Int J Clin Exp Med 2025;18(4):78-89
www.ijcem.com /ISSN:1940-5901/IJCEM0162386

Original Article

Development and validation of a nomogram to predict liver metastases in patients with gastric cancer

Bo Li[1*], Yuxiao Yang[2*], Haiyu Wang[3*], Jinhong Yu[1], Yongchen Zhang[1]

[1]Department of Laboratory Medicine, Nanjing Hospital Affiliated to Nanjing University of Chinese Medicine, The Second Hospital of Nanjing, Nanjing 210003, Jiangsu, China; [2]In Vitro Diagnostics (IVD) Clinical Application Department, Shenzhen Mindray Bio-Medical Electronics Co., Ltd, Shenzhen 518055, Guangdong, China; [3]Department of Oncology, Nanjing Hospital Affiliated to Nanjing University of Chinese Medicine, The Second Hospital of Nanjing, Nanjing 210003, Jiangsu, China. [*]Equal contributors.

Received November 30, 2024; Accepted March 4, 2025; Epub April 15, 2025; Published April 30, 2025

Abstract: Objective: Gastric cancer liver metastasis (GCLM) has become one of the major contributors of gastric cancer (GC) fatality. It is essential to assess the risk of liver metastasis in GC patients so that surgeries can be scheduled promptly. The nomogram-based prediction model has been well exploited in recent studies to evaluate overall survival in various cancers, including GC. Still, such a model was rarely proposed for predicting GCLM risk. This study aimed to propose and validate a statistical model to predict the risk of liver metastasis in GC patients. Methods: The retrospective study uses data extracted from the SEER database. A total of 7,787 patients were divided into a training set (n=5,444) and a validation set (n=2,343). Results: A univariate and a multivariate analysis were carried out to screen out eight characteristics significantly related to the GCLM outcome, namely age, gender, T stage, N stage, tumor size, number of tumors, surgery, and radiotherapy (P<0.05), and a nomogram was subsequently constructed. The receiver operating characteristic curve (ROC) indicated a good discriminative ability of the model. The area under the curve (AUC) of the training cohort and validation cohort was 0.859 (95% CI, 0.846-0.871) and 0.850 (95% CI, 0.832-0.868), respectively. The calibration curve showed a good agreement between the prediction and observed outcomes in both data sets. The decision curve analysis (DCA) revealed that the threshold probability for diagnosing GCLM was between 70% and 90%. Conclusion: The statistical performance demonstrated that the model performed well in predicting GCLM risk and its capability to support treatment regimen adjustment.

Keywords: Gastric cancer, liver metastases, nomogram

Introduction

Gastric cancer, also known as stomach cancer, ranks as the fifth most commonly diagnosed cancer worldwide, trailing behind breast, lung, colorectal, and prostate cancer. Furthermore, it stands as the fourth leading cause of cancer-related mortality among the 36 major cancer categories identified in a global analysis conducted in 2020 [1].

The liver is a hotspot for GC metastasis, accounting for 48% of metastatic cases, followed by the peritoneum (32%), lung (15%), and bone (12%) [2]. GCLM is identified in 4%-14% of primary GC and 37% of post-gastrectomy cases [3, 4]. The 1-, 3-, and 5-year survival rates for GCLM are approximately 4%, 8%, and 24%, respectively [5]. Radical resections of primary and metastatic tumors accompanied by palliative chemotherapies are proposed as a promising treatment pattern to improve overall survival [6]. In recent years, surgical treatment has been recognized as a practical approach to improve the survival of gastric cancer liver metastasis (GCLM) patients, especially for patients with limited liver metastasis [7, 8]. However, the benefits of surgical intervention vary significantly from patient to patient, influenced by the substantial diversity in patient characteristics, tumor biology, and the array of therapies they receive [8].

Clinical imaging is a traditional method of diagnosing metastasis. Imaging techniques convert noninvasive medical images into high-dimensional, mineable data via high-throughput extraction of quantitative features, followed by

https://doi.org/10.62347/LHSW4839

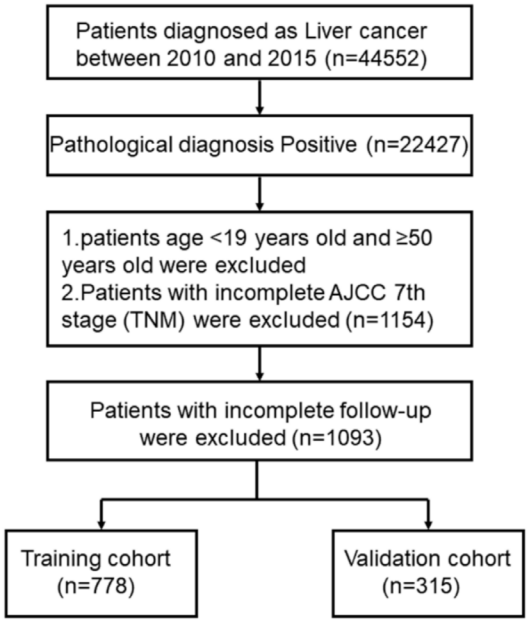

Figure 1. Flowchart of patient screening from SEER database.

subsequent data analysis for decision-making [9]. CT and PET/CT provide systemic information that is preferred for assessing distant metastasis but is limited by sensitivity and inability to identify malignant nodes accurately [10-13]. Considering the essential role of early screening and therapeutic involvement for curative intent in GCLM patients, timely and accurate prediction of metastasis should be highlighted.

Nomograms are standard tools practically used in predicting oncological prognosis and estimating clinical events to support clinicians in decision-making or therapy adjustment. Nomograms translate a variety of determinant variables into numerical scores based on their relative importance and integrate them into a statistical model to output the probability of a specific event [14]. Recent research, including studies by Zhao et al. [15], Li et al. [16], and Kim et al. [17], has effectively tested and improved the application of nomograms in predicting lymph node metastasis based on different biomarker signatures. Similarly, nomograms have been widely utilized in evaluating overall survival in gastric cancer [18]. However, few studies have been conducted to predict liver metastasis risk in GC patients.

