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Retrospective Study

Evaluating log odds of positive lymph nodes as a prognostic tool in differentiated gastric cancer: A retrospective study

Deng MC *et al.* LODDS in GC prognosis

Abstract

BACKGROUND

The log odds of positive lymph nodes (LODDS) are correlated with survival outcomes in gastric cancer (GC) patients. However, its prognostic value across different tumor differentiation levels remains unclear.

AIM

To evaluate the independent prognostic value of LODDS and its stratified predictive efficacy in GC patients with different histologic differentiations.

METHODS

We conducted a retrospective analysis of 2103 GC patients who underwent radical gastrectomy at Zhejiang Cancer Hospital. The prognostic value of the LODDS was compared with that of other lymph node-based metrics, including the pathologic N stage, number of positive lymph nodes, number of total lymph nodes, and lymph node ratio, stratified by tumor differentiation.

RESULTS

LODDS was identified as an independent prognostic factor for overall survival in moderately to poorly differentiated GC patients. LODDS demonstrated superior

predictive accuracy over the other lymph node metrics. A nomogram incorporating LODDS, age, carbohydrate antigen (CA) 125, carcinoembryonic antigen, and tumor differentiation showed good predictive accuracy (C-index = 0.703). A higher LODDS was significantly associated with an increased risk of recurrence or metastasis, poorly differentiated tumors, advanced cancer, mucinous gastric adenocarcinoma, nerve invasion, and vascular tumor thrombus. Additionally, LODDS was positively correlated with the tumor markers CA19-9, CA72-4, CA125, and CA242 (all $P < 0.05$).

CONCLUSION

LODDS is an independent prognostic indicator for patients with moderately and poorly differentiated GC, and its predictive performance is superior to that of other models.

Key Words: Gastric cancer; Log odds of positive lymph nodes; Tumor differentiation; Tumor marker; Overall survival

Deng MC, Chen K, Bao QM, Huang YX, Zhang CK, Zhong YK, He HY, Zu D, Liang C, Liu HD, Hu YC, Liu GX, He YH, Wu WX, Zhou JN, Teng YS, Jing J, Shi Y, Chung CYS, Yu CH, Du YA, Ye Z, Dong CX. Evaluating log odds of positive lymph nodes as a prognostic tool in differentiated gastric cancer: A retrospective study. *World J Gastroenterol* 2025; In press

Core Tip: This study highlights the log odds of positive lymph nodes (LODDS) as a reliable independent prognostic tool for moderately and poorly differentiated gastric cancer, providing more precise risk stratification than traditional systems such as pathologic N stage. Patients with higher LODDS values, which are associated with more aggressive tumor behavior, may benefit from more frequent follow-ups and intensified treatments. The incorporation of the LODDS into a clinical nomogram is expected to improve individualized survival prediction and the development of therapeutic strategies.

INTRODUCTION

Cancer is one of the most challenging diseases worldwide, with its development governed by a complex interplay of factors. These include intrinsic factors[1-6], such as genetic mutations, genomic instability, and the activation of oncogenes, as well as extrinsic factors[7-12], such as chronic inflammation induced by external stimuli and immune system dysregulation, which collectively contribute to the progression from inflammation to malignancy. ³ Gastric cancer (GC) is the fifth most common cancer worldwide and the third leading cause of cancer-related mortality, following lung and liver cancer[13,14]. According to the GLOBOCAN global cancer burden report, GC causes more than 780000 deaths annually, with its mortality rate remaining high worldwide, especially among patients with advanced disease accompanied by lymph node metastasis, who generally have a poor prognosis[15-17]. In clinical practice, lymph nodes are a primary route of metastasis for GC[18-20]. Cancer cells spread through the lymphatic system to nearby lymph nodes and may subsequently metastasize to distant lymph nodes or other organs[21-25].

Lymph node metastasis not only reflects the invasiveness and spreading capability of tumor cells but also typically signifies that cancer has progressed to a locally advanced stage[26-28]. Postoperatively, the number and distribution of metastatic lymph nodes directly influence patient survival rates and recurrence risk, and the extent of lymph node metastasis can further inform the staging of GC and potential treatment response[29,30]. Currently, prognosis assessment for GC patients relies primarily on ¹ the 8th edition of the American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) staging system[31-33]. Pathologic N stage in this system is determined on the basis of pathologic examination of the lymph nodes removed during surgery, and in particular, the number of metastatic lymph nodes is evaluated to assess the extent of disease progression[34-36]. However, this system does not account for ratio-based lymph node classification, which may provide more precise prognostic insights and better guide personalized treatment strategies.

