



Research article

Prognostic value analysis and survival model construction of different treatment methods for advanced intestinal type gastric adenocarcinoma

Shuangai Liu^{a,b,c,1}, Yizhou Zhuang^d, Qibo Fu^e, Zhongyuan Zhang^c, Kai Hang^c, Ting Tao^c, Lei Liu^f, Jiheng Wu^{c,e,**}, Yuanmei Liu^{a,b,g,***}, Jinhu Wang^{c,h,*}

^a Department of Pediatric Surgery, Affiliated Hospital of Zunyi Medical University, Zunyi, China

^b Guizhou Children's Hospital, Zunyi, China

^c Pediatric Cancer Research Center, National Clinical Research Center for Child Health, Hangzhou, China

^d Fujian Provincial Key Laboratory of Geriatric Diseases, Fujian Medical University, Fujian Provincial Hospital, Fujian Provincial Institute of Clinical Geriatrics, Fuzhou, China

^e National Clinical Trial Institute, The Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou, China

^f Department of Pathology, Children's Hospital Affiliated to Zhejiang University School of Medicine, Hangzhou, China

^g Department of Pediatric Surgery, Affiliated Hospital of Zunyi Medical University, Zunyi, China

^h Department of Surgical Oncology, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China

ARTICLE INFO

Keywords:

Intestinal type gastric adenocarcinoma

Prognosis analysis

Nomogram

OS

CSS

ABSTRACT

Background: Intestinal-type gastric adenocarcinoma, representing 95 % of gastric malignancies, originates from the malignant transformation of gastric gland cells. Despite its prevalence, existing methods for prognosis evaluation of this cancer subtype are inadequate. This study aims to enhance patient-specific prognosis evaluation by analyzing the clinicopathological characteristics and prognostic risk factors of intestinal-type gastric adenocarcinoma patients using data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI).

Methods: We extracted clinical data for patients diagnosed with intestinal-type gastric adenocarcinoma between 2010 and 2015 from the SEER database, selecting 257 cases based on pre-defined inclusion and exclusion criteria. Independent risk factors for overall survival (OS) and cancer-specific survival (CSS) were identified using a Cox regression model. A nomogram model for predicting OS or CSS was developed from the Cox risk regression analysis and validated through the consistency index (C-index), ROC curve, and calibration curve.

Results: Age, primary tumor resection, chemotherapy, lymph node metastasis, and tumor size were identified as independent prognostic factors for OS and CSS ($P < 0.05$). The nomogram model, constructed from these indicators, demonstrated superior predictive consistency for OS and CSS compared to the AJCC-TNM staging system. ROC curve analysis confirmed the model's

* Corresponding author. Department of Surgical Oncology, Children's Hospital Zhejiang University School of Medicine, Hangzhou, China.

** Corresponding author. Pediatric Cancer Research Center, National Clinical Research Center for Child Health, Hangzhou, China.

*** Corresponding author. Department of Pediatric Surgery, Affiliated Hospital of Zunyi Medical University, Zunyi, China.

E-mail addresses: liushuangai@zmu.edu.cn (S. Liu), wjh@zju.edu.cn (J. Wang).

¹ First author.

<https://doi.org/10.1016/j.heliyon.2024.e32238>

Received 4 March 2024; Received in revised form 29 May 2024; Accepted 30 May 2024

Available online 31 May 2024

2405-8440/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).

higher accuracy, and calibration curve analysis indicated good agreement between the nomogram's predictions and actual observed outcomes.

Conclusion: The nomogram model derived from SEER database analyses accurately predicts OS and CSS for patients with intestinal-type gastric adenocarcinoma. This model promises to facilitate more tailored treatments in clinical practice.

1. Introduction

Gastric cancer, a prevalent malignancy within the digestive system, is characterized by its high invasiveness, poor prognosis, and significant threat to human health. GLOBOCAN 2020 reports rank its global incidence and mortality rates as the fifth and fourth highest, respectively [1]. The Asian population experiences the highest incidence rates worldwide [2,3]. Key risk factors include dietary habits, smoking history, *Helicobacter pylori* infection, and genetic mutations [4–8]. The early stages of gastric cancer often present with diverse and subtle symptoms, leading to frequent underdiagnosis and progression to advanced stages by the time of diagnosis [9–11], culminating in a dismal five-year survival rate of approximately 20 % [12]. Gastric cancer demonstrates considerable heterogeneity in histological patterns and treatment response rates [13,14]. Notably, gastric adenocarcinoma constitutes about 90 % of all gastric cancer cases [15]. Statistics reveal that 46 % of patients undergoing gastric cancer resection experience recurrence, with 53 % of these recurrences occurring in patients with intestinal-type gastric adenocarcinoma and 47 % in those with diffuse or mixed types [16].

Current clinical practice predominantly relies on the American Joint Committee on Cancer (AJCC) staging guidelines for risk stratification and prognostic survival assessment [17]. These guidelines incorporate pathological indicators such as tumor depth, lymph node metastasis count, and extent of organ invasion. However, they overlook dynamic factors crucial for personalized prognosis, including age, surgical interventions, and chemotherapy, thereby limiting their prognostic utility. In contrast, the nomogram prediction model offers a more nuanced approach by quantitatively integrating multiple independent prognostic factors into a comprehensive statistical model, allowing for a more detailed prognostic survival estimation [18–20]. To date, there has been a lack of research specifically addressing the prognosis and survival evaluation of enteric gastric adenocarcinoma.