The present study aims to develop a nomogram for predicting GCLM based on patients' demographic and clinical characteristics using data from the Surveillance, Epidemiology, and End Results Program (SEER) database. The SEER database is a comprehensive and widely used cancer registry in the United States. It is maintained by the National Cancer Institute (NCI) and collects data on cancer incidence, prevalence, survival, and mortality. Diagnostic-related clinical-pathologic features were identified through multivariable analysis, and a high-performance diagnostic prediction model was established and validated. The model incorporates a series of risk factors to enable early prediction of GCLM. This research contributes to the growing body of evidence supporting the utility of nomograms in predicting cancer prognosis and provides valuable insights for clinical practice.

Methods

Study design and patients

This study is a retrospective cohort study. Data were obtained from the SEER database using the SEERstat software version 8.4.0.1 between 2010 and 2015. The data for this study was obtained from the SEER database, which is publicly available. An ethical review of data obtained from the SEER database was not required. Gastric cancer in this study was defined as adenocarcinoma (ICD-O-3 histology code 8140/3) with a 7th AJCC pathological stage.

Patients diagnosed with gastric cancer from January 1, 2010 to December 31, 2015 were included in the study. Variables included in the clinical information of the study included gender, age at diagnosis, race, marital status, pathological type (8140/3), primary site, grade, TNM stage (AJCC 7th edition), surgery, radiotherapy, chemotherapy, tumor size, tumor number, and liver metastases. The inclusion criteria were as follows: 1) pathological type (8140/3); 2) diagnosis between 2010 and 2015; 3) pathological diagnosis positive; 4) grade (including I, II, III, IV); and 5) stomach cancer liver metastases (including Yes or No). The exclusion criteria were as follows: 1) the age was unknown; 2) the race was unknown; 3) the marital status was unknown; and 4) the tumor size was unknown. A total of 7,787 patients were collected from the SEER database, randomly divided into a training cohort (n=5,444) and a validation cohort (n=2,343) in a 7:3 ratio. The screening flowchart is shown in **Figure 1**.

Statistical analysis

Enumeration data were expressed as percentages and compared using the Chi-square or Fisher exact test among groups. In the univariate analysis, variables that reached significance with $P<0.05$ were entered into multivariate analysis using the logistic backward regression model to determine the covariates associated with GCLM. The hazard ratio of each variable with a 95% confidence interval (CI) was achieved and subsequently utilized to construct a nomogram. We evaluated the predictive effect of nomograms using the receiver operating characteristic curve (ROC). The Hosmer-Lemeshow goodness of fit test in multiple logistic regression was performed to assess the model calibration, and the calibration plot was plotted. A decision curve analysis (DCA) was also performed to determine the net benefit threshold of prediction. All statistical analyses were performed with Stata software (version 15.0) and SPSS statistical software (version 26.0). $P<0.05$ was considered statistically significant.

Results

Characteristics of patients in the training and validation cohorts

A total of 7,787 cases diagnosed with gastric cancer from the SEER database were grouped into training and validation cohorts. Among the 7,787 patients, 45.6% of the population was over 70 years old (n=3549), 30.4% (n=2,370) was between 60 and 70, with the rest (24.0%, n=1,868) below 60. A total of 71.1% of patients (n=5,535) were male, and 28.9% (n=2,252) were female. Most tumors diagnosed were poorly differentiated (57.7%) and located in the cardia (48.5%). Liver metastases were reported in 1,185 cases (41.2%), 4,566 patients (58.6%) underwent surgery, 4,382 patients (56.3%) were treated with chemotherapy, and 2,804 patients (36.1%) were treated with radiotherapy. Besides, the distribution of tumor size and number was similar in pattern between the training and validation cohorts (**Table 1**).

Univariate and multivariate analysis of the factors relating to GCLM in the training cohort

Univariate analysis identified ten variables significantly associated with all-cause mortality in the training cohorts, including age at diagnosis, gender, race, T stage, N stage, tumor size, number of tumors, surgery, radiotherapy, chemotherapy, and primary site (**Table 2**). Then, the multivariable logistic regression analysis screened out eight clinicopathologic factors significantly correlated with GCLM prognosis (**Table 2**), which were age, gender, T stage, N stage, tumor size, number of tumors, surgery, and radiotherapy (all $P<0.05$). Subsequently, a clinical pathological risk model based on independent diagnostic features was developed for accurate assessment of liver metastasis.

Development and evaluation of the prediction model

A nomogram was created with eight prognostic factors identified from the multivariate analysis (age, gender, T stage, N stage, tumor size, number of tumors, surgery, and radiotherapy) (**Figure 2**). The ROC curve analysis showed the area under the curve (AUC) of the training cohort was 0.859 (95% confidence interval [CI], 0.846-0.871) (**Figure 3A**), and that of the validation cohort was 0.850, comparatively (95% confidence interval [CI], 0.832-0.868) (**Figure 3B**).

Calibration curves for GCLM in training and validation cohorts

The calibration curves for liver metastasis in gastric cancer patients in training and validation cohorts were illustrated in **Figure 4A** and **4B**. The Hosmer-Lemeshow test, which assesses the goodness of fit in predictive models, yielded a P value of 0.172, suggesting no statistical departure from a perfect fit between the predicted and observed values.

DCA of the nomogram

DCA was also performed to evaluate its clinical application based on the nomogram. The decision curve revealed that the threshold probability for diagnosing GCLM was between 70% and 90% (**Figure 5A**, **5B**).

Discussion

The morbidity and mortality rate of gastric cancer (GC) have decreased over the past decade. The propensity for metastasis, recurrence, and poor prognosis contribute to the high preva-