The grade of tumor differentiation plays a crucial role in GC prognosis[37-39]. Tumor differentiation refers to the degree of similarity between tumor cells and normal tissue cells and reflects the level of maturation of tumor cells in terms of morphology, structure, and function[40-43]. Poorly differentiated tumors often exhibit higher cellular heterogeneity and invasiveness, which are closely associated with poorer prognosis and a higher risk of recurrence[44-47]. However, studies have shown that in patients with limited lymph node dissection or substantial variation in tumor differentiation, the American Joint Committee on Cancer pathologic N stage (pN) staging system may fail to accurately reflect individual prognosis, particularly in patients with poorly differentiated and highly invasive tumors[48-50]. Moreover, existing staging systems and prognostic models are often based on the overall GC population and inadequately address the specific impact of tumor differentiation, leading to potential bias in prognostic stratification for patients with moderate to poorly differentiated tumors[51-53]. Therefore, developing tools that can better reflect the true prognosis of such patients is highly important.

In recent years, the ⁶ **log odds of positive lymph nodes (LODDS) - a ratio-based lymph node staging system** - has gained attention. By integrating the ratio of positive to negative lymph nodes, LODDS has the potential to overcome the limitations of the traditional pN staging system, which solely depends on the number of positive lymph node. Additionally, the LODDS has demonstrated superior prognostic performance, especially in patients with inadequate lymph node dissection[54,55]. Studies across various cancer types have shown the prognostic accuracy of LODDS, which outperforms traditional pN staging in esophageal and colorectal cancers[56,57]. Although the LODDS has been applied in some GC studies, its effectiveness in the context of moderately to poorly differentiated GC remains unclear. This subgroup exhibits unique biological behaviors and a relatively higher recurrence risk, making it crucial to explore tailored staging and prognostic tools for this patient population.

This large-scale retrospective analysis aimed to systematically evaluate the prognostic value and potential applications of the LODDS in patients with moderately to poorly

differentiated GC. Additionally, we comprehensively compared the prognostic performance of the pN, number of positive lymph nodes (NPLN), lymph node ratio (LNR), number of total lymph nodes (NTLN), and LODDS systems, identifying a more accurate staging system for predicting survival outcomes in GC patients. Finally, we attempted to develop a prognostic nomogram for GC patients.

MATERIALS AND METHODS

Population

This retrospective cohort study analyzed data from GC patients treated at Zhejiang Cancer Hospital between April 2008 and December 2019. Patients included in the study underwent radical gastrectomy with D1/D2 lymph node dissection and had complete clinical data and follow-up records. The exclusion criteria were other malignant tumors, a lymph node-negative status, palliative care, missing preoperative or postoperative tumor marker data, or unsuccessful surgeries. Ultimately, 2103 GC patients met the inclusion criteria. Tumor staging was performed according to the 8th edition of the AJCC staging manual. All patients signed informed consent forms. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Zhejiang Cancer Hospital, approval No. IRB-2024-604.

Data collection

Patient data, including sex, age, body mass index, family history, smoking history, drinking history, tumor differentiation, positive lymph nodes, total lymph nodes, pathological type, nerve invasion, vascular tumor thrombus, surgical method, N stage, pathological tumor-node-metastasis (pTNM) stage, survival status, recurrence or metastasis, tumor markers, and overall survival (OS), were collected. OS was defined as the time period from the initiation of treatment or diagnosis to the time of death from any cause. Patients with abnormal tumor marker outpatient levels were excluded from the analysis. All patients underwent regular follow-up after surgery, approximately

every 3 months to 6 months, until death or the end of the follow-up period. The median follow-up time was 40 months (range: 1-147 months). Follow-up assessments included computed tomography scans, ultrasound, and endoscopic examinations to assess survival and recurrence status.

