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Construction and validation of LODDS-based nomogram for prognosis of stage I-II gastric signet ring cell carcinoma

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Abstract: Objective To explore the predictive value of log odds of positive lymph nodes (LODDS) for survival outcomes in stage Ⅰ-Ⅱ gastric signet ring cell carcinoma patients, thus constructing and verifying a LODDS-based nomogram. **Methods** Clinical data of 680 cases from the Surveillance, Epidemiology, and End Results (SEER) Program and 62 patients with stage Ⅰ-Ⅱ gastric signet ring cell carcinoma from Yixing People's Hospital Affiliated to Jiangsu University were retrospectively collected from 2013 to 2017 as the training set and validation set, respectively. The X-tile software was applied to identify best cut off values of LODDS. The Kaplan-Meier method was applied to plot survival curves according to LODDS categories, and the prognostic performance of LODDS was evaluated by receiver operating characteristic (ROC)curve analysis. The Cox regression analysis was used to identify independent risk factors for prognosis of stage Ⅰ-Ⅱ gastric signet ring cell carcinoma patients, which were further used to establish a LODDS-based nomogram. **Results** LODDS was associated with gender, and N stage in training set (P<0.05), while LODDS was related with N stage and chemotherapy status in validation set (P<0.05). According to overall survival (OS) and cancer specific survival (CSS) in both training and validation sets, low LODDS group had the best survival outcomes, followed by the medium LODDS group, while high LODDS group had the worst survival outcomes (P<0.05). Additionally, high T stage, receiving chemotherapy and high LODDS were independent risk factors for prognosis of stage Ⅰ-Ⅱ gastric signet ring cell carcinoma patients. The LODDS-based nomogram was further constructed, and the area under the curve (AUC)for predicting 3-year CSS was 0.765 and 0.809 in internal and external validation, respectively. Meanwhile, calibration curve showed the good predictive value of this nomogram. **Conclusion** High LODDS can be served as an independent risk factor in stage Ⅰ-Ⅱ gastric signet ring cell carcinoma patients. The LODDS-based nomogram shows good predictive values for survival of these patients.

Keywords: Gastric tumor; Signet ring cell carcinoma; Gastric cancer, stages Ⅰ-Ⅱ; Log odds of positive lymph nodes; Nomogram; T stage; Prognosis

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Gastric cancer has a high incidence and mortality rate [1-3]. Signet ring cell gastric cancer accounts for approximately 9.9% of gastric cancer cases, commonly occurs in young women, and most patients with gastric signet ring cell carcinoma (GSRCC) present with metastasis at the time of initial diagnosis, leading to a poor prognosis [4-6]. Lymph node metastasis is a typical characteristic of its early metastasis. In recent years, an increasing number of studies have focused on exploring novel biomarkers associated with lymph node metastasis. The positive lymph node ratio (LNR) is an independent prognostic factor affecting the survival of gastric cancer patients [7], and a higher LNR is associated with a greater risk of death [8]. The prognostic value of LNR is superior to that of other biomarkers [9]. However, studies have shown that the log odds of positive lymph nodes (LODDS) demonstrate predictive value superior to other lymph node classification systems in patients undergoing radical resection for pancreatic ductal adenocarcinoma [10]. Due to the rarity of early-stage GSRCC, research has been largely limited to small-sample clinical studies, and there is currently a lack of studies on LODDS in early-stage GSRCC. This study aims to investigate the prognostic value of LODDS for survival in patients with stage I–II GSRCC [according to the comprehensive tumor-node-metastasis (TNM) staging system] and to construct and validate a LODDS-based nomogram, providing a powerful tool for prognosis prediction.

1 Data and Methods

1.1 Data Collection

This study was conducted based on previous research foundations [11]. A total of 680 patients with stage I–II GSRCC from 2013 to 2017 were collected from the Surveillance, Epidemiology, and End Results (SEER) database in the United States as the training set. Simultaneously, 62 patients with stage I–II GSRCC from the Affiliated Yixing Hospital of Jiangsu University (Yixing database) during the same period were collected as the validation set (**Figure 1**). The inclusion criteria were: (1) primary tumor site in the stomach; (2) pathological type of GSRCC; (3) TNM stage I or II. The exclusion criteria were: (1) non-primary malignant tumors; (2) lack of clinicopathological information.

The calculation formula for LODDS was: LODDS = lg [(number of positive lymph nodes+0.5) / (number of lymph nodes resected − number of positive lymph nodes+0.5)]. The clinical information collected included age, gender, T stage, N stage, and chemotherapy status.

1.2 Ethics and Follow-up

The data for the training set were obtained from the SEER database, which is a public database. The data were publicly accessed in 2022 (https://seerdataaccess.cancer.gov/seer-data-access). The data for the validation set were obtained from the Affiliated Yixing Hospital of Jiangsu University, and approval was obtained from the hospital's ethics committee (Approval Number: 2023-140). Informed consent was waived due to the retrospective nature of the data collection. The survival endpoints in this study included cancer-specific survival (CSS) and overall survival (OS). The survival status of patients in the validation set was confirmed through telephone follow-up.

1.3 Statistical Analysis

SPSS 21.0 and R 4.3.1 software packages were used for statistical analysis. The cut-off values for the study variable LODDS were determined using X-tile software (**Figure 2**). Based on the LODDS cut-off values, patients with stage I–II GSRCC in the training set and validation set were divided into three groups: -2.29 to < -1.47 as the low LODDS group, -1.47 to < -0.72 as the medium LODDS group, and -0.72 to 0.70 as the high LODDS group. The χ^2 test was used to analyze the correlation between LODDS and the clinical characteristics of patients with stage I–II GSRCC. The Kaplan-Meier method was used to analyze the predictive effect of LODDS on CSS and OS in patients with stage I–II GSRCC. Cox regression analysis was used to identify independent risk factors for CSS and OS in patients with stage I–II GSRCC. These independent risk factors were then used to construct a nomogram. Receiver operating characteristic (ROC) curves and calibration curves were used for internal and external validation. A P-value <0.05 was considered statistically significant.