Table 1. Characteristics of patients in the training and validation cohorts

Variables	Training cohort (*n*=5444)	Validation cohort (*n*=2343)	*P value*
Age (years) (%)			0.523
<60	1288 (23.7%)	580 (24.8%)	
60-70	1656 (30.4%)	714 (30.5%)	
>70	2500 (45.9%)	1049 (44.8%)	
Gender (%)			0.239
Male	3848 (70.7%)	1687 (72%)	
Female	1596 (29.3%)	656 (28%)	
Race (%)			0.141
Caucasian	4084 (75%)	1708 (72.9%)	
African	584 (10.7%)	276 (11.8%)	
Others	776 (14.3%)	359 (15.3%)	
Marital Status (%)			0.022
Married	3354 (61.6%)	1487 (63.5%)	
Single	768 (14.1%)	288 (12.3%)	
Divorced	444 (8.2%)	226 (9.6%)	
Separated	63 (1.2%)	30 (1.3%)	
Unmarried	17 (0.3%)	4 (0.2%)	
Widowed	798 (14.7%)	308 (13.1%)	
Grade (%)			0.904
I/II	2306 (42.4%)	989 (42.2%)	
III/IV	3138 (57.6%)	1354 (57.8%)	
T Stage (%)			0.774
T0	5 (0.1%)	4 (0.2%)	
T1	1386 (25.5%)	626 (26.7%)	
T2	596 (10.9%)	249 (10.6%)	
T3	1947 (35.8%)	826 (35.3%)	
T4	878 (16.1%)	367 (15.7%)	
TX	632 (11.6%)	271 (11.6%)	
N Stage (%)			0.790
N0	2359 (43.3%)	993 (42.4%)	
N1	1666 (30.6%)	724 (30.9%)	
N2	653 (12%)	292 (12.5%)	
N3	550 (10.1%)	230 (9.8%)	
NX	216 (4%)	104 (4.4%)	
Surgery (%)			0.552
No	2240 (41.1%)	981 (41.9%)	
Yes	3204 (58.9%)	1362 (58.1%)	
Radiotherapy (%)			0.311
No	3464 (63.6%)	1519 (64.8%)	
Yes	1980 (36.4%)	824 (35.2%)	
Chemotherapy (%)			0.242
No	2357 (43.3%)	1048 (44.7%)	
Yes	3087 (56.7%)	1295 (55.3%)	
Tumor size (cm) (%)			0.169
≤5	3741 (68.7%)	1573 (67.1%)	
>5	1703 (31.3%)	770 (32.9%)	

Tumor number (%)			0.651
≤2	5142 (94.5%)	2207 (94.2%)	
>2	302 (5.5%)	136 (5.8%)	
Liver Metastases (%)			0.288
No	4631 (85.1%)	1971 (84.1%)	
Yes	813 (14.9%)	372 (15.9%)	
Primary site (%)			0.994
Cardia	2626 (48.2%)	1153 (49.2%)	
Fundus of stomach	179 (3.3%)	80 (3.4%)	
Body of stomach	415 (7.6%)	174 (7.4%)	
Gastric antrum	861 (15.8%)	369 (15.7%)	
Pylorus	138 (2.5%)	59 (2.5%)	
Lesser curvature of the stomach	436 (8%)	183 (7.8%)	
Greater curvature of the stomach	195 (3.6%)	86 (3.7%)	
Overlapping lesion of the stomach	287 (5.3%)	114 (4.9%)	
Stomach	307 (5.6%)	125 (5.3%)	

Table 2. Univariate and multivariate analysis of the factors relating to GCLM in the training cohort

Variables	Univariate		Multivariate	
	OR (95% CI)	*P value*	*OR* (95% CI)	*P value*
Age (years)		<0.001		<0.001
<60	1.473 (1.226-1.769)	<0.001	1.670 (1.34-2.083)	
60-70	1.208 (1.012-1.442)	0.037	1.568 (1.270-1.935)	
>70	1		1	
Gender				
Female	0.722 (0.607-0.858)	<0.001	1.532 (1.252-1.874)	<0.001
Male	1		1	
Race		0.002		0.179
Caucasian	1.351 (1.067-1.711)	0.012	1.165 (0.884-1.536)	0.279
African	1.729 (1.277-2.342)	<0.001	1.397 (0.979-1.994)	0.065
Other	1		1	
Marital status		0.295		
Married	1.226 (0.976-1.541)	0.079		
Single	1.202 (0.902-1.601)	0.210		
Divorced	1.299 (0.936-1.803)	0.118		
Separated	1.774 (0.931-3.380)	0.081		
Unmarried	0.426 (0.056-3.250)	0.411		
Widowed	1			
Grade				
I/II	0.963 (0.828-1.120)	0.624		
III/IV	1			
T Stage		<0.001		<0.001
T0	0.807 (0.134-4.860)	0.814	0.703 (0.109-4.530)	0.711
T1	0.197 (0.158-0.245)	<0.001	0.532 (0.415-0.682)	<0.001
T2	0.042 (0.026-0.067)	<0.001	0.178 (0.108-0.296)	<0.001
T3	0.106 (0.085-0.133)	<0.001	0.342 (0.261-0.448)	<0.001
T4	0.257 (0.204-0.325)	<0.001	0.605 (0.456-0.804)	<0.001
TX	1		1	

N Stage		<0.001		<0.001
N0	0.175 (0.130-0.236)	<0.001	0.554 (0.395-0.775)	0.001
N1	0.379 (0.282-0.509)	<0.001	1.093 (0.778-1.533)	0.609
N2	0.136 (0.093-0.200)	<0.001	0.992 (0.631-1.558)	0.971
N3	0.134 (0.090-0.200)	<0.001	1.135 (0.703-1.834)	0.604
NX	1		1	
Surgery				
No	0.063 (0.050-0.079)	<0.001	12.699 (9.867-16.344)	<0.001
Yes	1		1	
Radiotherapy				
No	0.331 (0.274-0.400)	<0.001	3.239 (2.609-4.020)	<0.001
Yes	1		1	
Chemotherapy				
No	1.042 (0.896-1.212)	0.592		
Yes	1			
Tumor size (cm)				
≤5	1.621 (1.390-1.890)	<0.001	0.740 (0.614-0.892)	0.002
>5	1		1	
Number of tumors				
≤2	0.544 (0.364-0.814)	0.003	1.653 (1.054-2.592)	0.029
>2	1		1	
Primary site		0.024		0.832
Cardia	0.825 (0.603-1.127)	0.227	1.154 (0.792-1.683)	0.456
Fundus of stomach	1.348 (0.853-2.132)	0.201	1.092 (0.642-1.858)	0.746
Body of stomach	0.886 (0.597-1.314)	0.548	1.251 (0.787-1.990)	0.343
Gastric antrum	0.651 (0.455-0.931)	0.019	1.380 (0.905-2.105)	0.135
Pylorus	0.571 (0.310-1.053)	0.073	1.057 (0.505-2.209)	0.884
Lesser curvature of the stomach	0.806 (0.543-1.197)	0.286	1.208 (0.757-1.926)	0.428
Greater curvature of the stomach	0.753 (0.456-1.243)	0.267	1.209 (0.674-2.167)	0.524
Overlapping lesion of the stomach	0.965 (0.630-1.476)	0.868	0.951 (0.581-1.558)	0.842
Stomach	1		1	

lence and fatality of GC. Up to 80% of patients are diagnosed with distant metastasis or in advanced stages, with a 5-year overall survival rate of less than 30% [19, 20]. The liver is the most susceptible organ to GC metastasis. Guidelines commonly recommend using radiometric evidence and the AJCC TNM staging system [20-22]. However, these imaging techniques and staging systems only extract information on established lesions (both primary and metastatic) and regional lymph node involvement without giving due credit to objective risk factors for tumorigenesis, such as age, gender, and therapeutic implications.

