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Original Article

Risk factors of positive lymph node metastasis after radical gastrectomy for gastric cancer and construction of prediction models

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Abstract: Positive lymph node metastasis after radical gastrectomy for gastric cancer is a key factor affecting the prognosis of patients, and its mechanism is complex and multifactorial. The aim of this study is to identify the relevant risk factors for positive lymph node metastasis after radical gastrectomy for gastric cancer, and to construct corresponding predictive models. Through a retrospective analysis of clinical data of 316 gastric cancer patients who underwent radical surgery for gastric cancer, we found that age, maximum tumor diameter, degree of tumor differentiation, vascular invasion, depth of tumor infiltration, and CA199 were important factors affecting lymph node metastasis positivity in gastric cancer patients. Based on these factors, we constructed a Nomogram prediction model and found through internal validation that the model has good predictive performance. The area under the receiver operating characteristic curve (AUC) of the training and validation sets were 0.929 and 0.888, respectively. Clinical data of another 390 patients were collected for external verification. External validation results showed that the model had a predictive sensitivity of 75.76% (50/66), a specificity of 91.05% (295/324), and an accuracy of 88.46% (345/390). In addition, we also constructed a neural network prediction model and compared it with the Nomogram model. The results showed that the prediction performance of the Nomogram model was similar to that of the neural network model. The Nomogram model has been validated internally and externally, demonstrating high discrimination and accuracy, providing a convenient, intuitive, and personalized evaluation tool for clinicians, helping to optimize the postoperative management of gastric cancer patients and improve prognosis.

Keywords: Radical gastrectomy for gastric cancer, lymph node metastasis, logistic regression analysis, nomogram model, neural network model

Introduction

Gastric cancer, as a global health concern, poses a serious threat to human health due to its high incidence (4.9%) and mortality (6.80%) [1]. According to the global tumor epidemiological statistics, the incidence and mortality of gastric cancer are particularly high in Asia, and the prevention and treatment of gastric cancer is facing challenges [1]. The treatment strategies for gastric cancer include surgery, chemotherapy, radiotherapy, and targeted therapy, among which surgical resection, especially radical surgery, is a key means of treatment to improve patient survival rate [2-4]. However, even with curative surgery, lymph node metastasis remains a serious problem for gastric cancer patients. It not only indicates further deterioration of the disease, but also greatly affects the long-term survival rate and quality of life of patients [5].

Positive lymph node metastasis is indicated by pathological examination after curative surgery, which reveals that cancer cells have spread to the regional lymph nodes [6]. The mechanism is complex and involves various biological processes, including the invasion of tumor cells to lymphatic vessels and blood vessels, and changes in the tumor microenvironment [7, 8]. Positive lymph node metastasis is a serious condition after radical surgery, indicating that cancer cells have spread to other areas through the lymphatic system [9]. This diffusion not only

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increases the complexity of treatment, but also has a significant negative impact on the prognosis of patients. Specifically, gastric cancer patients with positive lymph node metastasis typically face poor prognosis and significantly increased risk of recurrence, which not only increases the difficulty of treatment but may also have an impact on the quality of life of patients [10]. In addition, treatment-related side effects and long-term health conditions may also lead to a decrease in the quality of life for patients. To cope with this situation, more aggressive treatment strategies such as adjuvant chemotherapy or radiotherapy may be necessary [11]. Ultimately, the survival period of gastric cancer patients with positive lymph node metastasis may be shortened due to difficulties in disease control. Therefore, in-depth study of the relevant risk factors for positive lymph node metastasis in gastric cancer is of great significance for individualized treatment and prognosis evaluation.

The occurrence of positive lymph node metastasis is closely related to the biological characteristics of tumors, as well as factors such as genetic background, lifestyle habits, and disease management [12-14]. A single factor often fails to fully reflect the full picture, as the degree of influence and mechanism of action of each factor may vary. In addition, the predictive power of individual factors may be lower as they do not cover the complex biological and environmental factors that affect lymph node metastasis [15]. For example, genetic background may affect an individual's response to tumor development, while lifestyle habits such as diet and smoking may affect the tumor microenvironment, thereby affecting the risk of lymph node metastasis [16]. Therefore, in order to accurately predict the risk of positive lymph node metastasis after radical gastrectomy for gastric cancer, multiple factors need to be comprehensively considered. By establishing a multi-factor predictive model, the patient's risk can be comprehensively evaluated, thereby improving the accuracy and reliability of predictions [17]. We conducted this retrospective analysis to explore the predictive factors for positive lymph node metastasis after radical surgery for gastric cancer, and established a comprehensive multi factor Nomogram to predict the risk of positive lymph node metastasis after the surgery, so as to help future personalized treatment in this population. Doctors can develop more precise treatment plans, optimize patient follow-up strategies, and potentially improve patient prognosis.

Materials and methods

Study population

Data of gastric cancer patients who underwent radical gastrectomy in Chongming Hospital Affiliated to Shanghai University of Medicine and Health Sciences between January 2018 and June 2020 were retrospectively analyzed.