Accordingly, this study leverages data from the Surveillance, Epidemiology, and End Results (SEER) database to systematically analyze 257 cases of enteric gastric adenocarcinoma, focusing on clinical characteristics and prognostic factors. The aim is to develop a prognostic evaluation model for enteric gastric adenocarcinoma, thereby offering a valuable tool for enhancing the accuracy of treatment and prognosis assessment in patients.

2. Methods

2.1. Data collection

SEER database [21] has meticulously documented patient incidences, pathology, treatments, and prognoses in various states and counties across the United States since 1973. Characterized by a vast array of cases and comprehensive clinical data, this study utilized the SEER*Stat software version 8.4.3 to extract data on patients diagnosed with enteric gastric adenocarcinoma between 2010 and 2015.

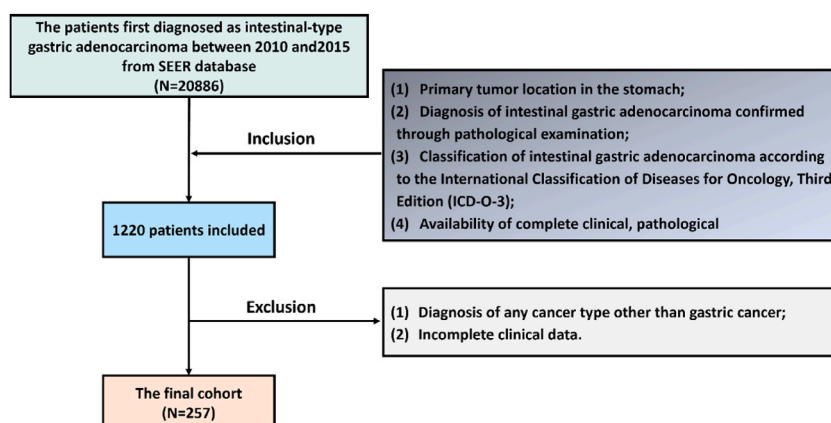


Fig. 1. Inclusion and exclusion of patient flow chart.

2.2. Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) Primary tumor location in the stomach; (2) Diagnosis of intestinal gastric adenocarcinoma confirmed through pathological examination; (3) Classification of intestinal gastric adenocarcinoma according to the International Classification of Diseases for Oncology, Third Edition (ICD-O-3); (4) Availability of complete clinical, pathological, and follow-up data: (1) Diagnosis of any cancer type other than gastric cancer; (2) Incomplete clinical data. The patient inclusion and exclusion flow chart is shown in Fig. 1.

2.3. Variables analyzed

The analysis encompassed the following variables: patient sex, age at diagnosis, primary tumor site, histologic type, ICD-O-3 code, stage (7th Edition), surgical treatment at primary site (RX Summ-Surg Prim Site), radiation therapy status (Radiation Recode), chemotherapy status (Chemotherapy Recode), number of regional nodes examined, tumor size, SEER-specific cause of death classification, other causes of death according to SEER, survival time in months, vital status, indicator of first malignant primary, race/ethnicity recode, AJCC T stage, and AJCC N stage.

2.4. Indicators analyzed

The study analyzed a comprehensive set of variables, encompassing 10 key indicators: gender, age, race, location of the tumor, tumor T stage, tumor N stage, utilization of radiotherapy, chemotherapy, primary surgery, presence of lymph node metastasis, survival status, cause of death, and duration of survival. Tumor staging was conducted in accordance with the 7th edition of the American Joint Committee on Cancer (AJCC) TNM staging criteria.

2.5. Statistical analysis

For statistical analysis, R software version 3.6.3 was employed. The chi-square (χ^2) test was utilized to assess differences in the composition ratios of variables across all groups. To evaluate the impact of each variable on overall survival (OS) and cancer-specific survival (CSS), Cox proportional hazards regression models and other relevant regression analyses were applied. Furthermore, survival curves for each variable were generated using Kaplan-Meier estimates and the Log-rank test, facilitated by R software.

Table 1

Basic characteristics of patients with intestinal-type gastric adenocarcinoma included in the study.

Variables		No chemotherapy group (N = 100)	Chemotherapy group (N = 157)	P value
Genders	Male	56(56.0 %)	98(62.4 %)	0.361
	Female	44(44.0 %)	59(37.6 %)	
Age (years)	> 75	58(58.0 %)	36(22.9 %)	< 0.001
	65–74	18(18.0 %)	46(29.3 %)	
	55–64	17(17.0 %)	51(32.5 %)	
	45–54	5(5.0 %)	19(21.1 %)	
	< 45	2(2.0 %)	5(3.2 %)	
Races	White	49 (49.0 %)	88 (56.1 %)	0.272
	Black	16 (16.0 %)	29 (18.5 %)	
	Other	35 (35.0 %)	40 (25.5 %)	
Surgical	Recommended but not performed	2(2.0 %)	2(1.3 %)	0.439
	Surgeries	48(48.0 %)	63(40.1 %)	
	No surgery	50(50.0 %)	92(58.6 %)	
Chemotherapy	Post-	–	46(29.3 %)	–
	Pre-	–	9(5.7 %)	
	Pre- and Post-	–	12(7.6 %)	
	No	–	90(57.3 %)	
Radiotherapy	Yes	1(1.0 %)	8(5.1 %)	0.16
	No	99(99.0 %)	149(94.9 %)	
T stage	T4	47(47.0 %)	56(35.7 %)	0.198
	T3	18(18.0 %)	33(21.0 %)	
	T2	3(3.0 %)	13(8.3 %)	
	T1	11(11.0 %)	25(15.9 %)	
	TX	21(21.0 %)	30(19.1 %)	
N stage	N3	20(20.0 %)	29(18.5 %)	0.259
	N2	22(22.0 %)	23(14.6 %)	
	N1	58(58.0 %)	105(66.9 %)	
M stage	M1	100(100 %)	157(100 %)	–

*Pre-: Preoperative Chemotherapy; Post-: Postoperative Chemotherapy; Pre- and Post-: Preoperative and Postoperative Chemotherapy.