Prognostic system and tumor marker grouping

The calculation formula for LODDS is as follows: $\text{LODDS} = \log [(NPLN + 0.5)/(NTLN - NPLN + 0.5)]$, where an offset of 0.5 is applied to avoid mathematical infinity or division by zero. The formula for the LNR is as follows: $\text{LNR} = NPLN/NTLN$. The optimal cutoff points for the NPLNs, NTLNs, LNR, and LODDS were determined by calculating Youden's index (sensitivity + specificity - 1). This index can be used to identify the optimal cutoff point, balance high-risk recognition with low-risk misdiagnosis, and improve survival prediction accuracy. On this basis, the following staging system was established: NPLN: NPLN1 ($1 \leq NPLN1 < 6$) and NPLN2 ($6 \leq NPLN2 \leq 34$); NTLN: NTLN1 ($1 \leq NTLN1 < 33$) and NTLN2 ($33 \leq NTLN2 \leq 73$); LNR: LNR1 ($0.01 \leq LNR1 < 0.16$) and LNR2 ($0.16 \leq LNR2 \leq 1.00$); LODDS: LODDS1 ($-1.68 \leq \text{LODDS1} < -0.69$) and LODDS2 ($-0.69 \leq \text{LODDS2} \leq 1.40$). According to the clinical laboratory standards at our hospital, the cutoff values for the tumor markers carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP), carbohydrate antigen (CA) 19-9, CA72-4, CA125, and CA242 were 5 ng/mL, 10 ng/mL, 37 U/mL, 6.9 U/mL, 35 U/mL, and 15 U/mL, respectively. The values above these thresholds were classified into the high group, whereas the values below the thresholds were classified into the low group.

Study design

This study first employed univariate and multivariate Cox proportional hazards regression models to analyze the hazard ratios (HRs) and 95% confidence intervals (CIs) of various factors, aiming to identify independent risk factors for OS in GC patients. Independent risk factors were then stratified by tumor differentiation to assess their

prognostic value in patients with different tumor differentiation levels. To minimize the influence of confounding factors, a 1:1 propensity score matching (PSM) analysis was performed with a matching tolerance of 0.05. Kaplan-Meier survival analysis was conducted on the matched data to determine survival rate differences among different LODDS groups and pN groups. Additionally, receiver operating characteristic (ROC) analysis was used to compare the prognostic predictive ability of the five staging systems. Finally, independent risk factors for GC patients with different degrees of tumor differentiation were incorporated into a nomogram for prognostic assessment. Decision curve analysis and ROC curve analysis were used to compare the prognostic predictive ability of the nomogram with that of the pTNM system. Calibration curves were used to evaluate the prognostic prediction ability of the model at different postoperative time points. The concordance index (C-index) was used to assess the predictive accuracy of the regression model.

Statistical analysis

Categorical variables in all baseline characteristic data are presented as frequencies and percentages, whereas continuous variables are expressed as the means and standard deviations. Categorical variables were analyzed *via* the χ^2 test, and continuous variables were analyzed *via* the independent-samples t test. Statistical analysis and visualization were performed *via* SPSS 27.0 and R 4.4.1 software, with a two-sided significance level set at $P < 0.05$ for all tests.

RESULTS

The impact of LODDS and tumor differentiation on the prognosis of all patients

After screening, 2103 GC patients who met the inclusion criteria were included in the study (Supplementary Figure 1A). Univariate Cox regression analysis was initially performed to evaluate the impact of various factors on OS, with factors showing $P < 0.05$ included in the multivariate Cox regression analysis. LODDS, pN, LNR, NPLN, and NTLN were analyzed by a variety of covariance analyses, and the variance inflation

factor was less than 10 (Supplementary Table 1). The results indicated that both LODDS (HR = 1.515, 95%CI: 1.185-1.938, $P < 0.001$) and tumor differentiation (HR = 1.268, 95%CI: 1.086-1.479, $P = 0.003$) were independent prognostic risk factors for GC patients (Table 1). ROC analysis revealed an area under the curve (AUC) of 0.694 for the LODDS, with an optimal cutoff value of -0.685, achieving a sensitivity of 72.9% and specificity of 56.0% (Supplementary Figure 1B). Kaplan-Meier survival analysis indicated that the OS rate for LODDS2 patients (with higher LODDS) was lower than that for LODDS1 patients (log-rank $P < 0.001$, Supplementary Figure 1C). Furthermore, patients with poorly differentiated tumors had lower survival rates compared to those with moderately differentiated tumors (log-rank $P < 0.001$, Supplementary Figure 1D).