The required sample size was calculated based on the empirical method (Events Per Variable, EPV): According to relevant literature, the positive rate of lymph node metastasis in gastric cancer patients after surgical treatment is about 13% to 23% [18, 19]. We estimated sample size based on a positive rate of 20%. Firstly, assuming EPV=10, it is estimated that there would be 6 variables entering the logistic regression analysis. The preliminary calculation led to a required sample size of 300 cases (10 * 6/0.2). The final sample size included in the study is 316 cases. Retrospective collection of clinical data from the 316 patients was conducted, and they were divided into a lymph node metastasis positive group and a lymph node metastasis negative group based on the characteristics of lymph node metastasis within 1 year after surgery. This study was approved by the Ethics Committee of Chongming Hospital Affiliated to Shanghai University of Medicine and Health Sciences.

Inclusion criteria: (1) Patients diagnosed with primary gastric cancer, confirmed by pathological examination as adenocarcinoma, and with regional lymph node metastasis [20]; (2) Patients received a standardized radical gastrectomy, with R0 resection (the complete removal of a tumor with no cancer cells visible at the margins of the resected tissue); (3) No distant metastasis was found during preoperative examinations; (4) No neoadjuvant chemotherapy was performed before surgery, and postoperative adjuvant chemotherapy was based on fluorouracil drugs; (5) Those with complete clinical and pathological data. Exclusion criteria: (1) Those with primary cancer in other areas; (2) Those with infectious diseases; (3) Those with immune system diseases; (4) Those with mental illness or consciousness disorder.

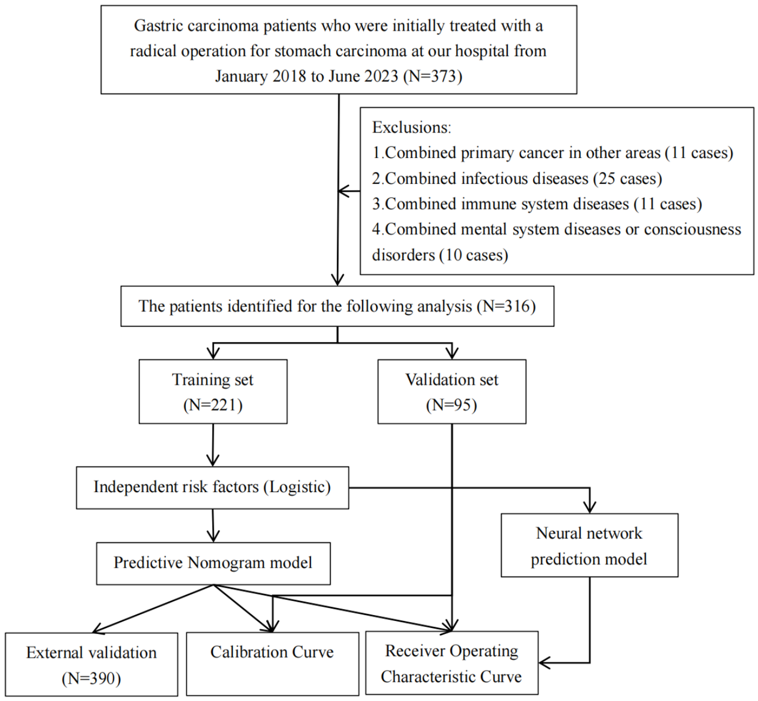

Figure 1. Study flow diagram.

Determination of positive lymph node metastasis and research process

Positive postoperative lymph node metastasis was defined as the presence of cancer cells in the original lymph node or nearby lymph nodes on pathological examination after the patient had undergone surgical treatment. This usually means that the primary tumor has spread through the lymphatic system to other parts of the body. To determine the positivity of postoperative lymph node metastasis, the lymph node tissue was observed under the microscope, and the sections of the postoperative tissue were observed by pathologists. The research subjects were randomly divided into a training cohort and a verification cohort with a ratio of 7:3. A detailed study flow chart is shown in **Figure 1**.

Data collection

We collect multidimensional data from patients for analysis. (1) General information: age, sex, place of residence, educational level, body mass index (BMI), drinking history, smoking history, hypertension history, diabetes history, coronary heart disease history, and genetic history. (2) Perioperative indexes: operation time, intraoperative blood loss, hospital stay, and number of lymph node dissection. (3) Pathological indexes: maximum diameter of cancer, lesion type, lesion number, gastric tumor location, degree of differentiation, vascular invasion, nerve invasion, intraoperative drug implantation, adjuvant chemotherapy, and tumor invasion depth. (4) Biochemical indicators: albumin (ALB), platelets (PLT), lymphocytes, D-dimer, fibrinogen, D-dimer/albumin (DA), platelets/lymphocytes (PLR), carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199), carbohydrate antigen 724 (CA-724), and alpha-fetoprotein (AFP).

Model building

(1) Construction of nomogram model: First, univariate and multivariate statistical analyses were performed to screen the predictive factors significantly associated with positive lymph node metastasis. Subsequently, logistic regression analysis was conducted to calculate the hazard ratio and confidence interval of each factor. These coefficients were visualized using R software to show their impact on the risk of lymph node metastasis. (2) The construction of neural network model: First, the collected data were preprocessed, including cleaning, standardization, and processing missing and abnormal values. Then, the back-propagation neural network was employed to build the prognosis evaluation model. The back-propagation neural network is composed of an input layer, a hidden layer and an output layer. There are a large number of neuronal nodes in each layer, and the nodes between layers are connected with each other. Each node is actually an activation function, and the connection between nodes is actually the weight assigned to the next node through this node. The back-propagation neural network model can be trained by adjusting the transmission weight and bias between nodes.