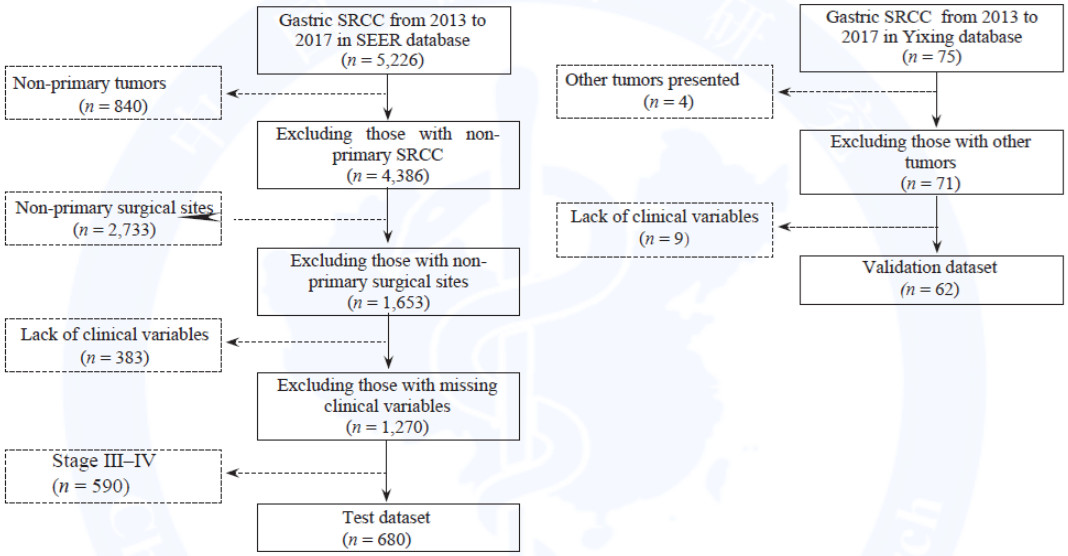
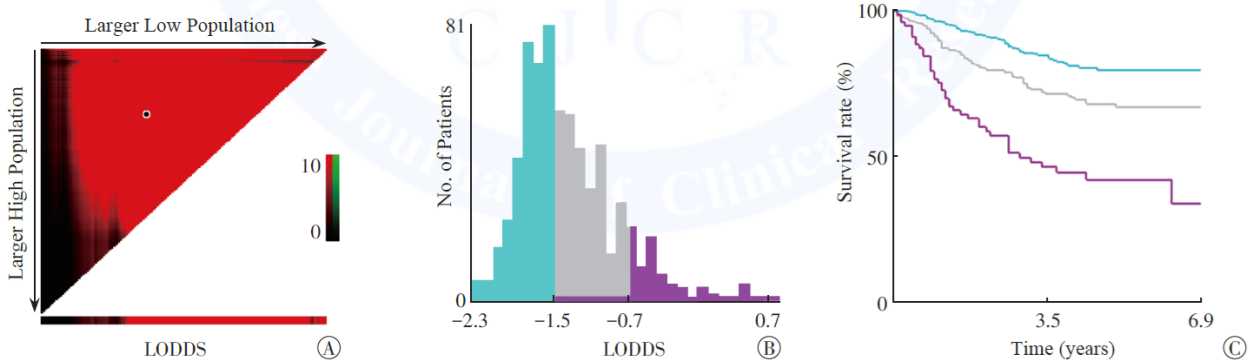


Fig.1 Flowchart of the research process



Grouping	No.	% Total	Events	Rate	Rank	Range
Low LODDS Group	321	47.21	51	15.89	0 to 51	-2.29 thru -1.48
Medium LODDS Group	280	41.18	78	27.86	52 to 104	-1.47 thru -0.73
High LODDS Group	79	11.62	42	53.16	105 to 138	-0.72 thru 0.70
Total	680	100.00	171	25.15	0 to 138	-2.29 thru 0.70

D

Chi-Sq Hi/Mid/Lo	58.9852	Max:61.5347
Lo *vs* Mid	12.3752	
Mid *vs* Hi	21.8614	
Lo *vs* Hi	62.6647	
Relative Risk 1 *vs* 2 *vs* 3	1.00/1.75/3.35	

E

Note: A, Correlation strength; B, Histogram of the optimal cutoff value distribution for LODDS; C, Kaplan Meier survival curve for LODDS optimal cutoff value grouping; D and E, the optimal truncation value of LODDS obtained from X-tile software.

Fig.2 Acquisition of the optimal cut-off value of LODDS

2 Results

2.1 Clinicopathological Characteristics of Patients with Stage I–II Gastric SRCC in Different LODDS Groups

In the training set, patients with stage I–II GSRCC included 321 cases in the low LODDS group, 280 cases in the medium LODDS group, and 79 cases in the high LODDS group. In the validation set, patients with stage I–II GSRCC included 23 cases in the low LODDS group, 33 cases in the medium LODDS group, and 6 cases in the high LODDS group. In the training set, LODDS was correlated with both sex and N stage (P<0.05). In the validation set, LODDS was correlated with N stage and chemotherapy status (P<0.05). See **Table 1**.

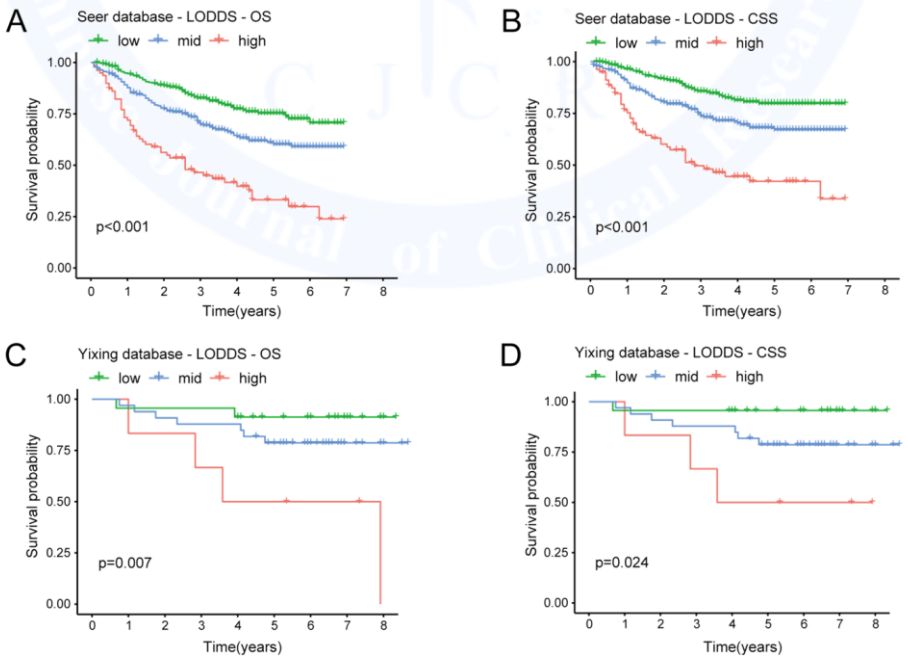
2.2 Survival Prognosis of Patients with Stage I–II GSRCC in Different LODDS Groups

In the training set, the OS of patients in the low LODDS group was superior to that of patients in the medium LODDS group and the high LODDS group (P<0.05) **(Figure 3A)**. Additionally, patients in the high LODDS group had the worst CSS, followed by patients in the medium LODDS group, while patients in the low LODDS group had relatively better CSS (P<0.05) **(Figure 3B)**. A similar phenomenon was observed in the validation set **(Figure 3C, 3D)**.

Tab.1 Association between clinical variables and LODDS in stage I-II GSRCC

Indicators	Testing set					Validation set				
	Low group (n=321)	Mid group (n=280)	High group (n=79)	χ^2 value	P value	Low group (n=23)	Mid group (n=33)	High group (n=6)	χ^2 value	P value
Gender				8.030	0.018				0.081	0.960
Male	142(44.23)	156(55.71)	41(51.89)			14(60.86)	20(60.60)	4(66.66)		
Female	179(55.77)	124(44.29)	38(48.11)			9(39.14)	13(39.40)	2(33.34)		
Age				5.169	0.075				0.196[a]	0.907
≤60 years	171(53.27)	131(46.78)	32(40.50)			9(39.14)	14(42.42)	2(33.34)		
>60 years	150(46.73)	149(53.22)	47(59.50)			14(60.86)	19(57.58)	4(66.66)		
T stage				1.705[b]	0.013				2.033[b]	0.288
T1	119(37.07)	101(36.07)	27(34.17)			17(73.91)	18(54.54)	4(66.66)		
T2	54(16.82)	61(21.78)	22(27.84)			1(4.34)	2(6.06)	1(16.67)		
T3	101(31.46)	97(34.68)	27(34.17)			4(17.41)	13(39.40)	1(16.67)		
T4	47(14.65)	21(7.51)	3(3.82)			1(4.34)	0	0		
N stage				244.672[b]	<0.001				28.767[b]	<0.001
N0	318(99.06)	180(64.28)	18(22.78)			23(100.00)	22(66.66)	0		
N1	3(0.94)	88(31.42)	39(49.36)			0	10(30.30)	2(33.33)		
N2	0	12(4.30)	18(22.78)			0	1(3.04)	2(33.33)		
N3	0	0	4(5.28)			0	0	2(33.34)		
Chemotherapy				3.015	0.221				6.204[a]	0.047
No	139(43.30)	111(39.64)	26(32.91)			12(52.17)	10(30.30)	0		
Yes	182(56.70)	169(60.36)	53(67.09)			11(47.83)	23(69.70)	6(100.00)		

Note: [a] uses Fisher's exact probability method; [b] uses the rank sum test.