This retrospective study introduced a nomogram to develop a diagnostic model for gastric cancer with liver metastasis (GCLM) by integrating various clinical variables. The main predictors of the nomogram, like age, gender, clinical stages (T- and N-stage), tumor size, tumor quantity, surgical intervention, and implications of radiotherapy were significantly associated with GCLM.

The relationship between clinical characteristics and the risk of GCLM was initially investigated in this study, and their predictive ability of GCLM was assessed subsequently. The results validated the predictive significance of age, gender, clinical stages (T- and N-stage), tumor size, quantity of tumors, surgical intervention, and implications of radiotherapy for GCLM.

Receiver operating characteristic (ROC) curves were constructed for both the training and validation cohorts to visualize the sensitivity and specificity of the prediction models. The ROC

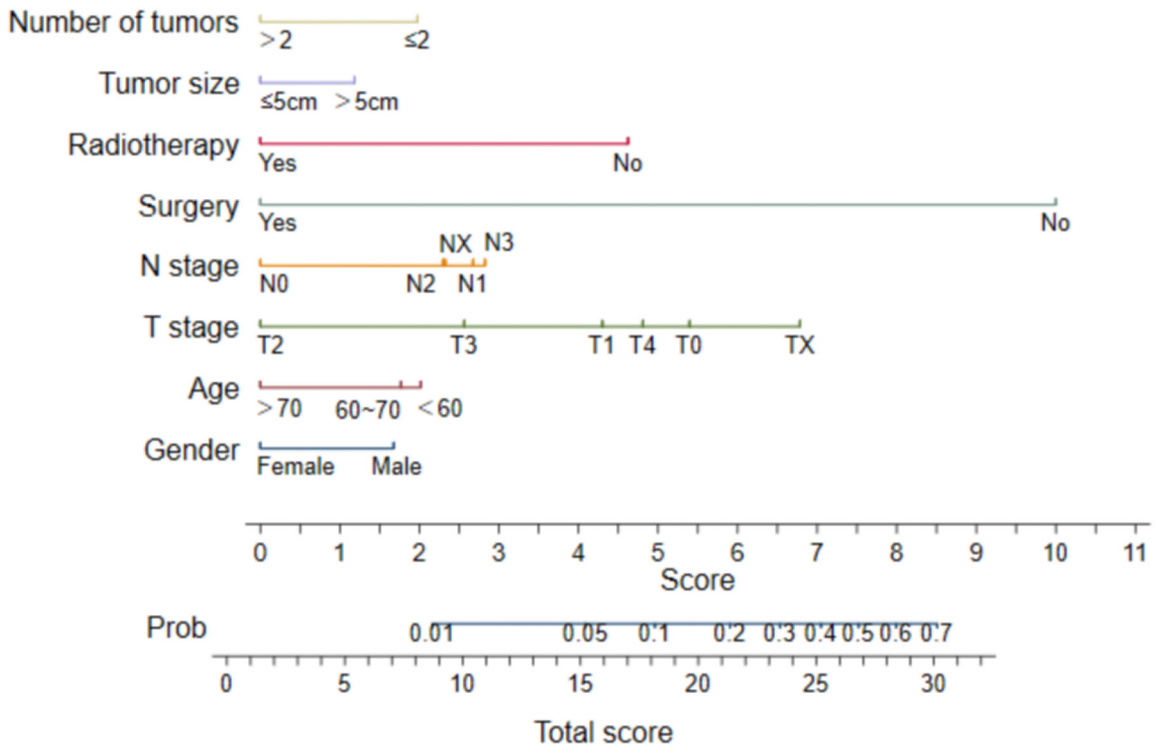

Figure 2. Nomogram of the training group.

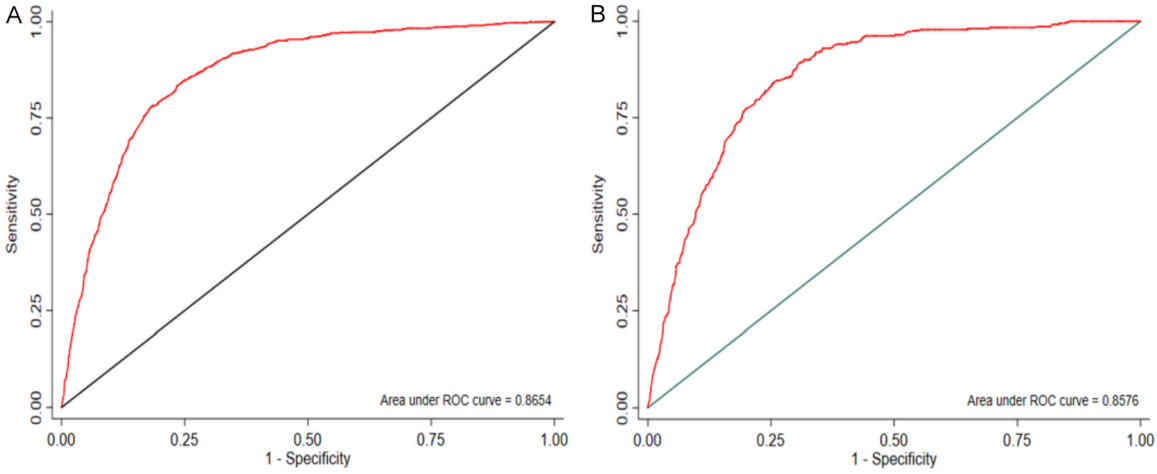

Figure 3. ROC curves for GCLM in training and validation cohorts. A. Training cohort. B. Validation cohort.

area under the curve (AUC) reflects the model's ability to classify patients with GCLM correctly. An AUC score between 0.5 and 1.0 is generally acceptable, with higher scores indicating better predictive abilities. Usually, an AUC score between 0.8 and 1.0 indicates that the model performs very well in predicting a positive GCLM outcome [23]. The AUC values for the training and validation cohorts were 0.859 and 0.850, respectively, indicating that the nomogram performs more accurately predicting patient prognosis in both training and validation sets.