Statistical analysis

SPSS 26.0 and R 4.2.1 were used for data analysis. The clinical data of patients with positive and negative lymph node metastases were

Table 1. Comparison of general data [$\overline{x}\pm s$, n (%)]

Index	Positive group (n=49)	Negative group (n=267)	t/χ^2	*P*
Age (year)	58.00 (56.00, 69.00)	55.00 (49.00, 61.00)	-3.505	<0.001
Sex			0.038	0.845
Man	29 (59.18)	162 (60.67)		
Woman	20 (40.82)	105 (39.33)		
Place of Residence			0.011	0.917
Lunar	31 (63.27)	171 (64.04)		
Urban	18 (36.73)	96 (35.96)		
Educational level			0.139	0.709
Junior college or below	34 (69.39)	178 (66.67)		
College or above	15 (30.61)	89 (33.33)		
BMI (kg/m^2)	24.06±2.03	23.45±2.10	1.860	0.064
History of drinking			0.802	0.371
Yes	30 (61.22)	145 (54.31)		
No	19 (38.78)	122 (45.69)		
History of smoking			0.442	0.506
Yes	21 (42.86)	101 (37.83)		
No	28 (57.14)	166 (62.17)		
History of hypertension			1.356	0.244
Yes	16 (32.65)	66 (24.72)		
No	33 (37.35)	201 (75.28)		
History of diabetes			0.368	0.544
Yes	11 (22.45)	50 (18.73)		
No	38 (77.55)	217 (81.27)		
History of coronary heart disease			1.064	0.302
Yes	10 (20.41)	39 (14.61)		
No	39 (79.59)	228 (85.39)		
History of heredity			1.980	0.159
Yes	8 (16.33)	23 (8.61)		
No	41 (83.67)	244 (91.39)		

Note: BMI: Body mass index.

compared and analyzed. The count data were expressed as rate [n (%)] and compared using Chi-square test. Measurement data were expressed as mean ± standard deviation and processed using independent sample t test. Logistic regression analysis was used to explore the independent risk factors for positive lymph node metastasis. R language was used to visualize the nomogram and the neural network prediction model to obtain the importance of the influencing factors. The area under receiver operating characteristic curve (AUC) and calibration curve were used to evaluate the predictive value of the models. *P*<0.05 indicates significant difference.

Results

General information

Among the 316 patients, there were 191 males (60.44%) and 125 females (39.56%), with an age of 56.00 (50.00, 63.00) years old and an average of BMI of (23.55±2.10) kg/m^2. There were 175 cases (55.38%) had a history of drinking, 122 cases (38.61%) with smoking history, 82 cases (25.95%) with a history of hypertension, and 61 cases (19.30%) with a history of diabetes.

Furthermore, 49 patients showed positive lymph node metastasis within 1 year, account-

Table 2. Comparison of pathological indexes, biochemical indicators and hospitalization related indicators [n (%)]

Index	Positive group (n=49)	Negative group (n=267)	χ^2	*P*
Maximum tumor diameter (cm)	5.00 (4.00, 6.00)	3.00 (3.00, 4.00)	-4.835	<0.001
Lesion classification			2.134	0.344
Protrude type	7 (14.29)	35 (13.11)		
Flat type	9 (18.37)	20 (11.24)		
Umbilicate type	33 (67.35)	202 (75.66)		
Number of lesions			1.806	0.179
A single lesion	39 (79.59)	232 (86.89)		
Multiple lesions	10 (20.41)	35 (13.11)		
Placement of gastric tumor			2.124	0.346
Upper third	12 (24.49)	61 (22.85)		
Middle third	20 (40.82)	85 (31.84)		
Lower third	17 (34.69)	121 (45.32)		
Degree of tumor differentiation			26.950	<0.001
Undifferentiated type	35 (71.43)	86 (32.21)		
Differentiated	14 (28.57)	181 (67.79)		
Vascular invasion			25.311	<0.001
Yes	15 (46.87)	23 (12.50)		
No	17 (53.13)	161 (87.50)		
Intraoperative drug implantation			0.574	0.449
Yes	17 (34.69)	108 (40.45)		
No	32 (65.31)	159 (59.55)		
Adjuvant chemotherapy			0.565	0.452
Yes	29 (59.18)	173 (64.79)		
No	20 (40.82)	94 (35.21)		
Depth of tumor invasion			14.772	<0.001
Layer of mucosa	11 (34.38)	110 (59.78)		
Submucosa	21 (65.62)	74 (40.22)		
ALB (g/L)	41.27±8.92	42.10±9.26	-0.581	0.562
PLT (10^9/L)	165.92±31.12	157.72±28.35	1.831	0.068
Lymphocytes (10^9/L)	1.63±0.48	1.69±0.55	-0.672	0.502
D-dimer (ng/mL)	101.57±20.88	96.61±18.61	1.685	0.093
Fibrinogen	3.42±1.22	3.20±1.02	1.362	0.174
DA	2.83±1.15	2.62±1.33	1.042	0.298
PLR	112.23±27.38	105.41±32.45	1.384	0.167
CEA (ng/mL)	4.52±1.16	4.21±1.54	1.327	0.186
CA199 (U/mL)	52.00 (45.00, 61.00)	37.00 (29.00, 46.00)	-6.214	<0.001
CA724 (U/mL)	6.29±1.66	5.90±1.35	1.790	0.074
AFP (ng/mL)	29.22±5.53	29.12±6.20	0.115	0.909
Duration of surgery (h)	3.78±0.97	3.68±0.81	0.769	0.442
Intraoperative blood loss (mL)	256.16±38.96	244.53±45.38	1.683	0.093
Length of stay (d)	7.34±2.18	7.65±2.25	0.891	0.374
Lymph node cleaning number	12.66±2.75	12.85±2.50	0.481	0.631