Patient characteristics before and after PSM

Before PSM, the LODDS1 group included 928 patients (44.1%), while the LODDS2 group included 1175 patients (55.9%). As shown in Table 2, significant differences were observed in the distributions of characteristics such as age, surgery method, pathological type, nerve invasion, vascular tumor thrombus, pTNM stage, CEA, CA19-9, CA72-4, CA242, and tumor differentiation between the LODDS1 and LODDS2 groups (all $P < 0.05$). To minimize the impact of distributional differences in confounding factors on the prognostic analysis, 1:1 PSM was performed on the basis of the collected clinical characteristics. After matching, a total of 1472 patients were included, with 736 patients in each group. To ensure the independent prognostic predictive power of the LODDS in patients with different degrees of tumor differentiation, key variables, including tumor differentiation and lymph node-related variables, were excluded from the matching process. After matching, no significant differences in any of the included clinical characteristics were observed between the two groups (all $P \geq 0.05$), indicating a significant improvement in the balance of clinical features between the groups. Notably, owing to the small sample size of patients with well-differentiated tumors, which accounted for only 0.8% of the total cases, these patients were not included in the subsequent analysis.

Accuracy of prognostic prediction by different systems for patients

ROC analysis was used to assess the prognostic prediction accuracy of the NPLN, LNR, LODDS, and N staging systems in GC patients with different degrees of tumor differentiation (Supplementary Figure 2, Supplementary Table 2). The results revealed that within 3 years post-surgery, the LODDS system had the highest predictive accuracy for all patients (AUC = 0.701, $P < 0.001$), as well as for patients with moderately differentiated tumors (AUC = 0.672, $P < 0.001$) and those with poorly differentiated tumors (AUC = 0.607, $P < 0.001$). Between 3-5 years post-surgery, the LODDS system again demonstrated the highest predictive accuracy for all patients (AUC = 0.654, $P < 0.001$), while the NPLN system was most accurate for patients with moderately differentiated tumors (AUC = 0.643, $P < 0.001$). After 5 years, none of the staging systems showed significant prognostic value.

Kaplan-Meier survival analysis after PSM revealed that in moderately differentiated GC patients, both the LODDS2 group and the N3a + N3b group had worse prognoses within 5 years after surgery (Figure 1A-D, all $P < 0.05$). Among poorly differentiated GC patients, those in the LODDS2 group also had a worse prognosis within 5 years (Figure 1E-G, all $P < 0.05$). However, pN stage did not significantly affect survival rates at 3 and 5 years after surgery in poorly differentiated tumor patients (Figure 1H, $P = 0.117$). Further analysis revealed that pN stage had a weak ability to stratify poorly differentiated GC patients (Supplementary Figure 3A), with no significant survival differences among the N1, N2, and N3a groups (Supplementary Table 2, all $P > 0.05$). In moderately differentiated GC patients, there was also no significant difference in survival between the N1 subgroup and the other three N stages (Supplementary Figure 3B, Supplementary Table 3, all $P > 0.05$). Additionally, multivariate Cox regression analysis incorporating the independent risk factors listed in Table 1, showed that age, CA125, CEA, and LODDS were prognostic factors for both moderately differentiated and poorly differentiated GC patients (Table 2, all $P < 0.05$).

Patients were stratified by the grade of tumor differentiation, and then LODDS, pN, LNR, and NPLN were subjected to multifactorial cox regression analyses with other independent prognostic influences separately. The results of the analysis revealed that the LODDS, LNR, pN, and NPLN were all risk factors for the prognosis of patients with moderately and poorly differentiated GC, and among patients with poorly differentiated GC, the HR value of patients with LODDS2 was 1.859, whereas in the group of moderately differentiated patients, the HR value of patients with LODDS2 was 2.391 compared with patients with LODDS1 (Supplementary Table 4), which indicated that the LODDS has a differential prognostic impact in differently differentiated patient groups. In addition, compared with other staging systems, the LODDS system consistently demonstrated higher prognostic predictive ability, with lower AIC and BIC values and higher C-index and linear trend χ^2 scores at different postoperative time points and in different tumor differentiation groups (Table 3). These findings suggest that the LODDS system has significant clinical potential for the prognostic management of GC patients with different levels of tumor differentiation.