Note: A, OS curve in the testing set; B, CSS curve in the testing set; C, OS curve in the validation set; D, CSS curve in the validation set.

Fig.3 Kaplan-Meier survival curves of LODDS

2.3 Independent Risk Factors and Relative Contribution in Patients with Stage I–II GSRCC

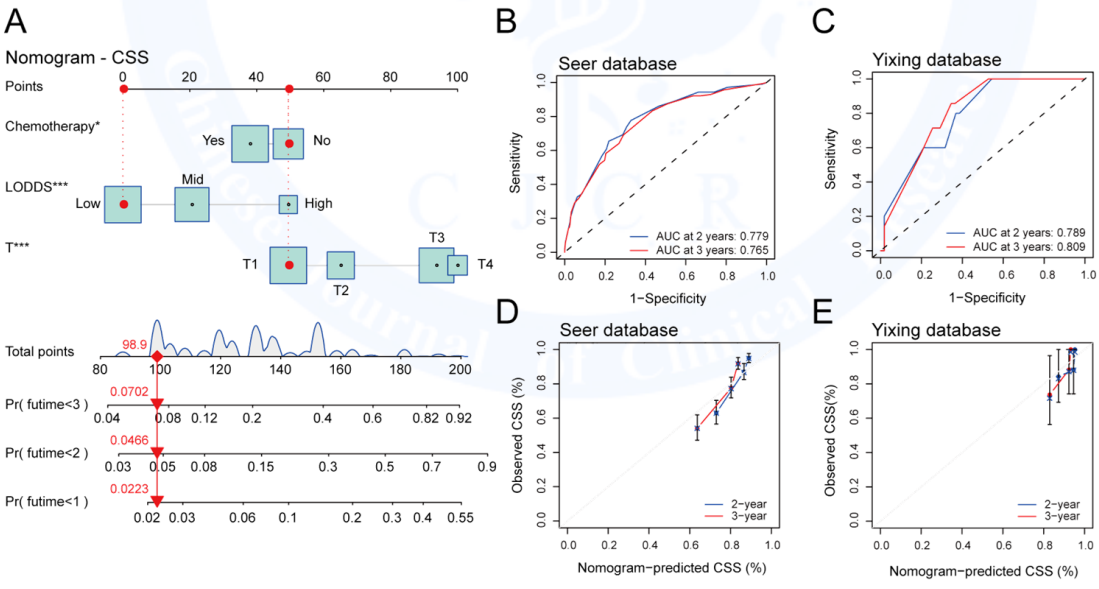
First, univariate Cox regression analysis was performed. Subsequently, significant clinical indicators were further included in multivariate Cox regression analysis, including age, sex, T stage, N stage, chemotherapy status, and LODDS. Multivariate Cox regression analysis showed that higher T stage, undergoing chemotherapy, and high LODDS were independent risk factors for patients with stage I–II GSRCC (P<0.05). See **Table 2, Figure 4A, and Figure 4B**.

2.4 Construction and Validation of a LODDS-Based Nomogram

Independent risk factors were further used to construct a nomogram for predicting CSS, including T stage, chemotherapy status, and LODDS (**Figure 4A**). Internal and external validation were performed. In the internal validation, the area under the curve (AUC) values for 2-year and 3-year CSS were 0.779 and 0.765, respectively. In the external validation, the AUC values for predicting 2-year and 3-year CSS were 0.789 and 0.809, respectively (Figure 4B, 4C). Meanwhile, the calibration curves also demonstrated the good predictive performance of the LODDS-based nomogram (**Figure 4D, 4E**).

Tab.2 Univariate and multivariate Cox analyses of CSS in stage I-II GSRCC

Indicators	Univariate		Multivariate	
	HR(95%*CI*)	*P* value	*HR*(95%*CI*)	*P* value
Age				
⩽60 years	1		1	
>60 years	1.446 (1.067-1.961)	0.017	1.315 (0.964-1.793)	0.084
Gender				
Male	1		1	
Female	0.710 (0.525-0.961)	0.027	0.837 (0.612-1.143)	0.263
T stage				
T1	1	<0.001	1	<0.001
T2	1.546 (0.926-2.580)	0.095	1.819 (1.038-3.188)	0.037
T3	3.645 (2.426-5.477)	<0.001	4.722 (2.862-7.790)	<0.001
T4	3.270 (1.947-5.490)	<0.001	6.428 (3.582-11.533)	<0.001
N stage				
N0	1	<0.001	1	0.173
N1	2.439 (1.759-3.381)	<0.001	1.311 (0.866-1.985)	0.2
N2	1.462 (0.712-3.002)	0.3	1.145 (0.509-2.576)	0.743
N3	3.758 (1.192-11.846)	0.024	3.739 (1.026-13.627)	0.046
Chemotherapy				
No	1		1	
Yes	1.527 (1.104-2.112)	0.011	0.635 (0.436-0.924)	0.018
LODDS				
Low	1	<0.001	1	<0.001
Mid	1.860 (1.307-2.648)	0.001	1.805 (1.221-2.669)	0.003
High	4.475 (2.973-6.736)	<0.001	4.489 (2.703-7.452)	<0.001



Note: A, Nomogram incorporating LODDS; B, ROC curve for internal validation; C, ROC curve for external validation; D, Calibration curve for internal validation; E, Calibration curve for external validation.

Fig.4 Construction and validation of the nomogram for CSS

3 Discussion

In recent years, the incidence of gastric cancer has been increasing year by year [12-13]. Among them, GSRCC is the most malignant subtype of gastric cancer, characterized by typical pathological features where the nucleus is pushed to one side by a large amount of intracellular mucus, resembling a signet ring [14-17].

Signet ring cell gastric cancer is highly aggressive and metastatic. Most patients are already at an advanced stage at the time of diagnosis, losing the opportunity for surgical treatment and having a poor prognosis. Therefore, screening for novel biomarkers for GSRCC is particularly critical, especially for early-stage stage I–II GSRCC. This study collected data from 680 patients with stage I–II GSRCC from the SEER database and 62 patients from the Affiliated Yixing Hospital of Jiangsu University. It was found that LODDS could effectively predict the survival of patients with stage I–II GSRCC. Low LODDS indicated better survival, followed by medium LODDS, while high LODDS indicated poorer survival. Furthermore, the authors constructed a nomogram based on LODDS and performed internal and external validation. The AUC values for 3-year CSS were 0.765 and 0.809 in internal and external validation, respectively. Additionally, the calibration curves indicated that the nomogram had good predictive performance.