Note: ALB: albumin; PLT: Platelets; DA: D-dimer/ALB; PLR: PLT/lymphocyte; CEA: Carcinoembryonic antigen; CA199: carbohydrate antigen 199; CA724: Carbohydrate antigen 724; AFP: Alpha-fetoprotein.

ing for 15.51%. After analysis, it was found that there was only one significant difference in general data between the negative and positive lymph node metastasis groups, with the posi-

Table 3. Multivariate Logistic regression analysis of factors associated with positive lymph node metastasis

Variable	*B*	*SE*	*Wald* χ^2	*P*	*OR*	95% CI
Age	0.071	0.023	9.325	0.002	1.074	1.026-1.124
Maximum tumor diameter	0.475	0.144	10.871	0.001	1.608	1.213-2.134
Degree of tumor differentiation	1.697	0.440	14.865	<0.001	5.458	2.303-12.935
Vascular invasion	1.599	0.462	11.993	0.001	4.946	2.001-12.223
Depth of tumor invasion	1.379	0.450	9.401	0.002	3.907	1.644-9.583
CA199	0.096	0.019	25.858	<0.001	1.101	1.061-1.143
Constant	-14.128	2.094	45.522	-	-	-

Note: CA199: carbohydrate antigen 199.

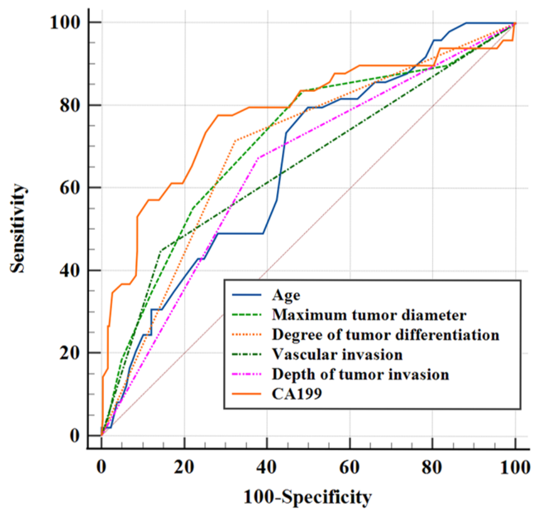

Figure 2. Predictive value of influencing factors for positive lymph node metastasis.

tive group having an older age (*P*<0.05); There were no significant differences between the two groups in gender, residence, education level, BMI, drinking history, smoking history, hypertension history, diabetes history, coronary heart disease history and genetic history (*P*>0.05), as shown in **Table 1**.

Comparison of pathological indexes and biochemical indicators

In the comparison of pathological indicators, it was found that compared with the negative group, the positive group had a larger tumor diameter, a higher proportion of undifferentiated tumors, vascular invasion, and tumor infiltration depth in the lower layer, with statistically significant differences (*P*<0.05). There was no significant difference other pathological indexes such as lesion type, lesion number, gastric tumor location, nerve invasion, intraoperative drug implantation, and adjuvant chemotherapy between the two groups (*P*>0.05). In terms of biochemical indicators, the positive group exhibited significantly increased CA199 level (*P*<0.05). There were no significant differences in other biochemical indicators (*P*>0.05), as shown in **Table 2**.

Multivariate Logistic regression analysis risk factors

Significant variables from the above univariant analyses were included in multivariate Logistic regression analysis, which showed that age, maximum tumor diameter, tumor differentiation degree, vascular invasion, depth of tumor invasion, and CA199 were independent risk factors for positive lymph node metastasis (*P*<0.05), as shown in **Table 3**.

ROC analysis of the influencing factors

The ROC analysis was performed on the independent factors in the above logistic regression analysis. The results showed that all influencing factors had a certain degree of discrimination in predicting lymph node metastasis positivity (AUC>0.5), among which maximum tumor diameter and CA199 had a good discrimination level (AUC>0.7), as shown in **Figure 2** and **Table 4**.

Establishment of nomogram prediction model

Based on the results of the multivariate analysis, the prediction formula P = exp (Y)/[1 + exp (Y)] was derived, where Y = -14.128 + 0.071 * age + 0.475 * maximum tumor diameter + 1.697 * degree of tumor differentiation + 1.599 * vascular invasion + 1.379 * depth of tumor infiltration + 0.096 * CA199. A visualiza-

Table 4. ROC analysis of factors associated with positive lymph node metastasis

Indicators	AUC	Sensitivity (%)	Specificity (%)	*P*	95% CI
Age	0.657	79.59	50.19	<0.001	0.602-0.710
Maximum tumor diameter	0.711	83.67	51.31	<0.001	0.658-0.761
Degree of tumor differentiation	0.696	71.43	67.79	<0.001	0.642-0.746
Vascular invasion	0.653	44.90	85.77	<0.001	0.598-0.706
Depth of tumor invasion	0.648	67.35	62.17	<0.001	0.559-0.692
CA199	0.779	77.55	71.91	<0.001	0.729-0.824

Note: ROC: Receiver operating characteristic; CA199: carbohydrate antigen 199.