3. Results

3.1. Patient characteristics

Clinical baseline characteristics of patients: According to the study's inclusion criteria, 257 patients diagnosed with intestinal-type gastric adenocarcinoma were enrolled, comprising 154 males and 103 females. These patients were categorized into two groups based on whether they received chemotherapy. Table 1 presents the baseline characteristics of these patients. Comparative analysis revealed

Table 2
Cox regression analysis affecting patients' OS and CSS.

variables	OS-Cox regression analysis					CSS-Cox regression analysis			
		one-way survival analysis		multifactorial Cox regression analysis		one-way survival analysis		multifactorial Cox regression analysis	
		HR (95 % CI)	P value	HR (95 % CI)	P value	HR (95 % CI)	P value	HR (95 % CI)	P value
Genders	Male	0.892 (0.688,1.157)	0.39	0.892 (0.394,2.020)	0.785	0.870 (0.665,1.14)	0.313		
<i>Reference</i>	Female					Female			
Age (years)	> 75	0.978 (0.453, 2.112)	0.955	0.671 (0.300,1.502)	0.332	0.829 (0.382,1.800)	0.636	0.583 (0.271,1.365)	0.196
	65–74	0.695 (0.317, 1.523)	0.363	0.397 (0.175,0.904)	0.028 ^a	0.657 (0.299,1.444)	0.296	0.373 (0.181,0.951)	0.020 ^a
	55–64	0.582 (0.265, 1.276)	0.176	0.299 (0.128,0.701)	0.005**	0.563 (0.256,1.24)	0.152	0.288 (0.136,0.732)	0.005 **
	45–54	0.480 (0.202,1.139)	0.096	0.291 (0.117,0.720)	0.008**	0.479 (0.202,1.136)	0.095	0.286 (0.131,0.807)	0.007 **
<i>Reference</i>	< 45					< 45			
Races	White	1.150 (0.806,1.641)	0.836	1.157 (0.536,1.221)	0.452	1.109 (0.769,1.599)	0.581	1.112 (0.751,1.206)	0.596
	Other	0.959 (0.648,1.420)	0.441	0.809 (0.791,1.692)	0.312	0.938 (0.626,1.405)	0.756	0.789 (0.516,1.206)	0.273
<i>Reference</i>	Black					Black			
Surgical	Recommended but not performed Surgeries	1.021 (0.324,3.216)	0.971	0.940 (0.291, 3.037)	0.918	1.083 (0.3436,3.4135)	0.892	0.948 (0.292,3.076)	0.930
		0.630 (0.484,0.818)	0.001***	0.554 (0.352,0.871)	0.010 ^a	0.58972 (0.4482,0.7759)	0.001 ***	0.467 (0.291,0.751)	0.002 **
<i>Reference</i>	No surgery					No surgery			
Chemotherapy	Post-	0.491 (0.349,0.692)	4.65e-05 ***	0.498 (0.324,0.766)	0.0015 **	0.466 (0.3241,0.6701)	3.77e-05 ***	0.481 (0.305,0.758)	0.002 **
	Pre-	0.473 (0.221,1.011)	0.053	0.866 (0.369,2.032)	0.742	0.509 (0.2378,1.0897)	0.082	0.973 (0.411,2.305)	0.951
	Pre- and Post-	0.376 (0.198,0.714)	0.003 **	0.410 (0.199,0.847)	0.016 ^a	0.4086 (0.2149,0.7768)	0.006**	0.497 (0.237,1.043)	0.065
<i>Reference</i>	No chemotherapy					No chemotherapy			
Radiotherapy	Yes	0.606 (0.299,1.231)	0.166	0.892 (0.394,2.020)	0.784	0.6538 (0.3216,1.329)	0.241	0.905 (0.397,2.066)	0.813
<i>Reference</i>	No					No			
T stage	T3	0.761 (0.486,1.189)	0.230	0.637 (0.401,1.012)	0.056	0.6477 (0.402,1.044)	0.075	0.553 (0.337,0.906)	0.019 ^a
	T2	0.4366 (0.235,0.810)	0.009 **	0.562 (0.295,1.071)	0.080	0.386 (0.199,0.749)	0.005 **	0.499 (0.250,0.996)	0.049 ^a
	T1	0.496 (0.329,0.747)	0.001 ***	0.520 (0.321,0.843)	0.008 **	0.4708 (0.308,0.720)	0.001 ***	0.533 (0.325,0.873)	0.012 ^a
	TX	0.686 (0.484,0.973)	0.034 ^a	0.883 (0.570,1.369)	0.578	0.6857 (0.480,0.980)	0.038 ^a	0.974 (0.624,1.519)	0.906
<i>Reference</i>	T4					T4			
N stage	N2	1.042 (0.738,1.470)	0.816	1.788 (1.161,2.751)	0.008 **	1.0162545 (0.708,1.458)	0.930	1.796 (1.145,2.821)	0.011 ^a
	N3	0.996 (0.715,1.387)	0.980	2.016 (1.309,3.104)	0.001 **	0.9997223 (0.709,1.409)	0.999	2.140 (1.370,3.343)	0.001 ***
<i>Reference</i>	N1					N1			

^a Pre-: Preoperative Chemotherapy; Post-: Postoperative Chemotherapy; Pre- and Post-: Preoperative and Postoperative Chemotherapy.