Lymph node-related novel biomarkers have been a research hotspot in recent years and have been explored extensively in malignant tumors other than gastric cancer. Łochowski *et al.* [18] found that in patients with N2 stage non-small cell lung cancer, LNR > 0.26 was an independent poor prognostic factor. Ke *et al.* [19] suggested that postoperative patients with non-metastatic cervical cancer and LNR ≤ 10% could benefit from adjuvant radiotherapy to improve survival, while concurrent chemoradiotherapy was recommended for patients with LNR between 10% and 30%. Khomiak et al. [20] discovered in their study on gallbladder cancer that patients with high LNR expression had poorer survival outcomes. Liu et al. [21] collected data from the SEER database and the First Affiliated Hospital of Dalian Medical University and found that age, T stage, and LODDS were associated with the survival of ovarian clear cell carcinoma. Gao *et al*. [22] reported that LODDS is a powerful novel biomarker for predicting survival in patients with small cell lung cancer. In patients with advanced colorectal cancer receiving neoadjuvant therapy, LODDS was also found to predict prognosis [23]. These findings all indicate that lymph node-based classification systems hold certain value in predicting the prognosis of malignant tumors. This study analyzed early-stage GSRCC using the SEER database and data from a Chinese hospital and found that LODDS could serve as an independent prognostic factor for stage I–II GSRCC. Further validation in a prognostic prediction model demonstrated its clinical utility.

Of course, this study also has limitations. The retrospective validation using the SEER database and data from the Affiliated Yixing Hospital of Jiangsu University did not specify the details of chemotherapy drugs or treatment courses, which to some extent affects the study results. Future studies should incorporate multi-center validation to improve the stability of the results. Nevertheless, this study confirms that LODDS has prognostic value for patients with stage I–II GSRCC and is expected to provide new insights for the diagnosis and treatment of this patient population.

Conflict of Interest None

References

[1] Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024[J] CACancer J Clin, 2024, 74(1):12-49.
[2] SmythEC, NilssonM, GrabschHI, etal. Gastric cancer[J]. Lancet, 2020, 396(10251):635-648.
[3] Zong L, Abe M, Seto Y, et al. The challenge of screening for early gastric cancer in China[J]. Lancet, 2016, 388(10060):2606.
[4] Dal Cero M, Bencivenga M, Liu DHW, et al. Clinical features of gastric signet ring cell cancer:results from a systematic review and meta-analysis[J].Cancers, 2023, 15(21):5191.
[5] Wang YK, Li YY, Wang B, et al. Early onset, development and histological features of gastric signet-ring cell carcinoma[J]. Front Oncol, 2023, 13:1166549.
[6] Belkaïd S, Crumbach L, de Bernardi A, et al. Gastric signet-ring cell adenocarcinoma masquerading as sarcoidosis[J]. Lancet Oncol, 2024, 25(4):e173.
[7] Zhuo M, Tian L, Han T, et al. Predictive value of positive lymph node ratio in patients with locally advanced gastric remnant cancer [J]. World J Gastrointest Oncol, 2024, 16(3):833-843.
[8] Liu W, WuHY, Lin JX, et al. Combining lymph node ratio to develop prognostic models for postoperative gastric neuroendocrine neoplasm patients[J]. World J Gastrointest Oncol, 2024, 16(8): 3507-3520.
[9] Chen S, Ding PA, Zhao Q. Comparison of the predictive performance of three lymph node staging systems for late-onset gastric cancer patients after surgery[J]. Front Surg, 2024, 11:1376702.
[10] Prassas D, Safi SA, Stylianidi MC, et al. N, LNR or LODDS: which is the most appropriate lymph node classification scheme for patients with radically resected pancreatic cancer?[J]. Cancers, 2022, 14(7):1834.
[11] Wang CZ, Fang Y, Zhang YH, et al. A LODDS-based nomogram for overall and cancer-specific survival in stage III-IV gastric signet ring cell carcinoma[J].Front Mol Biosci, 2025, 12:1600626.
[12] Liou JM, Malfertheiner P, Smith SI, et al. 40 years after the discovery of Helicobacter pylori:towards elimination of H pylori for gastric cancer prevention[J].Lancet, 2024, 403(10444):2570-2572.
[13] Joshi SS, Badgwell BD. Current treatment and recent progress in gastric cancer[J].CA Cancer J Clin, 2021, 71(3):264-279.
[14] Yin MY, Zhang RF, Lin JX, et al. Identification of gastric signet ring cell carcinoma based on endoscopic images using few shot learning[J]. Dig Liver Dis, 2023, 55(12):1725-1734.
[15] Roncati L, Manenti A, Barbolini G, et al. Deep inside of gastric signet-ring cell carcinoma[J].Neoplasma, 2018, 65(4):579-584.
[16] Li Y, Zhu ZK, Ma FH, et al. Gastric signet ring cell carcinoma: current management and future challenges[J]. Cancer Manag Res, 2020, 12:7973-7981.
[17] Machlowska J, Pucułek M, Sitarz M, et al. State of the art for gastric signet ring cell carcinoma:from classification, prognosis, and genomic characteristics to specified treatments[J]. Cancer Manag Res, 2019, 11:2151-2161.
[18] Łochowski MP, Chałubińska Fendler J, Szlachcińska A, et al. Prognostic value of lymph node ratio(LNR)in patients with postoperative N2 feature in non-small cell lung cancer(NSCLC)[J]. J Clin Med, 2024, 13(15):4570.
[19] Ke YY, Zhang ZJ, Li YC, et al. Prognostic value of lymph node ratio in patients with non-metastatic cervical cancer treated with radical hysterectomy:a population-based study[J]. Eur J Surg Oncol, 2024, 50(4):108258.
[20] Khomiak A, Ghaffar SA, Rodriguez Franco S, et al. The impact of lymph node ratio on survival in gallbladder cancer:a national cancer database analysis[J].Hpb, 2024, 26(12):1544-1552.
[21] Liu ZS, Jing CL, Hooblal YM, et al. Construction and validation of log odds of positive lymph nodes (LODDS)-based nomograms for predicting overall survival and cancer-specific survival in ovarian clear cell carcinoma patients[J]. Front Oncol, 2024, 14:1370272.
[22] Gao T, Chang YX, Yue HM. Association of log odds of positive lymph nodes with survival in patients with small cell lung cancer: results from the SEER database[J]. Clinics, 2024, 79:100369.
[23] Han Z, Yang H, Qiao Q, Wu T, et al. The survival prediction of advanced colorectal cancer received neoadjuvant therapy-a study of SEER database[J]. World J Surg Oncol, 2024, 22(1):175.