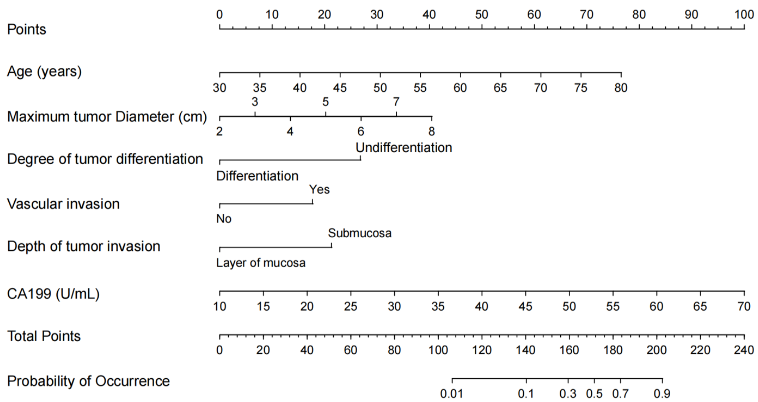

Figure 3. Nomogram model. Note: CA199: carbohydrate antigen 199.

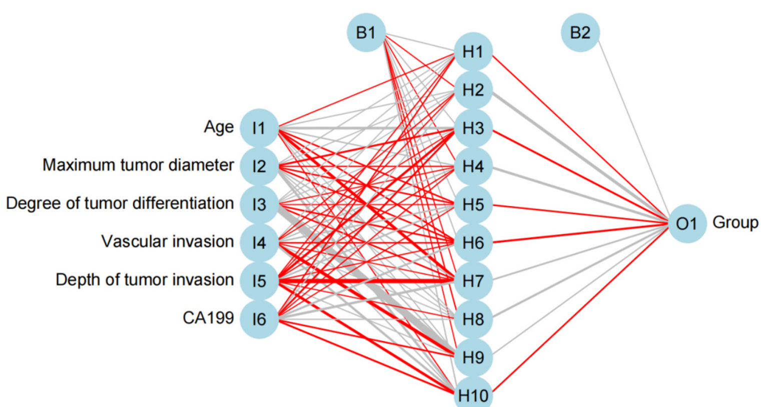

Figure 4. Network structure diagram of the neural network prediction model.

tion of the prediction formula and a line graph model are shown in **Figure 3**. While using nomogram prediction models, users can map various influencing factors to the "points" scale at the top of the graph to obtain the corresponding scores for each factor. Various scores are added up to calculate a total score, and the total score can be mapped to a "Probability of occurrence" scale below to obtain the risk value of lymph node metastasis for the patient.

Establishment of neural network prediction model

A neural network model was constructed based on the results of the multivariate logistic regression analysis. In this model, the network structure illustrates the connection weights between neurons: positive weights are connected by red lines, negative weights are connected by gray lines, and the thickness of each line indicates the magnitude of the weight, as shown in **Figure 4**. Additionally, to highlight the significance of variables associated with lymph node metastasis positivity, the normalized importance ranking of various factors is shown in **Figure 5**.

Internal validation of the nomogram model

Internal validation of the nomogram model showed that the AUC of the model in the training and validation sets were 0.929 and 0.888, respectively (**Figure 6**). This indicates that the model has good discrimination in internal validation. In addition, the calibration curve shows that the probability predicted by the model is close to the actual observed frequency of events, which further confirms the accuracy and reliability of the model (**Figure 7**).

External validation of the nomogram model

To further validate the generalization ability of the model, external validation was performed.

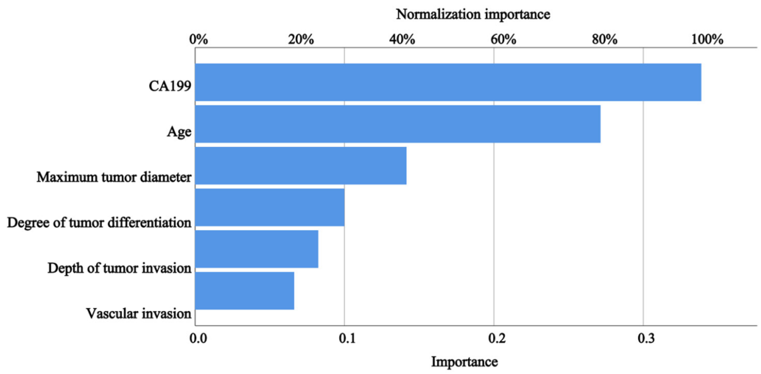

Figure 5. Analysis of variable importance in neural network prediction model.