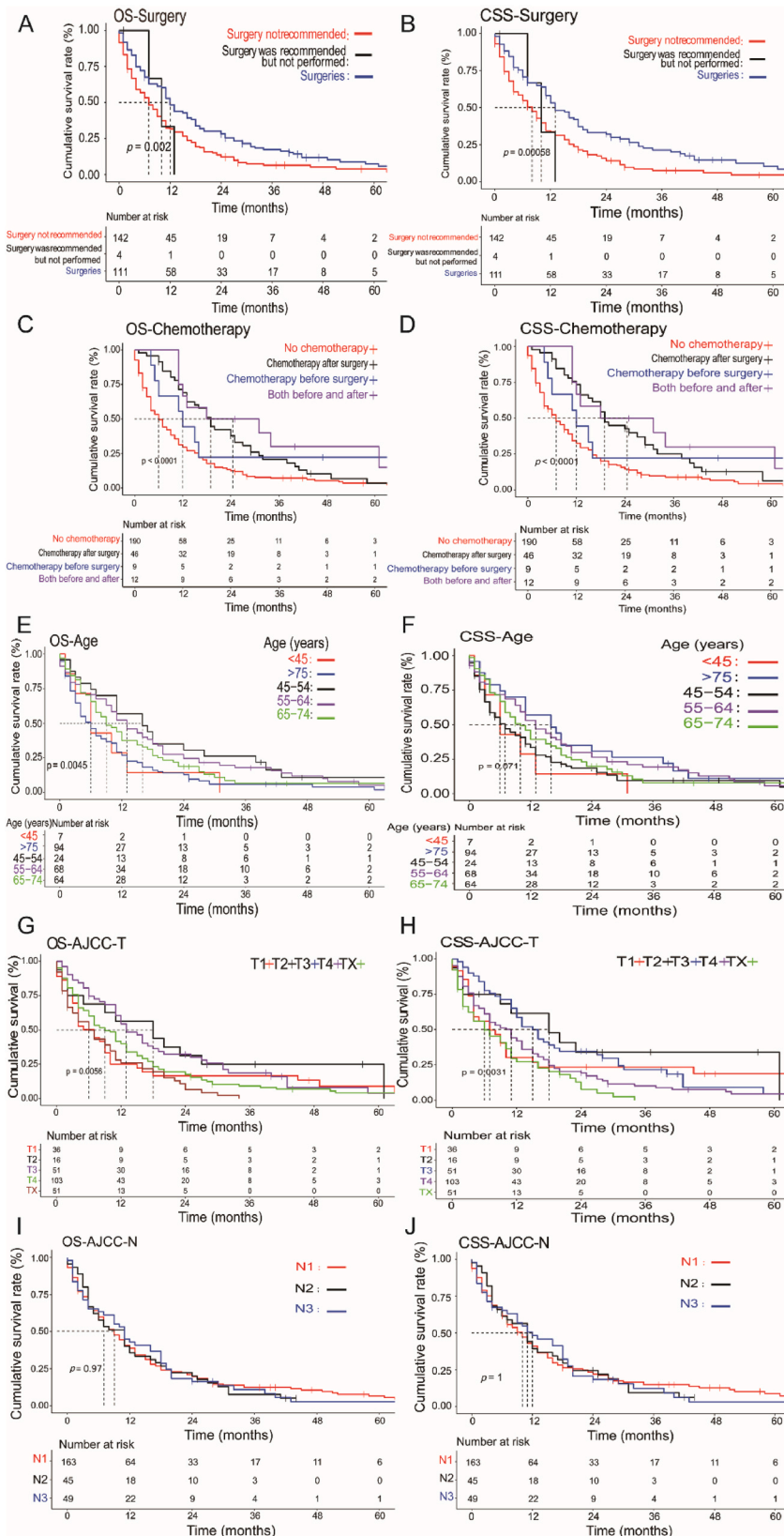


Fig. 2. Effect of major variables on OS and CSS in patients with intestinal-type gastric adenocarcinoma.

no significant disparities in gender, race, local tumor surgery, radiotherapy, T stage, and N stage between the groups receiving chemotherapy and those not receiving it ($P > 0.05$). However, a notable variance was observed in the age distribution.

3.2. Analysis of the variables affecting patients' OS and CSS

Univariate Cox regression analysis identified significant correlations between OS and several factors, including primary tumor surgery, chemotherapy (both preoperative and postoperative, as well as postoperative only), T stage, and N stage in patients with intestinal-type gastric adenocarcinoma ($P < 0.05$). Subsequent multivariate Cox regression analysis confirmed these factors, along with age, as significant independent predictors of OS in this patient population ($P < 0.05$), as detailed in Table 2. Survival curves for these key independent predictors were generated using the Kaplan-Meier method and analyzed with the Log-rank test, as illustrated in Fig. 2. Further multivariate analysis highlighted a notably poorer prognosis for patients younger than 45 or older than 75 years compared to those aged 45–74 years (Table 2). Significant survival advantages were observed in patients who underwent primary tumor resection and/or chemotherapy, with those diagnosed at an earlier T-stage showing better outcomes, and those with advanced lymph node involvement exhibiting poorer prognoses. The findings for CSS mirrored those for OS, as demonstrated in Table 2.