LODDS correlation with clinical features and tumor markers in GC

The LODDS value was correlated with various clinicopathological features and tumor markers. Specifically, elderly patients aged over 60 years, those with mucinous gastric adenocarcinoma, vascular tumor thrombus, nerve invasion, or poorly differentiated tumors exhibited significantly higher LODDS values (Figure 2A-F, all $P < 0.05$). The LODDS values did not correlate with patient body mass index (Figure 2D, $P > 0.05$). Furthermore, patients with higher LODDS values were associated with advanced pTNM stages and an increased likelihood of tumor metastasis and recurrence (Figure 2G and H, all $P < 0.05$). Scatter plot analysis revealed positive correlations between the LODDS values and the levels of the tumor markers CA19-9, CA242, CA72-4, and CA125 (Figure 3A, C, D, and E, R values = 0.065, 0.095, 0.13, and 0.15, respectively; all $P < 0.01$), and no correlation was detected between the LODDS values and CEA and AFP (Figure 3B and F, all $P > 0.05$).

Construction and validation of a prognostic nomogram for OS in GC patients

In the multivariate Cox regression analysis for patients with different tumor differentiation levels, the LODDS, Age, CA125 and CEA were identified as independent prognostic factors for OS in patients with GC (Supplementary Table 4, $P < 0.05$). Tumor differentiation was also included as a risk factor (Table 1, $P < 0.05$). Based on these four factors, a nomogram was constructed to predict 1-year, 3-year, and 5-year OS (Figure 4A). The nomogram demonstrated a C-index of 0.703. The calibration curves demonstrated excellent concordance between the predicted and observed values, confirming that the nomogram provides reliable prognostic predictions (Figure 4B). The AUCs for predicting 1-year, 3-year, and 5-year OS were 0.738, 0.730, and 0.722, respectively, which were higher than those of the pTNM staging system (Figure 4C and Supplementary Figure 4A and B, all $P < 0.001$), confirming that the sensitivity and specificity of this model were superior to those of the pTNM system. The ability of this model to predict patient prognosis was greater than that of individual prognostic indicators (Supplementary Figures 4C-E). The Kaplan-Meier curve successfully distinguished high-risk patients from low-risk patients, with the high-risk group showing poorer OS (Figure 4D, $P < 0.001$). Decision curve analysis revealed that the nomogram provided a greater clinical net benefit in prognostic prediction than did the AJCC 8th edition TNM staging system (Figure 4E). These findings further support the clinical utility of the LODDS in predicting OS in GC patients.

DISCUSSION

Currently, the pN staging system remains the most widely used lymph node staging method in clinical practice. This system, established by the AJCC and the Union for International Cancer Control, evaluates the number and distribution of positive lymph nodes, providing critical information about the extent of tumor spread[58,59]. However, the pN staging system has notable limitations in GC patients, particularly when factors such as insufficient lymph node collection, tumor differentiation, and changes in tumor

markers affect its accuracy. These shortcomings potentially lead to reduced staging precision[60]. To address these limitations of the traditional pN system, alternative staging methods, such as the LODDS and LNR, have emerged. By incorporating the ratio of positive to negative lymph nodes, these methods offer more precise prognostic assessments[61].

Existing studies have highlighted the advantages of the LODDS and LNR for prognostic prediction. For example, Fortea-Sanchis *et al*[62] reported that in patients with colorectal cancer, even with a lower number of lymph nodes collected, the LODDS still exhibited high predictive efficacy. Similarly, Teng *et al*[63] noted the significant value of the LNR in predicting OS in breast cancer patients. Despite the abundant evidence supporting the strong prognostic value of the LODDS and LNR, their prognostic ability across different cancers is still debated. Jin *et al*[64] reported that the LODDS more accurately predicts prognosis in muscle-invasive bladder cancer patients than do pN and the LNR, whereas Deng *et al*[65] reported that in non-small cell lung cancer patients, the LODDS and LNR each have their own advantages depending on the NPLN. Thus, our study sought to comprehensively evaluate the prognostic value of various staging systems in GC patients. Through a comprehensive ROC comparison analysis, we found that the LODDS demonstrated superior prognostic ability compared with the N, NPLN, NTLN, and LNR systems in GC patients.