The calculation of required sample size for external validation also used the EPV method. In this study, the positive rate of postoperative lymph node metastasis in the training set was 15.51%, and the final predictive factor was 6. Therefore, the sample size for external validation was estimated to be N = 6 * 10/15.51% = 386 cases. In the end, 390 patients from July 2020 to July 2023 were included for external validation. The age of 390 patients ranged from 34 to 84 years old, with an average of (58.37±8.85) years. Among them, there were 257 males (65.90%) and 133 females (34.10%); 266 cases (68.21%) living in rural areas and 124 cases (31.79%) in urban areas; 229 cases (58.72%) with an educational level below college level and 161 cases (41.28%) with an educational level above college level. Furthermore, 203 cases (52.05%) had a history of alcohol consumption, 141 cases (36.15%) with a history of smoking, 91 cases (23.33%) with a history of hypertension, 79 cases (20.26%) with a history of diabetes, 85 cases (21.79%) with a history of coronary heart disease, and 52 cases (13.33%) with a genetic history. The external validation results are shown in **Table 5**. Among the 390 patients, the positive rate of postoperative lymph node metastasis was 16.92% (66/390). The positive predictive value of the column chart model was calculated to be 63.29% (50/79), with a sensitivity of 75.76% (50/66), a specificity of 91.05% (295/324), and an accuracy of 88.46% (345/390).

Comparison of predictive performance between the nomogram model and individual influencing factors

We compared the predictive performance of the nomogram model with the influencing factors with an AUC greater than 0.7, and the results showed that the predictive performance of the model was significantly higher than that of each individual factor (Z=4.910 and 3.941, P<0.05), as shown in **Figure 8** and **Table 6**.

Validation of the neural network model and comparison with the nomogram model

As shown in **Figure 9**, the ROC of the neural network model in the training set and validation set are 0.949 and 0.809, respectively, indicating that the neural network model also has a good discrimination ability. The Delong test results showed that there was no significant difference in ROC between the column chart model and the neural network model in the training set (Z=-0.788, P=0.430) and the validation set (Z=1.012, P=0.313).

Discussion

Radical gastrectomy for gastric cancer can significantly improve the survival rate and quality of life of patients by completely removing tumor tissue [21, 22]. However, positive postoperative lymph node metastasis remains a serious challenge, which not only affects patient prognosis, but also increase the complexity and difficulty of treatment [23, 24]. This study analyzed the clinical data of 316 patients who underwent gastric cancer radical treatment, and found 49 cases with lymph node metastasis, with a positive rate of 15.51%. Our result is similar to that of previous research [18, 19, 25].

Advanced age is a key factor associated with increased risk of postoperative lymph node metastasis [26]. As people age, the gastric mucosa becomes more susceptible to inflammation and damage, increasing the risk of cancer [27, 28]. Additionally, the immune function of elderly people declines, weakening their defense against tumors, which promotes immune escape and lymphatic metastasis of tumors [29]. Mao et al. [30] found that age ≥45 years was associated with an increased risk of cancer lymph node metastasis. In addition, the healing ability of elderly people decreases, which may prolong the survival and spread time of tumor cells. Therefore, for elderly gastric can-

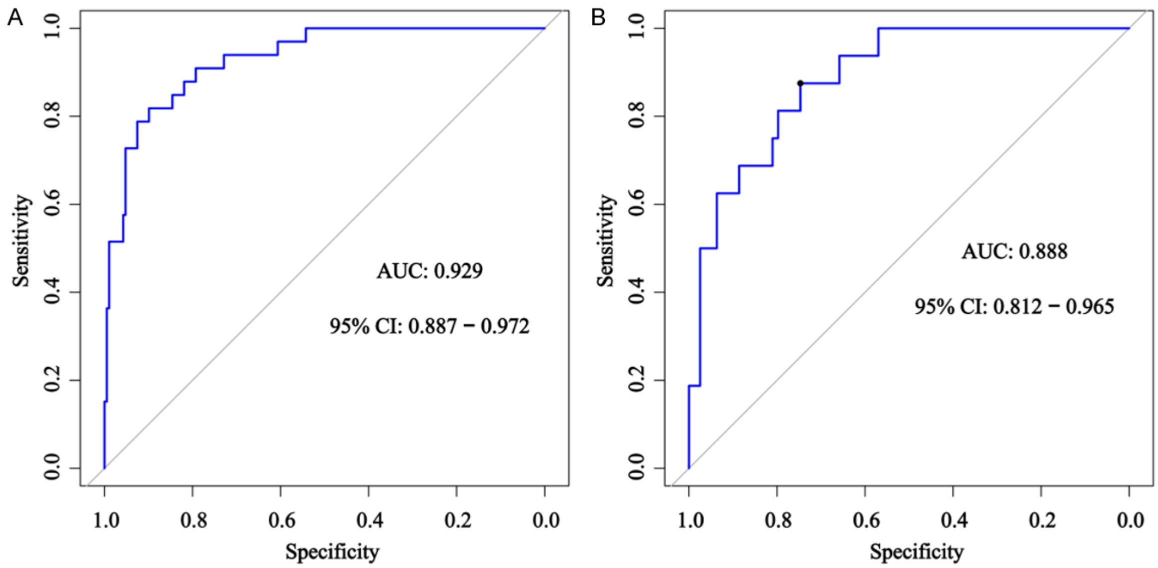

Figure 6. Area under the curve (AUC) of the model in the internal validation. A. Training set; B. Validation set.