3.3. Construction of the nomogram model for prognostic survival

Utilizing the outcomes from the Cox analysis in the modeling cohort, variables identified as statistically significant in multivariate Cox regression were integrated into the nomogram for predicting OS in patients with intestinal-type gastric adenocarcinoma. Similarly, variables significant in the competing risk analyses were included in the nomogram for CSS prognosis. This comprehensive nomogram aims to forecast 1- and 5-year survival rates for these patients, as depicted in Fig. 3.

3.4. Validation of the nomogram predictive model

The nomogram underwent internal validation using designated modeling and validation cohorts, demonstrating high predictive accuracy for OS and CSS in gastric cancer lymph node metastasis (GCLM) patients. Notably, the concordance indices (C-indices) for OS in both cohorts surpassed those of the traditional TNM staging system (0.706 vs. 0.560; 0.670 vs. 0.554), as did the C-indices for CSS (0.769 vs. 0.534; 0.744 vs. 0.518), detailed in Table 3. Receiver Operating Characteristic (ROC) curve analysis further confirmed the superior accuracy of the nomogram models, with larger areas under the curve indicating enhanced predictive capability, shown in Fig. 4. To mitigate overfitting of the C-index, a correction was applied. The study focused on the 1-year survival predictions, generating correction curves that closely aligned with the diagonal, illustrating the nomogram's precise congruence with actual 1-year survival rates. This alignment, highlighted in Fig. 5, underscores the model's exceptional discrimination and accuracy.

4. Discussion

Intestinal-type gastric adenocarcinoma, a malignancy characterized by severe outcomes, often leads to metastasis at diagnosis due to the subtlety of early symptoms [22,23]. Recent advancements in surgical and adjuvant therapies have established multidisciplinary treatment as the cornerstone for managing this cancer type, significantly enhancing patient survival rates. Research indicates a strong association between patient prognosis and factors such as the clinical management approach, disease stage, and others [10]. Consequently, optimizing treatment strategies and prognostic tools necessitates the integration of all pertinent metrics. This study presents a novel, effective tumor prognosis assessment model derived from an extensive clinical case dataset, aimed at facilitating personalized and precise patient care. Firstly, our prognostic model can assist clinicians in more accurately assessing patients' prognosis and devising personalized treatment plans for each individual. By incorporating patients' individual and tumor characteristics, physicians can estimate patients' survival rates more precisely, thus providing more targeted guidance for treatment decisions. This helps to avoid overtreatment or undertreatment and maximizes treatment efficacy. Secondly, our research results also

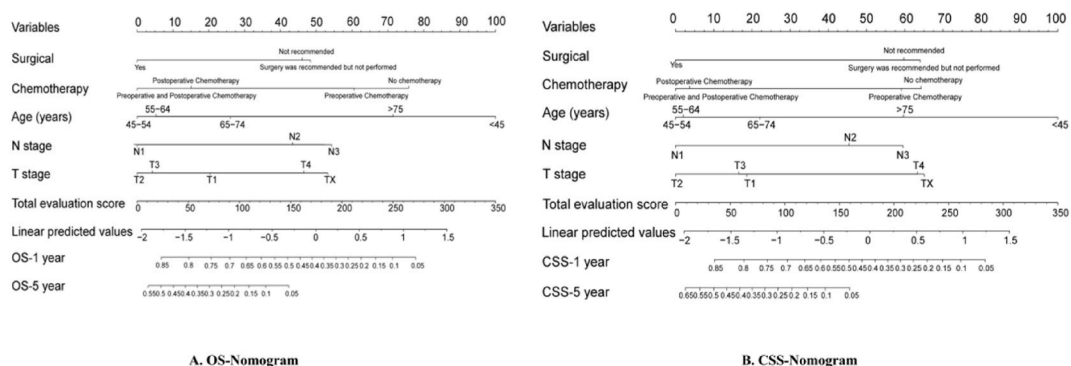
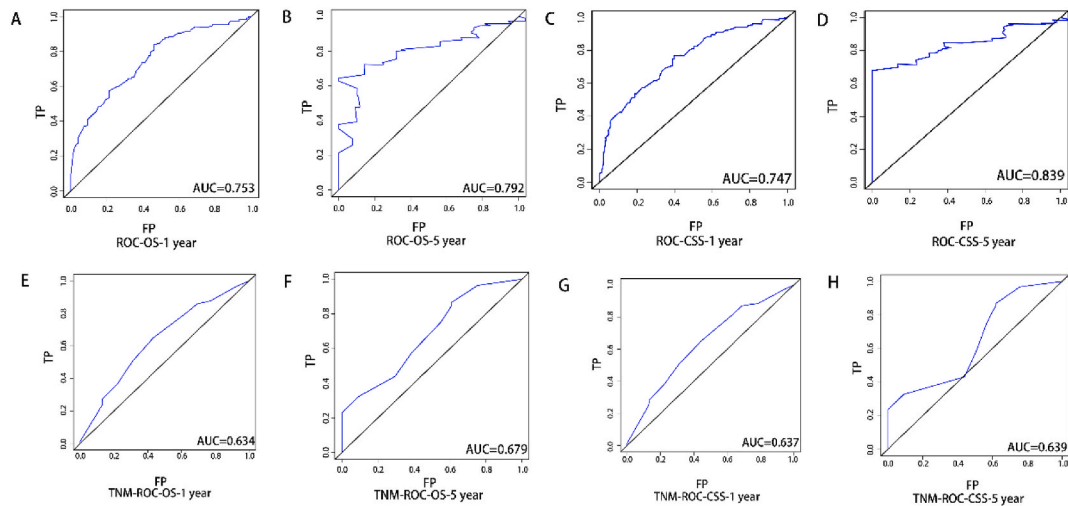
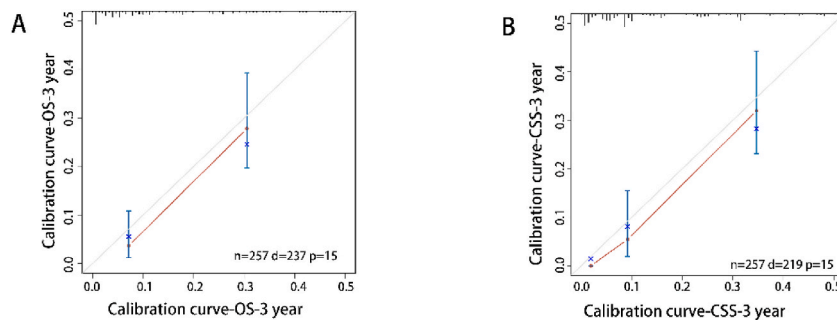


