and ROC curve analysis. The calibration plots were applied to verify the performance characteristics of the predictive nomogram. The significance level for all statistical tests was set at 0.05, and all tests were 2-sided.

Figure 4. Nomogram for predicting 3- and 5-year OS of GC patients after surgery. (A) Nomogram for predicting 3- and 5-year OS of GC patients after surgery. Calibration plot of the nomogram for (B) 3-year and (C) 5-year survival. The dashed line represents the performance of an ideal nomogram. The blue line indicates the performance of the proposed nomogram. Blue circles are sub-cohorts of the data set; X is the bootstrapped corrected estimate of nomogram with 200 resamples. Vertical bars represent 95% CI. It seems that the nomogram predicts accurately 3- and 5-year OS.
Figure 5. Time-dependent receiver operating characteristic curve analysis for the sensitivity and specificity of the nomograms. Receiver operating characteristic of the nomogram for (A) 3-yr survival and (B) 5-yr survival.

Data availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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**Author contributions**

X.M.C. and P.X.W. designed the study; H.J.W., J.H.L., G.L.Q., and J.I. collected the data; P.X.W. and L.F. interpreted the results; P.X.W. and X.H.L. prepared the manuscript; All authors approved the final version of the manuscript.

**Competing interests**

The authors declare no competing interests.

**Additional information**

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