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基于阳性淋巴结对数比的Ⅰ~Ⅱ期胃印戒细胞癌预后列线图预测模型的构建及验证

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摘要：目的 探讨阳性淋巴结对数比（LODDS）对Ⅰ~Ⅱ期胃印戒细胞癌患者生存预后的预测价值，并构建基于LODDS的列线图并进行验证。**方法** 回顾性收集2013年至2017年680例美国监测、流行病学和最终结果（SEER）数据库、62例江苏大学附属宜兴市人民医院Ⅰ~Ⅱ期胃印戒细胞癌患者的临床资料，分别作为试验集和验证集。应用X-tile软件获取LODDS的最佳截断值。应用Kaplan-Meier法分析LODDS的生存曲线，应用受试者工作特征（ROC）曲线分析LODDS对生存的预测作用，应用Cox回归分析Ⅰ~Ⅱ期胃印戒细胞癌患者预后的独立危险因素，并构建、验证基于LODDS的列线图。**结果** LODDS在试验集中与患者性别、N分期相关（$P<0.05$），LODDS在验证集中与N分期、化疗状态相关（$P<0.05$）；在试验、验证集中，低LODDS组患者的总生存率（OS）、癌症特异性生存率（CSS）最佳，中LODDS组患者次之，高LODDS组患者则最差（$P<0.05$）。T分期高、不接受化疗及高LODDS分别为Ⅰ~Ⅱ期胃印戒细胞癌患者的独立危险因素（$P<0.05$）。基于LODDS进一步构建列线图，其预测3年CSS的曲线下面积（AUC）在内部、外部验证中分别为0.765、0.809。此外，校正曲线也提示该列线图具有较好的预测效应。**结论** 高LODDS为Ⅰ~Ⅱ期胃印戒细胞癌患者的独立危险因素，基于LODDS的列线图具有较好的生存预测价值。

关键词： 胃肿瘤；印戒细胞癌；胃癌，Ⅰ~Ⅱ期；阳性淋巴结对数比；列线图；T分期；预后
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Construction and validation of LODDS-based nomogram for prognosis of stage Ⅰ－Ⅱ gastric signet ring cell carcinoma

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Abstract: Objective To explore the predictive value of log odds of positive lymph nodes (LODDS) for survival outcomes in stage Ⅰ－Ⅱ gastric signet ring cell carcinoma patients, thus constructing and verifying a LODDS-based nomogram. **Methods** Clinical data of 680 cases from the Surveillance, Epidemiology, and End Results (SEER) Program and 62 patients with stage Ⅰ－Ⅱ gastric signet ring cell carcinoma from Yixing People's Hospital Affiliated to Jiangsu University were retrospectively collected from 2013 to 2017 as the training set and validation set, respectively. The X-tile software was applied to identify best cut off values of LODDS. The Kaplan-Meier method was applied to plot survival curves according to LODDS categories, and the prognostic performance of LODDS was evaluated by receiver operating characteristic (ROC) curve analysis. The Cox regression analysis was used to identify independent risk factors for prognosis of stage Ⅰ－Ⅱ gastric signet ring cell carcinoma patients, which were further used to establish a LODDS-

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QR code for English version

based nomogram. **Results**　LODDS was associated with gender and N stage in training set (P<0.05), while LODDS was related with N stage and chemotherapy status in validation set (P<0.05). According to overall survival (OS) and cancer specific survival (CSS) in both training and validation sets, low LODDS group had the best survival outcomes, followed by the medium LODDS group, while high LODDS group had the worst survival outcomes (P<0.05). Additionally, high T stage, not receiving chemotherapy and high LODDS were independent risk factors for prognosis of stage Ⅰ-Ⅱ gastric signet ring cell carcinoma patients. The LODDS-based nomogram was further constructed, and the area under the curve (AUC) for predicting 3-year CSS was 0.765 and 0.809 in internal and external validation, respectively. Meanwhile, calibration curve showed the good predictive value of this nomogram. **Conclusion**　High LODDS can be served as an independent risk factor in stage Ⅰ-Ⅱ gastric signet ring cell carcinoma patients. The LODDS-based nomogram shows good predictive values for survival of these patients.

Keywords: Gastric tumor; Signet ring cell carcinoma; Gastric cancer, stage Ⅰ-Ⅱ; Log odds of positive lymph nodes; Nomogram; T stage; Prognosis

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胃癌具有较高的发病率及死亡率[1-3]，胃印戒细胞癌约占胃癌的9.9%，好发于青年女性，大部分胃印戒细胞癌患者初诊时即伴随转移，预后较差[4-6]。淋巴结转移是其早期转移的典型特征。近年来，越来越多的研究侧重于探索淋巴结转移相关的新型生物标志物，而淋巴结阳性率（positive lymph node ratio，LNR）是影响胃癌生存的独立预后因素[7]，且LNR越高死亡风险越大[8]，LNR的生存预测价值优于其他标志物[9]。但有研究显示，阳性淋巴结对数比（log odds of positive lymph nodes，LODDS），在根治性切除的胰腺导管腺癌中展现出优于其他淋巴结分类系统的预测价值[10]。由于早期胃印戒细胞癌的罕见性，研究多局限于小样本临床研究，目前尚缺乏关于LODDS在早期胃印戒细胞癌中的研究。本研究旨在探讨LODDS对TNM综合分期Ⅰ~Ⅱ期胃印戒细胞癌患者生存预后的预测价值，并构建、验证基于LODDS的列线图，以期为预后预测提供有力工具。

1　资料与方法

1.1　*数据收集*　本研究基于前期研究基础开展[11]。收集美国监测、流行病学和最终结果（Surveillance, Epidemiology, and End Results，SEER）数据库中2013年至2017年的Ⅰ~Ⅱ期胃印戒细胞癌患者680例作为试验集，收集同期江苏大学附属宜兴市人民医院（宜兴数据库）的Ⅰ~Ⅱ期胃印戒细胞癌患者62例作为验证集（图1）。纳入标准为：（1）原发部位为胃；（2）病理类型为胃印戒细胞癌；（3）TNM分期为Ⅰ

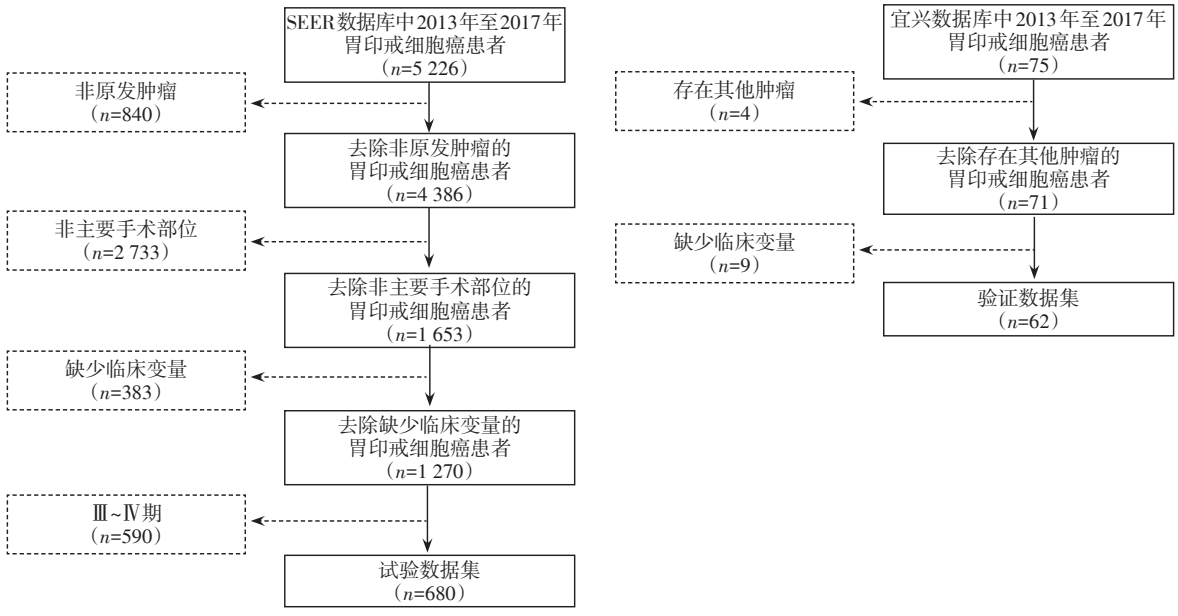


图1　研究流程图

Fig.1　Flowchart of the research process

期或Ⅱ期。排除标准为：(1) 非原发性恶性肿瘤；(2) 临床病理信息缺乏。LODDS的计算公式：LODDS=lg[(阳性淋巴结个数+0.5)/(切除淋巴结个数−阳性淋巴结个数+0.5)]。本研究收集的临床信息包括：年龄、性别、T分期、N分期、化疗状态。