Surgery

Surgery has a significant association with liver metastasis in gastric cancer. It has been observed that GC patients who undergo surgical resection, particularly those in advanced stages, have a lower risk of liver metastasis [24]. Kinoshita et al. [25] have also used the similar

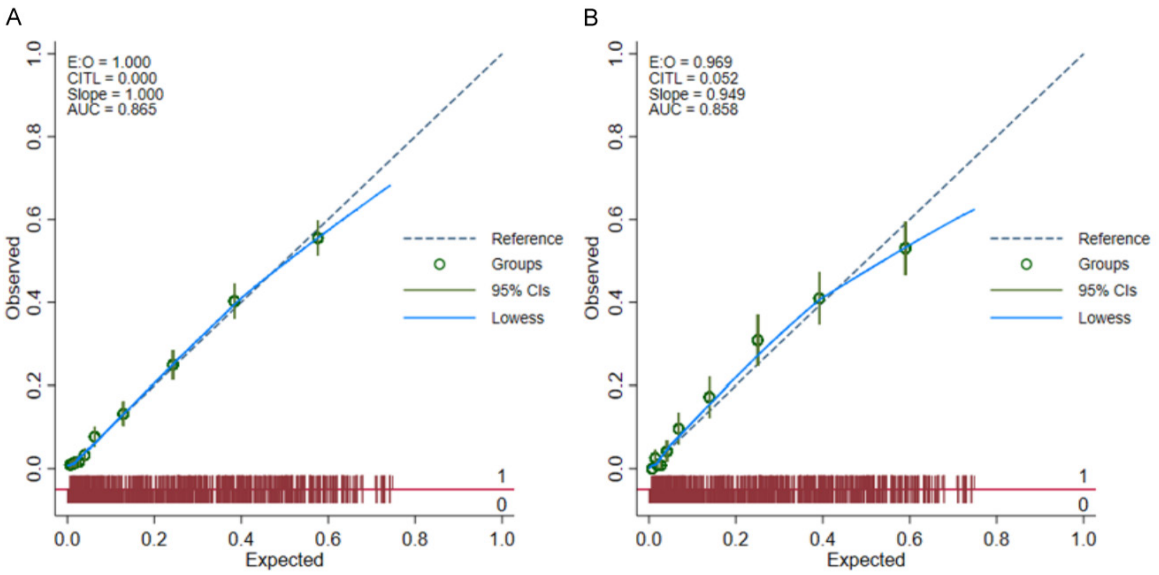

Figure 4. Calibration curves for GCLM in training and validation cohorts. A. Training cohort. B. Validation cohort.

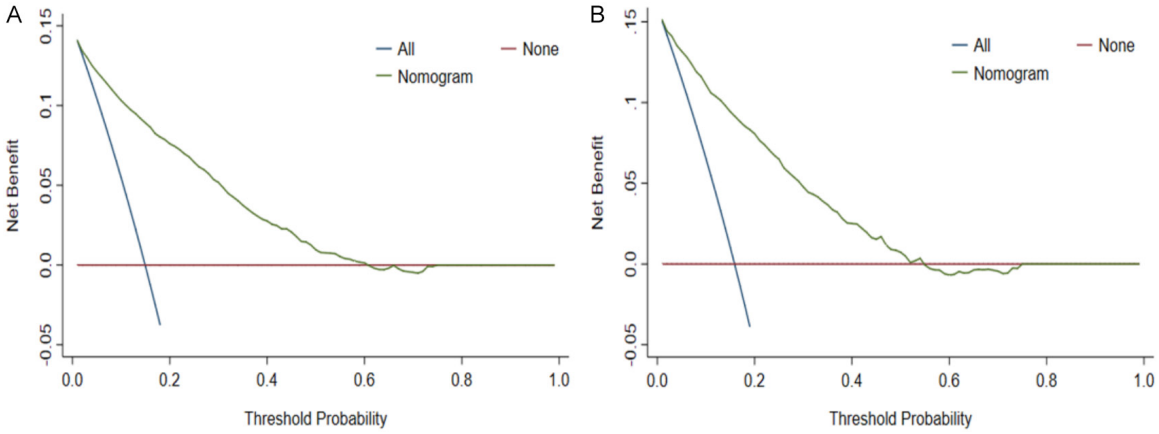

Figure 5. DCA of the nomogram. A. Training cohort. B. Validation cohort. The x-axis indicates the threshold probability, and the y-axis indicates the net benefit. The red line shows the "treat-none" line, and the blue curve shows the "treat-all" line.

clinical characteristics in the establishment of GC metastasis prediction models. A survey conducted by European and Japanese oncological study groups has concluded that the preferred regimen for resectable GCLM patients without extrahepatic metastasis is preoperative chemotherapy followed by surgical resection of both primary and liver lesions [26]. Similarly, another study indicated that gastric cancer (GC) patients undergoing surgical intervention exhibited a reduced risk of liver metastasis [27]. Consistent with previous studies, this study demonstrated that urgery patients had a lower risk of developing GCLM than patients without.

Decisive surgical resection is also crucial in improving survival outcomes [28], although the standardization of surgery remains a topic of debate. Various constraints on surgical resection, such as the extent of resection, postoperative complications, and patient selection, make the prognosis and recurrence of metastasis less predictable and varied among patients [29].