Fig. 3. Predictive model for OS/CSS at 1 and 5 years in patients with intestinal-type gastric adenocarcinoma by nomograms.

Table 3

Comparison of heterogeneity indices between the column chart evaluation model and the AJCC-TNM evaluation system.

C-index	OS	CSS
Nomogram	0.675 (0.641,0.709)	0.680 (0.645,0.715)
AJCC-TNM	0.581 (0.539,0.623)	0.588 (0.547,0.631)

**Fig. 4.** ROC curves for the nomogram model.**Fig. 5.** Calibration curves for nomogram correction curve.

provide clinicians with more comprehensive information support, aiding in optimizing clinical decision-making. By understanding the prognosis of different patient subgroups, physicians can better assess patients' disease risks and tailor treatment strategies accordingly.

Nomograms [24], innovative statistical tools for forecasting, offer a more objective and systematic approach to prognosis than traditional indices and have gained widespread application across various cancers, including liver [25], lung [26], and pediatric tumors [27]. Our study developed nomogram models to predict OS and CSS in patients with intestinal-type gastric adenocarcinoma. The models' accuracy and reliability were validated through concordance indices, receiver operating characteristic (ROC) curves, and calibration curve analysis, affirming their efficacy in prognosticating OS and CSS and underscoring their robustness and reliability.

This study identified age, tumor size, T-grade, lymph node metastasis, primary site surgery, and adjuvant chemotherapy as independent risk factors influencing survival outcomes in patients with intestinal-type gastric adenocarcinoma, incorporating these factors into the prognostic columnar graph model. Specifically, diagnosis at ages below 45 or above 75 years was associated with poorer outcomes, with no significant differences observed across racial (white, black, and other) or gender (male and female) groups. This may be attributed to poor lifestyle choices and delayed screening in younger individuals, whereas diminished physiological resilience and increased palliative care reliance may affect older patients. Treatment predominantly involves surgery (either radical or palliative), adjuvant chemotherapy (pre and postoperative), and radiation, yet the application of these modalities remains under debate. A surgical approach combined with other treatments is considered optimal [28,29]. This study's findings underscore the significant impact of primary site surgery on prognostic survival (OS: 0.62958, $P = 0.000543$; CSS: 0.58972, $P = 0.000162$),

highlighting the crucial role of postoperative and perioperative chemotherapy in enhancing prognosis, unlike preoperative chemotherapy alone. Ballhausen et al. [30] multicenter retrospective analysis corroborates the beneficial effects of perioperative chemotherapy on disease-free survival (DFS) and OS in this patient group. Our study findings are consistent with those of Ballhausen et al. demonstrating the positive impact of perioperative chemotherapy on the prognosis of gastric cancer patients. Additionally, our research aligns with other relevant studies [31,32], indicating that perioperative chemotherapy significantly improves both the survival rates and disease progression of gastric cancer patients. The consistency of these findings further emphasizes the importance of perioperative chemotherapy in gastric cancer treatment and underscores its potential impact on patient prognosis. Although our study results are consistent with previous research, there are some differences in sample size, study design, and analytical methods.

However, our study had several limitations, including ambiguities in disease metastasis details, unspecified chemotherapeutic regimens, the retrospective study design, and absence of external validation. Data limitations in our study prevented the inclusion of factors such as genetic mutations and biomarkers, which could have influenced the survival prognosis of patients with intestinal-type gastric adenocarcinoma. Subsequent research should investigate the influence of these potential prognostic factors on patient survival outcomes. Therefore, future research should prioritize the additional validation and refinement of the model. Initially, we will actively seek collaborations with other institutions to acquire multicenter datasets for external validation. Moreover, we will explore the use of prospective cohort study designs to enhance the assessment of the model's performance in actual clinical environments. These endeavors aim to validate and refine the model further, thereby bolstering its utility in clinical practice. It is important to note that the model's predictions should be used in conjunction with clinical judgment and patient preferences, rather than as a standalone tool.

In summary, this research leveraged clinicopathological data from the SEER database to analyze prognostic factors in patients with intestinal gastric adenocarcinoma, developing a nomogram prediction model. This model, significant for its clinical applicability, enables precise survival prognoses assessment in terms of OS and CSS. Thus, it serves as a valuable adjunct tool for the clinical management of this condition. Furthermore, our study also has potential implications for health policy and resource allocation. For instance, within healthcare systems, resources can be adjusted based on individual characteristics determined by our prognostic model, thereby optimizing resource allocation strategies and enhancing the distribution of personalized treatment methods.