1.2　伦理及随访　试验集的数据来自SEER数据库，SEER数据库为公共数据库，其数据为2022年公开获取（https://seerdataaccess.cancer.gov/seer-data-access）。验证集的数据来自江苏大学附属宜兴市人民医院，已获得医院伦理委员会的批准（批准文号：2023-140），回顾性收集已免除知情同意书。本研究的生存终点为癌症特异性生存率（cancer specific survival，CSS）及总生存率（overall survival，OS）。验证集患者的生存状态通过电话随访确认。

1.3　统计学方法　采用SPSS 21.0及R 4.3.1软件包分析数据。依据X-tile软件获取研究变量LODDS的截断值（图2）。依据LODDS的截断值，将试验集及验证集的Ⅰ～Ⅱ期胃印戒细胞癌患者分为3组：−2.29~<−1.47为低LODDS组，−1.47~<−0.72为中LODDS组，−0.72~0.70为高LODDS组。应用χ^2检验、Fisher确切概率法及秩和检验分析LODDS与Ⅰ～Ⅱ期胃印戒细胞癌患者临床特征的相关性；采用Kaplan-Meier法分析不同LODDS组胃印戒细胞癌患者的CSS和OS；利用Cox回归分析Ⅰ～Ⅱ期胃印戒细胞癌患者CSS、OS的独立危险因素，并将其独立危险因素绘制成列线图，采用受试者工作特征（receiver operating characteristic，ROC）曲线及校正曲线进行内部及外部验证。P<0.05为差异有统计学意义。

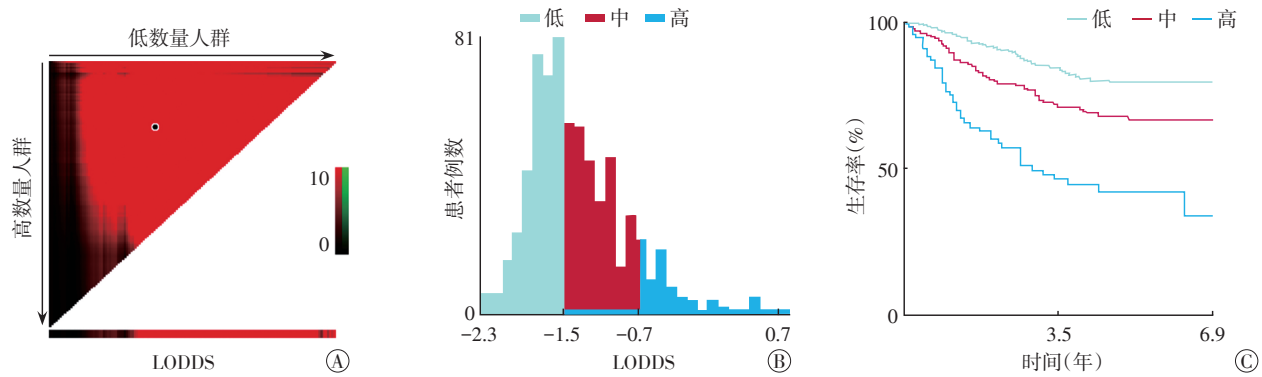
2　结　果

2.1　不同LODDS组Ⅰ～Ⅱ期胃印戒细胞癌患者的临床病理特征　试验集的Ⅰ～Ⅱ期胃印戒细胞癌患者包括321例低LODDS组，280例中LODDS组，79例高LODDS组；验证集的Ⅰ～Ⅱ期胃印戒细胞癌患者包括23例低LODDS组，33例中LODDS组，6例高LODDS组。在试验集中，LODDS与性别、N分期均相关（P<0.05）；在验证集中，LODDS与N分期、化疗状态相关（P<0.05）。见表1。

2.2　不同LODDS组Ⅰ～Ⅱ期胃印戒细胞癌患者的生存预后　在试验集中，低LODDS组患者的OS优于中LODDS组和高LODDS组（P<0.05）（图3A）。同时，高LODDS组患者有最差的CSS，其次为中LODDS组患者，低LODDS组患者CSS相对较好（P<0.05）（图3B）。在验证集中显现出类似现象（图3C、3D）。

2.3　Ⅰ～Ⅱ期胃印戒细胞癌患者的独立危险因素及相对贡献度　首先进行Cox单因素回归分析，然后将有意义的临床指标进一步纳入Cox多因素回归分析，包括年龄、性别、T分期、N分期、化疗状态及LODDS。多因素Cox回归分析显示，T分期高、不进行化疗及高LODDS分别为Ⅰ～Ⅱ期胃印戒细胞癌患者的独立危险因素（P<0.05）。见表2。

2.4　基于LODDS的列线图构建及验证　进一步将



组别	数量	占比%	发生数	发生率	等级	范围
低LODDS组	321	47.20	51	15.89	0 to 51	−2.29~<−1.47
中LODDS组	280	41.18	78	27.86	52 to 104	−1.47~<−0.72
高LODDS组	79	11.62	42	53.16	105 to 138	−0.72~0.70
总计	680	100.00	171	25.15	0 to 138	−2.29~0.70

Ⓓ

卡方 高/中/低	58.9852	最大值：61.5347
低 *vs* 中	12.3752	
中 *vs* 高	21.8614	
低 *vs* 高	62.6647	
相对风险 1 *vs* 2 *vs* 3	1.00/1.75/3.35	

Ⓔ

注：A，相关性强度；B，LODDS最佳截断值分布的直方图；C，LODDS最佳截断值分组的Kaplan-Meier生存曲线；D、E，X-tile软件获取LODDS的最佳截断值。

图2　LODDS最佳截断值的获取

Fig.2　Acquisition of the optimal cut-off value of LODDS

表 1　Ⅰ~Ⅱ期胃印戒细胞癌临床变量与LODDS之间的关联

Tab.1　Association between clinical variables and LODDS in stage Ⅰ-Ⅱ gastric signet ring cell carcinoma