TNM staging

The risk of GCLM increases with higher grading in the T and N stages. This finding is consistent with previous studies by Huang and Fang [24]

and Zhu et al. [30]. The T stage describes the invasion of primary tumors into parietal tissues and organs, while the N stage refers to cancer spread into surrounding lymph nodes. In higher stages, there is a deeper depth of tumor infiltration into stomach sublayers and lymph nodes, which promotes further stage migration and distant metastasis, such as in the liver, lung, or other organs [30]. Advanced TNM stage and poor pathological tissue differentiation were identified as independent risk factors for liver metastasis in gastric cancer [31]. Furthermore, tumors originating in the cardia and fundus were reported to be more prone to liver metastasis [32]. Consistent with previous studies, In our study, the higher the N and T stages of GC, the higher the risk of liver metastasis.

Radiotherapy

The nomogram identified that patients who did not undergo radiotherapy had higher risk scores for GCLM. However, it was observed that the actual effectiveness of radiotherapy in controlling GCLM had not been extensively studied after reviewing numerous research articles. Some investigations did report clinical benefits of radiotherapy [33-35], including a reduction of distant metastasis in resected gastric cancer by 75% using intraoperative and external beam radiation therapy [35]. Radiotherapy was found to upregulate cancer cell death through continuous irradiation, suppressing the metastatic cycles of proliferating cancer cells and reducing cell diffusion into plasma [36]. However, it is important to note that therapeutic manipulation, including radiotherapy and chemotherapy, may subsequently facilitate recurrence and distant metastasis, possibly due to the awakening and attraction of dormant circulating tumor cells after the elimination of primary tumors.

Additionally, irradiation-induced angiogenesis suppression can create a tumor-favored hypoxic microenvironment [37, 38]. The complexity of the systemic post-therapeutic response makes the effect of radiotherapy ambiguous, and the optimal treatment strategy remains controversial. It was noted that the function of radiotherapy can be maximized in patients below grade III or those undergoing surgeries such as D2-reaction [39]. The significance of radiotherapy recognized in this study may be attributed to the population selected that conforms to such criteria. Consistent with previous studies [35], this study demonstrated that radiotherapy had a lower risk for gastric cancer liver metastasis.

Tumor size

Tumor size was found to be positively correlated with metastasis. Larger tumors are associated with poor differentiation, more active cell replication, and abundant angiogenesis, making larger tumors prone to metastasis [40, 41]. It was reported that tumor size is related to the depth of tumor invasion, lymphatic metastasis, and the development of liver metastasis [40]. Previous studies have shown that tumor size was an independent prognostic risk factor for liver metastasis in GC [27]. Furthermore, Huang and Fang have suggested that tumors larger than 25 mm are a risk factor for liver metastasis [24]. Additionally, Yang et al. discovered that tumors larger than 50 mm are more likely to metastasize in the liver exclusively [42]. Therefore, the tumor size might play an important role in the process of GCLM.

Notably, the study also pointed out that a tumor number ≤2 was a risk factor for GCLM, which had not been given enough credit in other investigations. The correlation between tumor number and liver metastasis was not well-supported in the literature, but it was proposed that primary tumors at early stages with highly aggressive biology might grow more rapidly and be more favorable to invade the bloodstream towards distant organs. Further, cancer cell dissemination could occur early, and metastatic cells may have already spread to the liver before tumors became numerous or large and technically visible in the stomach. Additionally, cell microenvironment and genetic factors may also play a role in promoting liver metastasis in the presence of smaller or fewer tumors.

Age and gender

The study found that age was negatively associated with the risk of GCLM, indicating that younger individuals were more likely to develop distant metastasis in the liver, lungs, bones, and brain [43-45]. This result was consistent with findings from other research, showing that younger patients could undergo more vigorous tumor biology and tend to develop higher-grade tumors. Males were also found to be at higher risk than females for GCLM, which was consis-

tent with previous research [2, 42, 46]. It was hypothesized that prolonged exposure to estrogen may mitigate the risk of gastric cancer, but the underlying mechanism requires further exploration and comprehensive validation [47]. In our study, we found that the risk of liver metastasis in female patients with gastric cancer was significantly lower than that in male patients. At the same time, the risk of liver metastasis in gastric cancer patients over 70 years old was significantly lower than that in young patients.

Limitations

This study has some shortcomings. The data was extracted from the SEER database, and the selected variables may be limited. Essential prognostic biomarkers were not taken into consideration, such as radiometric information, cancer cell differentiation, helicobacter pylori infection, and serological biomarkers (CEA, AFP, CA19-9, CA72-4, *et cetera*), have been widely employed as an auxiliary diagnosis in clinical. Serum tumor marker levels are usually positively associated with disease progression. They have high diagnostic accuracy but low positive predictive values. It is recommended to incorporate tumor markers with other clinical examinations to improve screening efficiency [48, 49]. It can be considered prospective work to introduce other biomarkers and make the model more varied and balanced. Secondly, the training model is examined by an internal validation group. External validation is required to objectively explore how the model functions in a different population. Last but not least, the model can be further optimized by reducing the endpoints to make it less redundant without over-fitting, which could make the AUC falsely high and lead to potential confusion.

Conclusion

This article carried out a SEER-based study and identified surgery, radiotherapy, T-stage, N-stage, tumor size, tumor number, age, and gender as significant risk factors of liver metastasis for gastric cancer patients. The prediction model was proven capable of predicting GCLM with high accuracy. In brief, our work has provided a unique perspective on diagnosing GCLM patients.

Acknowledgements

We are deeply grateful to all the participants who contributed to this study. This study was supported by the Nanjing Second Hospital Reserve Talent Research Project, China (Award Number: HBRCYL05).

Disclosure of conflict of interest

None.

Address correspondence to: Jinhong Yu and Yongchen Zhang, Department of Laboratory Medicine, Nanjing Hospital Affiliated to Nanjing University of Chinese Medicine, The Second Hospital of Nanjing, No. 1-1, Zhongfu Road, Gulou District, Nanjing 210003, Jiangsu, China. Tel: +86-025-83626496; E-mail: jhyu2023@16.com (JHY); Tel: +86-025-83626171; E-mail: zhangyongchen@126.com (YCZ)

References

[1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71: 209-249.

[2] Riihimaki M, Hemminki A, Sundquist K, Sundquist J and Hemminki K. Metastatic spread in patients with gastric cancer. Oncotarget 2016; 7: 52307-52316.

[3] Nishi M, Shimada M, Yoshikawa K, Higashijima J, Tokunaga T, Kashihara H, Takasu C, Ishikawa D, Wada Y and Eto S. Results of hepatic resection for liver metastasis of gastric cancer. J Med Invest 2018; 65: 27-31.