Ethics approval and consent to participate

The data of this study is obtained from the SEER database. The patients' data is public and anonymous, so this study does not require ethical approval and informed consent.

Funding

Supported by grant (No. 2024C03181) from "Pioneer" and "Leading Goose" R&D Program of Zhejiang Province.

Data availability statement

The dataset supporting the conclusions of this article is available in the SEER repository, and hyperlink to dataset in <https://seer.cancer.gov/seerstat/>.

CRedit authorship contribution statement

Shuangai Liu: Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. **Yizhou Zhuang:** Data curation. **Qibo Fu:** Resources, Data curation. **Zhongyuan Zhang:** Visualization, Data curation. **Kai Hang:** Investigation, Data curation. **Ting Tao:** Validation, Methodology, Data curation. **Lei Liu:** Software. **Jiheng Wu:** Writing – review & editing, Formal analysis, Data curation, Conceptualization. **Yuanmei Liu:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Jinhu Wang:** Writing – review & editing, Supervision, Resources, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- [1] H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, F. Bray, Global cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, *Ca - Cancer J. Clin.* 71 (3) (2021) 209–249.
- [2] A.P. Thrift, H.B. El-Serag, Burden of gastric cancer, *Clin. Gastroenterol. Hepatol.* 18 (3) (2020) 534–542.
- [3] L. Yang, R. Zheng, N. Wang, Y. Yuan, S. Liu, H. Li, S. Zhang, H. Zeng, W. Chen, Incidence and mortality of stomach cancer in China, 2014, *Chin. J. Cancer Res.* 30 (3) (2018) 291–298.
- [4] A.R. Yusefi, K. Bagheri Lankarani, P. Bastani, M. Radinmanesh, Z. Kavosi, Risk factors for gastric cancer: a systematic review, *Asian Pac. J. Cancer Prev. APJCP* 19 (3) (2018) 591–603.
- [5] A.P. Gobert, K.T. Wilson, Induction and regulation of the innate immune response in *Helicobacter pylori* infection, *Cell Mol Gastroenterol Hepatol* 13 (5) (2022) 1347–1363.