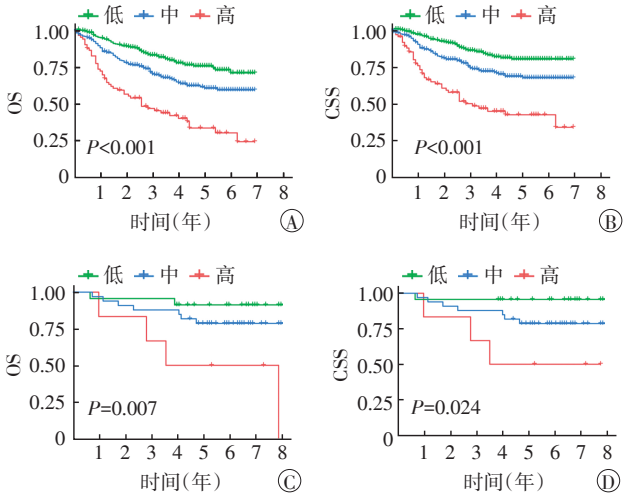
项目	试验集					验证集				
	低LODDS组(*n*=321)	中LODDS组(*n*=280)	高LODDS组(*n*=79)	χ^2值	*P*值	低LODDS组(*n*=23)	中LODDS组(*n*=33)	高LODD组(*n*=6)	χ^2值	*P*值
性别										
男	142(44.23)	156(55.71)	41(51.89)	8.030	0.018	14(60.86)	20(60.60)	4(66.66)	0.081	0.960
女	179(55.77)	124(44.29)	38(48.11)			9(39.14)	13(39.40)	2(33.34)		
年龄										
≤60岁	171(53.27)	131(46.78)	32(40.50)	5.169	0.075	9(39.14)	14(42.42)	2(33.34)	0.196[a]	0.907
>60岁	150(46.73)	149(53.22)	47(59.50)			14(60.86)	19(57.58)	4(66.66)		
T分期										
T1	119(37.07)	101(36.07)	27(34.17)	1.705[b]	0.426	17(73.91)	18(54.54)	4(66.66)	2.033[b]	0.362
T2	54(16.82)	61(21.78)	22(27.84)			1(4.34)	2(6.06)	1(16.67)		
T3	101(31.46)	97(34.68)	27(34.17)			4(17.41)	13(39.40)	1(16.67)		
T4	47(14.65)	21(7.51)	3(3.82)			1(4.34)	0	0		
N分期										
N0	318(99.06)	180(64.28)	18(22.78)	244.672[b]	<0.001	23(100.00)	22(66.66)	0	28.767[b]	<0.001
N1	3(0.94)	88(31.42)	39(49.36)			0	10(30.30)	2(33.33)		
N2	0	12(4.30)	18(22.78)			0	1(3.04)	2(33.33)		
N3	0	0	4(5.28)			0	0	2(33.34)		
化疗										
否	139(43.30)	111(39.64)	26(32.91)	3.015	0.221	12(52.17)	10(30.30)	0	6.204[a]	0.047
是	182(56.70)	169(60.36)	53(67.09)			11(47.83)	23(69.70)	6(100.00)		

注：[a]为采用Fisher确切概率法；[b]为采用秩和检验。

表 2　Ⅰ~Ⅱ期胃印戒细胞癌中CSS的单因素和多因素Cox分析

Tab.2　Univariate and multivariate Cox analyses of CSS in stage Ⅰ-Ⅱ gastric signet ring cell carcinoma

项目	单因素		多因素	
	HR(95%*CI*)	*P*值	*HR*(95%*CI*)	*P*值
年龄				
≤60岁	1		1	
>60岁	1.446(1.067~1.961)	0.017	1.315(0.964~1.793)	0.084
性别				
男	1		1	
女	0.710(0.525~0.961)	0.027	0.837(0.612~1.143)	0.263
T分期				
T1	1		1	
T2	1.546(0.926~2.580)	0.095	1.819(1.038~3.188)	0.037
T3	3.645(2.426~5.477)	<0.001	4.722(2.862~7.790)	<0.001
T4	3.270(1.947~5.490)	<0.001	6.428(3.582~11.533)	<0.001
N分期				
N0	1		1	
N1	2.439(1.759~3.381)	<0.001	1.311(0.866~1.985)	0.200
N2	1.462(0.712~3.002)	0.300	1.145(0.509~2.576)	0.743
N3	3.758(1.192~11.846)	0.024	3.739(1.026~13.627)	0.046
化疗				
否	1		1	
是	0.655(0.474~0.906)	0.011	0.635(0.436~0.924)	0.018
LODDS				
低	1		1	
中	1.860(1.307~2.648)	0.001	1.805(1.221~2.669)	0.003
高	4.475(2.973~6.736)	<0.001	4.489(2.703~7.452)	<0.001

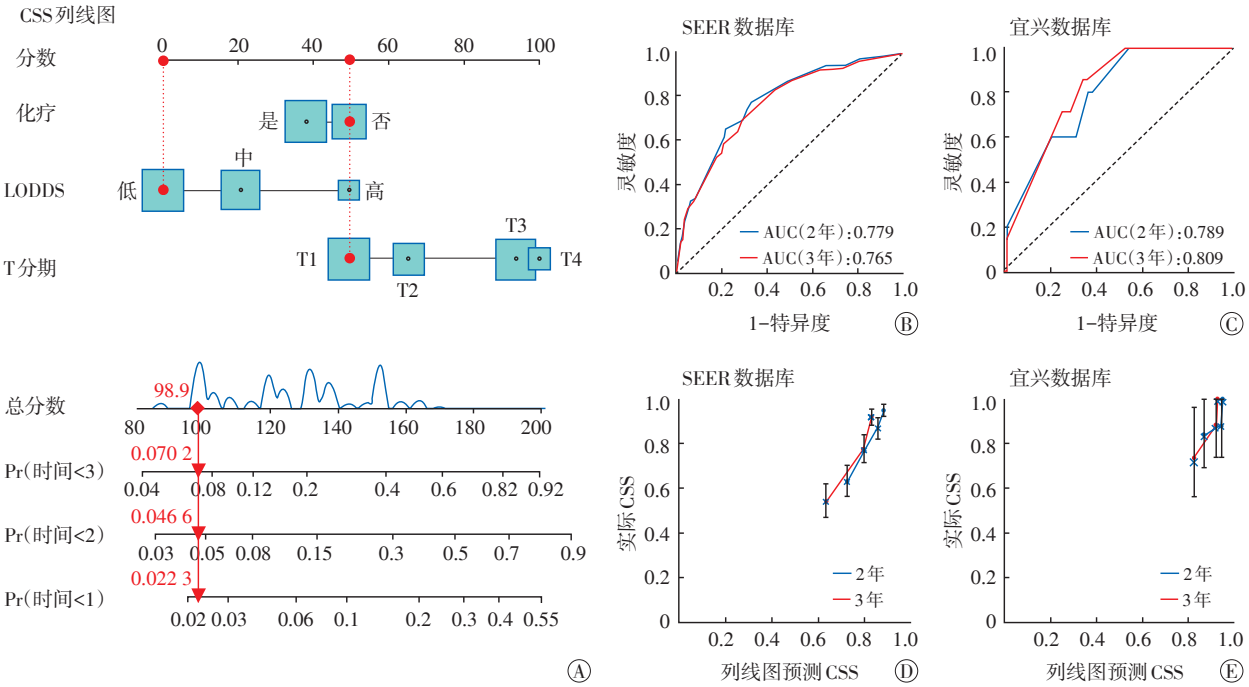


注：A，试验集中LODDS的OS曲线；B，试验集中LODDS的CSS曲线；C，验证集中LODDS的OS曲线；D，验证集中LODDS的CSS曲线。

图 3　LODDS的Kaplan-Meier生存曲线

Fig.3　Kaplan-Meier survival curves of LODDS

独立危险因素构建CSS预测列线图，包括T分期、化疗状态及LODDS（图4A）。并进行内部及外部验证。在内部验证中，2年、3年CSS的曲线下面积（area under the curve，AUC）值为0.779、0.765；在外部验证中，预测2年、3年CSS的AUC值为0.789、0.809（图4B、图C）。同时，校正曲线也显示基于LODDS的列线图有较好的预测效能（图4D、图4E）。