[4] Yu P, Zhang Y, Ye Z, Chen X, Huang L, Du Y and Cheng X. Treatment of synchronous liver metastases from gastric cancer: a single-center study. Cancer Manag Res 2020; 12: 7905-7911.

[5] Shinohara T, Maeda Y, Hamada T and Futakawa N. Survival benefit of surgical treatment for liver metastases from gastric cancer. J Gastrointest Surg 2015; 19: 1043-1051.

[6] Stahl KA, Olecki EJ, Dixon ME, Peng JS, Torres MB, Gusani NJ and Shen C. Gastric cancer treatments and survival trends in the United States. Curr Oncol 2020; 28: 138-151.

[7] Kamarajah SK, Markar SR, Phillips AW, Salti GI, Dahdaleh F and Griffiths EA. Palliative gastrectomy for metastatic gastric adenocarcinoma: a national population-based cohort study. Surgery 2021; 170: 1702-1710.

[8] Granieri S, Altomare M, Bruno F, Paleino S, Bonomi A, Germini A, Facciorusso A, Fagnani

D, Bovo G and Cotsoglou C. Surgical treatment of gastric cancer liver metastases: systematic review and meta-analysis of long-term outcomes and prognostic factors. Crit Rev Oncol Hematol 2021; 163: 103313.
[9] Sun Y, Hu P, Wang J, Shen L, Xia F, Qing G, Hu W, Zhang Z, Xin C, Peng W, Tong T and Gu Y. Radiomic features of pretreatment MRI could identify T stage in patients with rectal cancer: preliminary findings. J Magn Reson Imaging 2018; [Epub ahead of print].
[10] Renzulli M, Clemente A, Ierardi AM, Pettinari I, Tovoli F, Brocchi S, Peta G, Cappabianca S, Carrafiello G and Golfieri R. Imaging of colorectal liver metastases: new developments and pending issues. Cancers (Basel) 2020; 12: 151.
[11] Hu Q, Shi Y, Hua ZY, Bao L, Li F, Wei H, Song P, Ou-Yang HJ, Li Q and Wang M. A prediction nomogram for acute kidney injury in very-low-birth-weight infants: a retrospective study. Front Pediatr 2020; 8: 575097.
[12] Drzezga A, Souvatzoglou M, Eiber M, Beer AJ, Furst S, Martinez-Moller A, Nekolla SG, Ziegler S, Ganter C, Rummeny EJ and Schwaiger M. First clinical experience with integrated whole-body PET/MR: comparison to PET/CT in patients with oncologic diagnoses. J Nucl Med 2012; 53: 845-855.
[13] Glynne-Jones R, Wyrwicz L, Tiret E, Brown G, Rodel C, Cervantes A and Arnold D; ESMO Guidelines Committee. Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017; 28 Suppl 4: iv22-iv40.
[14] Balachandran VP, Gonen M, Smith JJ and DeMatteo RP. Nomograms in oncology: more than meets the eye. Lancet Oncol 2015; 16: e173-e180.
[15] Zhao L, Han W, Niu P, Lu Y, Zhang F, Jiao F, Zhou X, Wang W, Luan X, He M, Guan Q, Li Y, Nie Y, Wu K, Zhao D and Chen Y. Using nomogram, decision tree, and deep learning models to predict lymph node metastasis in patients with early gastric cancer: a multi-cohort study. Am J Cancer Res 2023; 13: 204-215.
[16] Li S, Zhao Z, Yang H, Wang D, Sun W, Li S, Zhang Z and Fu W. Construction and validation of a nomogram for the preoperative prediction of lymph node metastasis in gastric cancer. Cancer Control 2021; 28: 10732748211027160.
[17] Kim SM, Min BH, Ahn JH, Jung SH, An JY, Choi MG, Sohn TS, Bae JM, Kim S, Lee H, Lee JH, Kim YW, Ryu KW, Kim JJ and Lee JH. Nomogram to predict lymph node metastasis in patients with early gastric cancer: a useful clinical tool to reduce gastrectomy after endoscopic resection. Endoscopy 2020; 52: 435-443.
[18] Dong Z, Zhang Y, Geng H, Ni B, Xia X, Zhu C, Liu J and Zhang Z. Development and validation of two nomograms for predicting overall survival and cancer-specific survival in gastric cancer patients with liver metastases: a retrospective cohort study from SEER database. Transl Oncol 2022; 24: 101480.
[19] Wang B, Zhang Y, Qing T, Xing K, Li J, Zhen T, Zhu S and Zhan X. Comprehensive analysis of metastatic gastric cancer tumour cells using single-cell RNA-seq. Sci Rep 2021; 11: 1141.
[20] Mranda GM, Xue Y, Zhou XG, Yu W, Wei T, Xiang ZP, Liu JJ and Ding YL. Revisiting the 8th AJCC system for gastric cancer: a review on validations, nomograms, lymph nodes impact, and proposed modifications. Ann Med Surg (Lond) 2022; 75: 103411.
[21] Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition). Gastric Cancer 2021; 24: 1-21.
[22] Chinese College of Surgeons; Section of Gastrointestinal Surgery, Branch of Surgery, Chinese Medical Association; Section of Colorectal Surgery, Branch of Surgery, Chinese Medical Association; Section of Colorectal Oncology, Oncology Branch, Chinese Medical Association; Colorectal Cancer Professional Committee, Chinese Anti-Cancer Association; Colorectal Cancer Professional Committee, Chinese Medical Doctor Association; Colorectal Cancer Expert Committee, Chinese Society of Clinical Oncology; Chinese Society of Colon and Rectal Surgeons, Chinese College of Surgeons, Chinese Medical Doctor Association; Metastasis Research Committee, Anorectal Branch of Chinese Medical Doctor Association; Colorectal Liver Metastases Professional Committee, China International Exchange and Promotive Association for Medical and Health Care. China guideline for diagnosis and comprehensive treatment of colorectal liver metastases (version 2020). Zhonghua Wei Chang Wai Ke Za Zhi 2021; 24: 1-13.
[23] Nahm FS. Receiver operating characteristic curve: overview and practical use for clinicians. Korean J Anesthesiol 2022; 75: 25-36.
[24] Huang F and Fang M. Prediction model of liver metastasis risk in patients with gastric cancer: a population-based study. Medicine (Baltimore) 2023; 102: e34702.
[25] Kawahara K, Makino H, Kametaka H, Hoshino I, Fukada T, Seike K, Kawasaki Y and Otsuka M. Outcomes of surgical resection for gastric cancer liver metastases: a retrospective analysis. World J Surg Oncol 2020; 18: 41.
[26] Kataoka K, Kinoshita T, Moehler M, Mauer M, Shitara K, Wagner AD, Schrauwen S, Yoshikawa T, Roviello F, Tokunaga M, Boku N, Ducreux M, Terashima M and Lordick F; EORTC GITCG