- [6] F. Lordick, F. Carneiro, S. Cascinu, T. Fleitas, K. Haustermans, G. Piessen, A. Vogel, E.C. Smyth, *clinicalguidelines@esmo.org* EGCEa, Gastric cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up, *Ann. Oncol.* 33 (10) (2022) 1005–1020.
- [7] I. Tramacere, C. Pelucchi, V. Bagnardi, M. Rota, L. Scotti, F. Islami, G. Corrao, P. Boffetta, C. La Vecchia, E. Negri, A meta-analysis on alcohol drinking and esophageal and gastric cardia adenocarcinoma risk, *Ann. Oncol.* 23 (2) (2012) 287–297.
- [8] L. Lu, C.S. Mullins, C. Schafmayer, S. Zeissig, M. Linnebacher, A global assessment of recent trends in gastrointestinal cancer and lifestyle-associated risk factors, *Cancer Commun.* 41 (11) (2021) 1137–1151.
- [9] P. Rawla, A. Barsouk, Epidemiology of gastric cancer: global trends, risk factors and prevention, *Przegląd Gastroenterol.* 14 (1) (2019) 26–38.
- [10] W.-J. Yang, H.-P. Zhao, Y. Yu, J.-H. Wang, L. Guo, J.-Y. Liu, J. Pu, J. Lv, Updates on global epidemiology, risk and prognostic factors of gastric cancer, *World J. Gastroenterol.* 29 (16) (2023) 2452–2468.
- [11] T. Ushiku, T. Arnason, S. Ban, T. Hishima, M. Shimizu, M. Fukayama, G.Y. Lauwers, Very well-differentiated gastric carcinoma of intestinal type: analysis of diagnostic criteria, *Mod. Pathol.* : an Official Journal of the United States and Canadian Academy of Pathology, Inc. 26 (12) (2013) 1620–1631.
- [12] E.C. Smyth, M. Nilsson, H.I. Grabsch, N.C. van Grieken, F. Lordick, Gastric cancer, *Lancet* 396 (10251) (2020) 635–648.
- [13] S. Bian, Y. Wang, Y. Zhou, W. Wang, L. Guo, L. Wen, W. Fu, X. Zhou, F. Tang, Integrative single-cell multiomics analyses dissect molecular signatures of intratumoral heterogeneities and differentiation states of human gastric cancer, *Natl. Sci. Rev.* 10 (6) (2023) nwad094.
- [14] M. Zhang, S. Hu, M. Min, Y. Ni, Z. Lu, X. Sun, J. Wu, B. Liu, X. Ying, Y. Liu, Dissecting transcriptional heterogeneity in primary gastric adenocarcinoma by single cell RNA sequencing, *Gut* 70 (3) (2021) 464–475.
- [15] F.H. Wang, X.T. Zhang, Y.F. Li, L. Tang, X.J. Qu, J.E. Ying, J. Zhang, L.Y. Sun, R.B. Lin, H. Qiu, et al., The Chinese Society of Clinical Oncology (CSCO): clinical guidelines for the diagnosis and treatment of gastric cancer, *Cancer Commun (Lond)*, 2021 41 (8) (2021) 747–795.
- [16] J.H. Lee, K.K. Chang, C. Yoon, L.H. Tang, V.E. Strong, S.S. Yoon, Lauren histologic type is the most important factor associated with pattern of recurrence following resection of gastric adenocarcinoma, *Ann. Surg.* 267 (1) (2018) 105–113.
- [17] R.J. Nicholls, R. Zinicola, N. Haboubi, Extramural Spread of Rectal Cancer and the AJCC Cancer Staging Manual 8th Edition, 2017, vol. 30, *Ann Oncol*, 2019, pp. 1394–1395, 8.
- [18] J. Lv, H. Ren, X. Guo, C. Meng, J. Fei, H. Mei, S. Mei, Nomogram predicting bullying victimization in adolescents, *J. Affect. Disord.* 303 (2022) 264–272.
- [19] J. WenTao, Z. GuoFu, W. TianPin, W. ShiJia, Z. HaiYan, L. WenTao, Nomogram for predicting the long-term outcomes of uterine artery embolization for adenomyosis, *Eur. J. Radiol.* 148 (2022).
- [20] E. Mazzucchi, Both the nomogram and the score system can represent an useful tool especially in those cases where the complication is foreseen by the surgeon, *Int. Braz. J. Urol.* 48 (5) (2022) 828–829.
- [21] K.M. Doll, A. Rademaker, J.A. Sosa, Practical guide to surgical data sets: surveillance, epidemiology, and End results (SEER) database, *JAMA Surg* 153 (6) (2018) 588–589.
- [22] C. Pun, S. Luu, C. Swallow, R. Kirsch, J.R. Conner, Prognostic significance of tumour budding and desmoplastic reaction in intestinal-type gastric adenocarcinoma, *Int. J. Surg. Pathol.* 31 (6) (2023) 957–966.
- [23] T. Kadota, N. Hasuike, H. Ono, N. Boku, J. Mizusawa, I. Oda, T. Oyama, Y. Horiuchi, K. Hirasawa, T. Yoshio, et al., Clinical factors associated with noncurative endoscopic submucosal dissection for the expanded indication of intestinal-type early gastric cancer: Post hoc analysis of a multi-institutional, single-arm, confirmatory trial (JCOG0607), *Dig. Endosc.* 35 (4) (2022) 494–502.
- [24] H. Cheng, F. Gong, Y. Shen, P. OuYang, R. Ni, H. Gao, A nomogram model predicting the risk of postpartum stress urinary incontinence in primiparas: a multicenter study, *Taiwan. J. Obstet. Gynecol.* 61 (4) (2022) 580–584.
- [25] W. Dong, Y. Xie, H. Huang, Prognostic value of cancer-associated fibroblast-related gene signatures in hepatocellular carcinoma, *Front. Endocrinol.* 13 (2022) 884777.
- [26] Y. Yang, C. Shen, J. Shao, Y. Wang, G. Wang, A. Shen, Based on the development and verification of a risk stratification nomogram: predicting the risk of lung cancer-specific mortality in stage IIIA-N2 unresectable large cell lung neuroendocrine cancer compared with lung squamous cell cancer and lung adenocarcinoma, *Front. Oncol.* 12 (2022) 825598.
- [27] J. Wu, X. Shou, J. Cai, J. Mao, J. Qian, J. Wang, S. Ni, Prognostic factors of pediatric pelvic and genitourinary rhabdomyosarcoma: an analysis based on SEER database, *Front. Oncol.* 12 (2022) 992738.
- [28] C. Schulz, F. Kullmann, V. Kunzmann, M. Fuchs, M. Geissler, U. Vehling-Kaiser, H. Stauder, A. Wein, S.-E. Al-Batran, T. Kubin, et al., NeoFLOT: multicenter phase II study of perioperative chemotherapy in resectable adenocarcinoma of the gastroesophageal junction or gastric adenocarcinoma-Very good response predominantly in patients with intestinal type tumors, *Int. J. Cancer* 137 (3) (2015) 678–685.
- [29] X. Cheng, S. Yu, Y. Wang, Y. Cui, W. Li, Y. Yu, C. Tang, H. Jiang, Y. Ji, Y. Sun, et al., The role of oxaliplatin in the adjuvant setting of different Lauren's type of gastric adenocarcinoma after D2 gastrectomy: a real-world study, *Gastric Cancer* 22 (3) (2019) 587–597.
- [30] A. Ballhausen, P. Bartels, I. Iacovella, A. Hoegner, A. Lorusso, D. Bichev, S. Daum, P. Thuss-Patience, Impact of postoperative chemotherapy in patients with gastric/gastroesophageal adenocarcinoma treated with perioperative chemotherapy, *Curr. Oncol.* 29 (3) (2022) 1983–1996.
- [31] F.J.F. Coimbra, V.H.F. de Jesus, H.S.C. Ribeiro, A.L. Diniz, A.L. de Godoy, I.C. de Farias, T. Felismino, C.A.L. Mello, M.F. Almeida, M.D.F.S. Begnami, et al., Impact of ypT, ypN, and adjuvant therapy on survival in gastric cancer patients treated with perioperative chemotherapy and radical surgery, *Ann. Surg. Oncol.* 26 (11) (2019) 3618–3626.
- [32] M. van Putten, V.E.P.P. Lemmens, H.W.M. van Laarhoven, H.F.M. Pruijt, G.A.P. Nieuwenhuijzen, R.H.A. Verhoeven, Poor compliance with perioperative chemotherapy for resectable gastric cancer and its impact on survival, *Eur. J. Surg. Oncol.* 45 (10) (2019) 1926–1933.