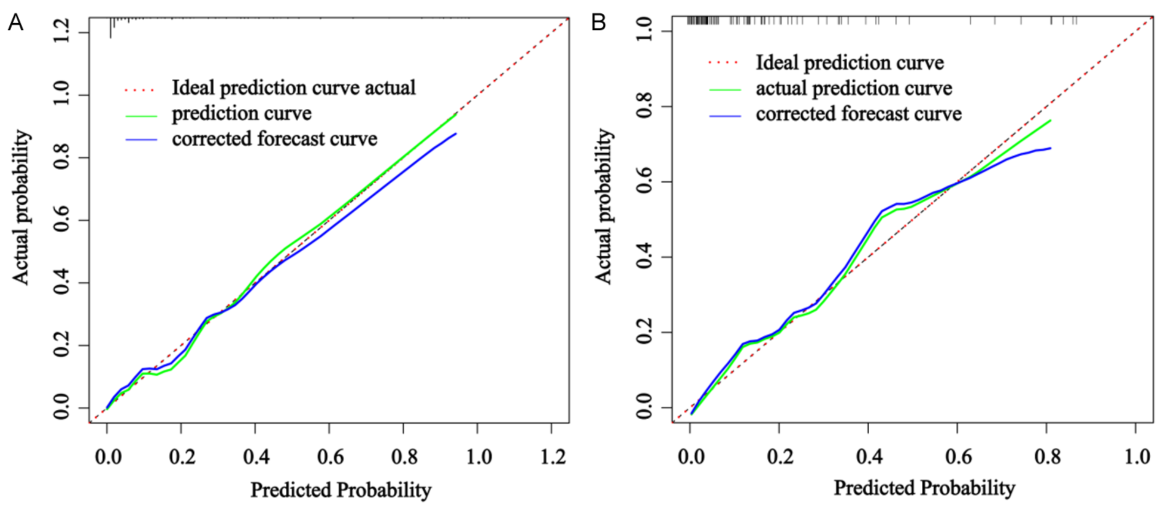

Figure 7. Calibration curve of the model. A. Training set; B. Validation set.

Table 5. External validation of the nomogram model

Actual	Predicted		Total
	Positive	Negative	
Positive	50	16	66
Negative	29	295	324
Total	79	311	390

cer patients, age-related physiological and immune function changes should be considered during treatment, and active measures should be taken to prevent tumor metastasis, in order to improve patient survival rate and quality of life.

A larger tumor diameter usually means a greater number of tumor cells and a larger tumor volume, which may be accompanied by increased invasiveness and spreading ability of tumor cells [31]. A gastric tumor with large diameter could herald a higher activity and invasive growth, increasing the cancer spread through the lymphatic system or the blood into the surrounding lymph nodes or other distant organs [32]. In addition, larger tumors may have caused some compression and invasion of the

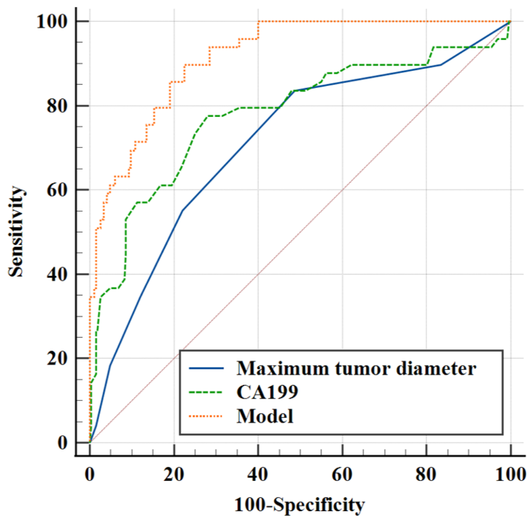

Figure 8. Comparison between the model and individual influencing factors.

surrounding tissues and lymph nodes, which lead to changes in the local microenvironment and provide favorable conditions for cancer cell invasion and metastasis [33]. A retrospective study on the basis of SEER database, categorizing patients with gastric cancer by tumor size into three groups, found that larger size (≥5.3 cm) were associated with poor prognosis [34]. Therefore, larger tumor diameter may be associated with an increased incidence of positive lymph node metastasis after radical gastrectomy for gastric cancer.

Lower tumor differentiation is associated with higher tumor malignancy, including increased potential for lymphatic invasion of surrounding tissues [35]. Several studies have pointed out that the lymph node metastasis rate of gastric cancer is closely linked to the degree of tumor cell differentiation [36, 37]. Specifically, Feng et al. [37] found that the worse the tumor cell differentiation, the higher the rate of lymph node metastasis in gastric cancer. Studies have shown that gastric cancer patients with positive lymph node metastasis had a higher incidence of vascular infiltration than the negative group [38]. This may be due to the invasive and proliferative nature of gastric tumors; as they grow and penetrate the lymphatic and vascular rich stomach wall, tumor emboli and vascular invasion can form more readily. Additionally, research suggests that vascular invasion can promote the spread and metastasis of tumor cells, thereby increasing the risk of lymph node metastasis in gastric cancer patients [39]. The invasion depth of gastric cancer is generally categorized by the specific layers affected: mucosa, submucosa, superficial muscle, deep muscle, serosa, and extra-serosa [40]. Studies have shown a direct correlation between lymph node metastasis and the depth of tumor invasion in gastric cancer [41]. In addition, the depth of invasion is also closely related to other factors, such as tumor differentiation and prognosis [42]. For patients with deeper infiltration, the risk of lymph node metastasis is higher, often corresponding to a poor prognosis.