Group and JCOG SCGC Group. Current management of liver metastases from gastric cancer: what is common practice? New challenge of EORTC and JCOG. Gastric Cancer 2017; 20: 904-912.
[27] Markar SR, Mackenzie H, Mikhail S, Mughal M, Preston SR, Maynard ND, Faiz O and Hanna GB. Surgical resection of hepatic metastases from gastric cancer: outcomes from national series in England. Gastric Cancer 2017; 20: 379-386.
[28] Zurleni T, Gjoni E, Altomare M and Rausei S. Conversion surgery for gastric cancer patients: a review. World J Gastrointest Oncol 2018; 10: 398-409.
[29] Mocan L. Surgical management of gastric cancer: a systematic review. J Clin Med 2021; 10: 2557.
[30] Zhu Z, Gong Y and Xu H. Clinical and pathological staging of gastric cancer: current perspectives and implications. Eur J Surg Oncol 2020; 46: e14-e19.
[31] Li Z, Wang Y, Ying X, Shan F, Wu Z, Zhang L, Li S, Jia Y, Ren H and Ji J. Different prognostic implication of ypTNM stage and pTNM stage for gastric cancer: a propensity score-matched analysis. BMC Cancer 2019; 19: 80.
[32] Qiu MZ, Shi SM, Chen ZH, Yu HE, Sheng H, Jin Y, Wang DS, Wang FH, Li YH, Xie D, Zhou ZW, Yang DJ and Xu RH. Frequency and clinicopathological features of metastasis to liver, lung, bone, and brain from gastric cancer: a SEER-based study. Cancer Med 2018; 7: 3662-3672.
[33] Tey J, Soon YY, Koh WY, Leong CN, Choo BA, Ho F, Vellayappan B, Lim K and Tham IW. Palliative radiotherapy for gastric cancer: a systematic review and meta-analysis. Oncotarget 2017; 8: 25797-25805.
[34] Ilson DH. The role of radiation therapy in upper gastrointestinal cancers. Clin Adv Hematol Oncol 2017; 15: 366-376.
[35] Budach VG. The role of radiation therapy in the management of gastric cancer. Ann Oncol 1994; 5 Suppl 3: 37-48.
[36] Baskar R, Dai J, Wenlong N, Yeo R and Yeoh KW. Biological response of cancer cells to radiation treatment. Front Mol Biosci 2014; 1: 24.
[37] Chen H, Han Z, Luo Q, Wang Y, Li Q, Zhou L and Zuo H. Radiotherapy modulates tumor cell fate decisions: a review. Radiat Oncol 2022; 17: 196.
[38] Vilalta M, Rafat M and Graves EE. Effects of radiation on metastasis and tumor cell migration. Cell Mol Life Sci 2016; 73: 2999-3007.
[39] Yu JI. Role of adjuvant radiotherapy in gastric cancer. J Gastric Cancer 2023; 23: 194-206.
[40] Maehara Y, Moriguchi S, Kakeji Y, Kohnoe S, Korenaga D, Haraguchi M and Sugimachi K. Pertinent risk factors and gastric carcinoma with synchronous peritoneal dissemination or liver metastasis. Surgery 1991; 110: 820-823.
[41] Feng F, Liu J, Wang F, Zheng G, Wang Q, Liu S, Xu G, Guo M, Lian X and Zhang H. Prognostic value of differentiation status in gastric cancer. BMC Cancer 2018; 18: 865.
[42] Yang DY, Wang X, Yuan WJ and Chen ZH. Metastatic pattern and prognosis of gastrointestinal stromal tumor (GIST): a SEER-based analysis. Clin Transl Oncol 2019; 21: 1654-1662.
[43] Luo P, Wei X, Liu C, Chen X, Yang Y, Zhang R, Kang X, Qin J, Qi X and Li Y. The risk and prognostic factors for liver metastases in esophageal cancer patients: a large-cohort based study. Thorac Cancer 2022; 13: 2960-2969.
[44] Zhang Y, Lin Y, Duan J, Xu K, Mao M and Wang X. A population-based analysis of distant metastasis in stage IV gastric cancer. Med Sci Monit 2020; 26: e923867.
[45] Lin Z, Wang R, Zhou Y, Wang Q, Yang CY, Hao BC and Ke CF. Prediction of distant metastasis and survival prediction of gastric cancer patients with metastasis to the liver, lung, bone, and brain: research based on the SEER database. Ann Transl Med 2022; 10: 16.
[46] Wang S, Feng Y, Swinnen J, Oyen R, Li Y and Ni Y. Incidence and prognosis of liver metastasis at diagnosis: a pan-cancer population-based study. Am J Cancer Res 2020; 10: 1477-1517.
[47] Camargo MC, Goto Y, Zabaleta J, Morgan DR, Correa P and Rabkin CS. Sex hormones, hormonal interventions, and gastric cancer risk: a meta-analysis. Cancer Epidemiol Biomarkers Prev 2012; 21: 20-38.
[48] Hu PJ, Chen MY, Wu MS, Lin YC, Shih PH, Lai CH and Lin HJ. Clinical evaluation of CA72-4 for screening gastric cancer in a healthy population: a multicenter retrospective study. Cancers (Basel) 2019; 11: 733.
[49] Kim DH, Oh SJ, Oh CA, Choi MG, Noh JH, Sohn TS, Bae JM and Kim S. The relationships between perioperative CEA, CA 19-9, and CA 72-4 and recurrence in gastric cancer patients after curative radical gastrectomy. J Surg Oncol 2011; 104: 585-591.