注：A，基于LODDS的列线图；B，内部验证的ROC曲线；C，外部验证的ROC曲线；D，内部验证的校正曲线；E，外部验证的校正曲线。

图4　CSS预测列线图的构建及验证

Fig.4　Construction and validation of the nomogram for CSS

3　讨　论

近年来，胃癌的发病率逐年增加[12-13]。其中，胃印戒细胞癌是胃癌恶性程度最高的亚型，具有典型的病理特征，其细胞核因细胞内大量的黏液而被挤压至一侧，形似戒指[14-17]。胃印戒细胞癌具有高度侵袭性和转移性，大部分患者确诊时已处于较晚的分期，丧失手术治疗的机会，预后欠佳，因而筛选胃印戒细胞癌的新型标志物尤为关键，尤其对处于较早期的Ⅰ~Ⅱ期胃印戒细胞癌。本研究分别收集680例SEER数据库、62例江苏大学附属宜兴市人民医院的Ⅰ~Ⅱ期胃印戒细胞癌患者，发现LODDS可较好预测Ⅰ~Ⅱ期胃印戒细胞癌患者的生存，低LODDS预示着较好的生存，中LODDS次之，高LODDS则预示着较差的生存。此外，作者构建了基于LODDS的列线图，进行内部及外部验证。3年CSS的AUC值在内部、外部验证中分别为0.765、0.809，并且，校正曲线也提示该列线图具有较好的预测效应。

淋巴结相关的新型生物标志物是近年来的研究热点，其在胃癌之外的其他恶性肿瘤中也有较广泛的探索。Łochowski等[18]研究发现，N2期非小细胞肺癌患者中，LNR>0.26是不良的独立预后因素。Ke等[19]认为，LNR≤10%的非转移性宫颈癌术后患者接受辅助放疗可改善生存，而LNR介于10%~30%的患者则推荐同步放化疗。Khomiak等[20]在关于胆囊癌的研究中发现，LNR高表达的患者有较差的生存预后。Liu等[21]收集了SEER数据库及大连医科大学第一附属医院的资料，发现年龄、T分期、LODDS与卵巢透明细胞癌的生存相关联。Gao等[22]报道LODDS是预测小细胞肺癌患者生存的有力新型生物标志物。在接受新辅助治疗的晚期结直肠癌患者中，也发现LODDS可预测预后[23]。这些均表明，基于淋巴结的分类系统在恶性肿瘤的预后预测方面具有一定的价值。本研究利用SEER数据库和中国医院数据分析早期胃印戒细胞癌，发现LODDS可作为Ⅰ~Ⅱ期胃印戒细胞癌独立的预后因素，在预后预测模型中，进一步验证显示其临床实用性。

当然，本研究亦存在不足之处。SEER数据库和江苏大学附属宜兴市人民医院回顾性验证未明细具体化疗药物以及疗程，这在一定程度上影响研究结果，未来需要增加多中心验证，以改善结果的稳定性。尽管如此，本研究证实LODDS对Ⅰ~Ⅱ期胃印戒细胞癌患者具有预后预测价值，有望为这类群体患者的诊治提供新的思路。

利益冲突　无

参考文献

[1]　Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024[J].

CA Cancer J Clin, 2024, 74(1): 12-49.
[2] Smyth EC, Nilsson M, Grabsch HI, et al. Gastric cancer[J]. Lancet, 2020, 396(10251): 635-648.
[3] Zong L, Abe M, Seto Y, et al. The challenge of screening for early gastric cancer in China[J]. Lancet, 2016, 388(10060): 2606.
[4] Dal Cero M, Bencivenga M, Liu DHW, et al. Clinical features of gastric signet ring cell cancer: results from a systematic review and meta-analysis[J]. Cancers, 2023, 15(21): 5191.
[5] Wang YK, Li YY, Wang B, et al. Early onset, development and histological features of gastric signet-ring cell carcinoma[J]. Front Oncol, 2023, 13: 1166549.
[6] Belkaïd S, Crumbach L, de Bernardi A, et al. Gastric signet-ring cell adenocarcinoma masquerading as sarcoidosis[J]. Lancet Oncol, 2024, 25(4): e173.
[7] Zhuo M, Tian L, Han T, et al. Predictive value of positive lymph node ratio in patients with locally advanced gastric remnant cancer [J]. World J Gastrointest Oncol, 2024, 16(3): 833-843.
[8] Liu W, Wu HY, Lin JX, et al. Combining lymph node ratio to develop prognostic models for postoperative gastric neuroendocrine neoplasm patients[J]. World J Gastrointest Oncol, 2024, 16(8): 3507-3520.
[9] Chen S, Ding PA, Zhao Q. Comparison of the predictive performance of three lymph node staging systems for late-onset gastric cancer patients after surgery[J]. Front Surg, 2024, 11: 1376702.
[10] Prassas D, Safi SA, Stylianidi MC, et al. N, LNR or LODDS: which is the most appropriate lymph node classification scheme for patients with radically resected pancreatic cancer?[J]. Cancers, 2022, 14(7): 1834.
[11] Wang CZ, Fang Y, Zhang YH, et al. A LODDS-based nomogram for overall and cancer-specific survival in stage Ⅲ-Ⅳ gastric signet ring cell carcinoma[J]. Front Mol Biosci, 2025, 12: 1600626.
[12] Liou JM, Malfertheiner P, Smith SI, et al. 40 years after the discovery of *Helicobacter pylori*: towards elimination of *H pylori* for gastric cancer prevention[J]. Lancet, 2024, 403(10444): 2570-2572.
[13] Joshi SS, Badgwell BD. Current treatment and recent progress in gastric cancer[J]. CA Cancer J Clin, 2021, 71(3): 264-279.
[14] Yin MY, Zhang RF, Lin JX, et al. Identification of gastric signet ring cell carcinoma based on endoscopic images using few-shot learning[J]. Dig Liver Dis, 2023, 55(12): 1725-1734.
[15] Roncati L, Manenti A, Barbolini G, et al. Deep inside of gastric signet-ring cell carcinoma[J]. Neoplasma, 2018, 65(4): 579-584.
[16] Li Y, Zhu ZK, Ma FH, et al. Gastric signet ring cell carcinoma: current management and future challenges[J]. Cancer Manag Res, 2020, 12: 7973-7981.
[17] Machlowska J, Pucułek M, Sitarz M, et al. State of the art for gastric signet ring cell carcinoma: from classification, prognosis, and genomic characteristics to specified treatments[J]. Cancer Manag Res, 2019, 11: 2151-2161.
[18] Łochowski MP, Chałubińska-Fendler J, Szlachcińska A, et al. Prognostic value of lymph node ratio (LNR) in patients with postoperative N2 feature in non-small cell lung cancer (NSCLC)[J]. J Clin Med, 2024, 13(15): 4570.
[19] Ke YY, Zhang ZJ, Li YC, et al. Prognostic value of lymph node ratio in patients with non-metastatic cervical cancer treated with radical hysterectomy: a population-based study[J]. Eur J Surg Oncol, 2024, 50(4): 108258.
[20] Khomiak A, Ghaffar SA, Rodriguez Franco S, et al. The impact of lymph node ratio on survival in gallbladder cancer: a national cancer database analysis[J]. HPB(Oxford), 2024, 26(12): 1544-1552.
[21] Liu ZS, Jing CL, Hooblal YM, et al. Construction and validation of log odds of positive lymph nodes (LODDS)-based nomograms for predicting overall survival and cancer-specific survival in ovarian clear cell carcinoma patients[J]. Front Oncol, 2024, 14: 1370272.
[22] Gao T, Chang YX, Yue HM. Association of log odds of positive lymph nodes with survival in patients with small cell lung cancer: results from the SEER database[J]. Clinics, 2024, 79: 100369.
[23] Han Z, Yang H, Qiao Q, Wu T, et al. The survival prediction of advanced colorectal cancer received neoadjuvant therapy-a study of SEER database[J]. World J Surg Oncol, 2024, 22(1): 175.

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