CA199, as a tumor marker, is upregulated in various cancers including gastric cancer and is associated with the invasiveness and metastatic potential of tumors [43]. High levels of CA199 may indicate that gastric cancer cells have developed to a stage with immune escape capabilities and potential for lymphatic spread [44]. In addition, high levels of CA199 may also be associated with changes in the tumor microenvironment, creating conditions for tumor invasion and metastasis [45]. Therefore, monitoring the levels of CA199 in gastric cancer patients before and after surgery can help evaluate the risk of metastasis and treatment efficacy. If CA199 continues to rise or does not return to normal after surgery, this may indicate a high risk of lymph node metastasis, warranting close monitoring and consideration of adjuvant therapy to improve patient prognosis.

At present, nomogram prediction models are widely used in clinical settings to assess cancer prognosis [46]. However, study has pointed out that the accuracy of nomogram prediction models are highly dependent on correct data representation, which can lead to overfitting [47]. In contrast, neural network prediction model provide a more visual representation of statistical relationships and offer clinical advantages due to their simplified quantification of risk factors over traditional digital model [48]. The results of this study showed that there was no significant difference in the AUCs between the nomogram model and the neural network model in both the training and validation sets. This suggests that a nomogram prediction model based on multidimensional clinical indicators can effectively predict lymph node metastasis in patients with gastric cancer undergoing radical surgery. Therefore, applying

Table 6. Comparison between the model and individual influencing factors

Indicators	AUC	95% CI	Z	*P*
Model	0.917	0.881-0.945	-	-
Maximum tumor diameter	0.711	0.658-0.761	4.910	<0.001
CA199	0.773	0.729-0.824	3.941	<0.001

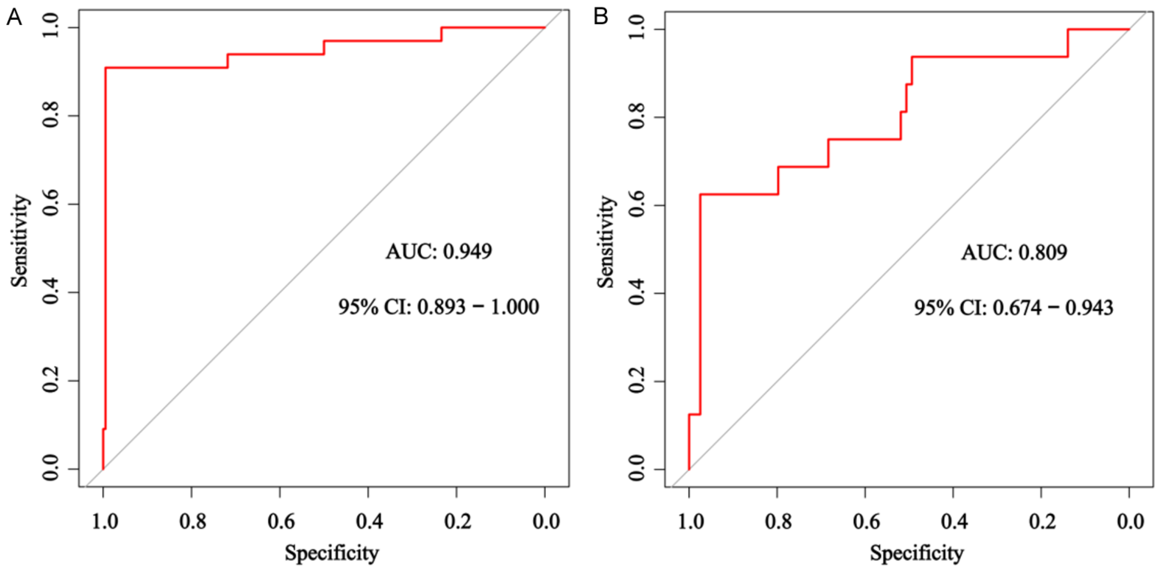

Figure 9. Area under the curve (AUC) of the neural network model. A. Training set; B. Validation set.

these models in clinical practice could provide valuable guidance for the prevention and management of lymph node metastasis in gastric cancer patients undergoing radical surgery.

This study delved into the risk factors for positive lymph node metastasis after radical gastrectomy for gastric cancer and established two predictive models. However, there are still some limitations. Firstly, as a single center study with a single-source sample, the findings may have limited generalizability. Variations in genetic and lifestyle across regions may affect the accuracy of the model. Secondly, the study adopts retrospective data collection, which may introduce selection and information bias, and the incompleteness and accuracy of historical records may also affect the reliability of the results. In addition, the retrospective design cannot fully control the variability of data collection, potentially overlooking important factors. In order to improve the generalization ability and clinical utility, future research should adopt a multicenter, prospective design, and incorporate a more diverse patient population.

Conclusion

This study analyzed the risk factors for positive lymph node metastasis after radical gastrectomy for gastric cancer, and developed a nomogram and a neural network prediction model to evaluate these risk factors. The results identified age, tumor diameter, degree of tumor differentiation, vascular invasion, tumor infiltration depth, and CA199 levels as key factors affecting the lymph node metastasis. The nomogram model based on these factors demonstrated strong predictive performance, providing valuable clinical reference value for assessing metastasis risk in gastric cancer patients undergoing radical gastrectomy.

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Disclosure of conflict of interest

None.

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