Unlike studies focused on the general GC population, recent research on the LODDS has gradually expanded to include more specific cancer subtypes. For instance, Zhou *et al*[66] compared different staging systems and found that for GC patients with distant metastases, the LODDS and LNR outperformed the PLN in terms of discriminative ability, prognostic homogeneity, and accuracy in predicting 1- or 2-year cancer-specific survival. Similarly, Zhang *et al*[67] demonstrated the significant role of the LODDS in predicting the prognosis of patients with gastric signet-ring cell carcinoma, suggesting that it can serve as an independent prognostic factor. Our study focused on patients with moderate to poorly differentiated GC, a group characterized by more aggressive behaviors and higher recurrence risk. We found that traditional systems, such as pN

and the LNR, struggled to stratify prognosis in this subgroup. In contrast, the LODDS provides effective risk stratification across different tumor differentiation levels and postoperative time points, underscoring its potential to refine individualized management strategies.

Moreover, our findings revealed a strong association between the LODDS score and clinicopathological features, including nerve invasion, vascular tumor thrombus, mucinous adenocarcinoma, and low tumor differentiation, all of which are linked to an increased risk of postoperative recurrence and poor prognosis[68]. The present study revealed a significant positive correlation between CA family tumor markers (CA19-9, CA72-4, CA125, CA242) and LODDS, whereas AFP and CEA did not show similar associations. This discrepancy may reflect heterogeneity in biological properties and metastatic mechanisms among these markers: CA family markers, as glycosylation-associated antigens, may promote lymph node metastatic microenvironment formation through modulating tumor cell adhesion, metabolic reprogramming (*e.g.*, CA19-9-mediated lactate metabolism), and stromal remodeling (*e.g.*, CA125-activated TGF- β pathway), thereby evolving synergistically with elevated LODDS. In contrast, the tissue specificity of AFP (*e.g.*, its association with intrahepatic dissemination in hepatocellular carcinoma) and temporal discordance in CEA secretion dynamics (*e.g.*, early-stage elevation misaligned with lymph node metastatic progression) may limit their correlation with LODDS[69,70]. Future studies should incorporate multi-timepoint monitoring and molecular subtyping (*e.g.*, MSI status or KRAS mutations) to evaluate the incremental prognostic value of CA family markers in lymph node metastasis prediction models. Clinically, CA family markers could complement TNM staging to optimize lymph node metastasis risk stratification and immunotherapy response prediction.

To increase the clinical applicability of the LODDS, we developed an individualized prognostic nomogram model specifically designed for GC patients with moderate to poorly differentiated tumors. When five key prognostic risk factors - LODDS, age, CA125, CEA, and tumor differentiation - were incorporated, this nomogram

demonstrated superior performance in terms of prediction accuracy, calibration, and clinical applicability compared with the AJCC 8th edition TNM staging system. The model provides precise guidance for clinical follow-up frequency and the formulation of individualized treatment plans. For example, ² high-risk patients identified by the model may require more frequent follow-up and intensified adjuvant therapy, whereas low-risk patients can avoid unnecessary overtreatment through personalized strategies. Research by Guo *et al*[71] and He *et al*[72] has also shown that incorporating LODDS into nomograms significantly improves prognostic evaluation accuracy and the practicality of individualized management in patients with colorectal and lung cancers, further confirming the broad potential of LODDS in personalized cancer treatment.

However, this study has several limitations. First, as a retrospective analysis, further prospective studies are needed to validate our findings. Second, there is currently no standardized staging method for systems such as the LODDS and LNR. In this study, we used Youden's index to determine the optimal cutoff value, balancing sensitivity and specificity to predict postoperative survival. Finally, this study included only moderately and poorly differentiated GC patients with positive lymph nodes. Future research should include highly differentiated and lymph node-negative patients to further assess the generalizability of the LODDS. The moderate AUC value (approximately 0.7) of our nomogram model suggests that further improvement in predictive accuracy is possible. Recent advances in computational methods, particularly deep learning and ensemble modeling, have shown promise in enhancing prognostic performance through several avenues. These include: (1) More sophisticated feature engineering that integrates additional clinical biomarkers and genomic data; (2) Multimodal data fusion combining imaging, molecular, and pathological inputs; and (3) Personalized model architectures tailored to specific patient subgroups. Integrating these advanced methods with our current model should facilitate the development of more powerful prognostic tools in the future. However, it is also important to acknowledge the trade-offs between model complexity and clinical interpretability. In medical practice, especially in oncology, the adoption of predictive models requires not

only accuracy but also transparency and ease of application, which must be carefully balanced in future research.

In conclusion, our study establishes the LODDS as an independent and superior prognostic factor for moderately to poorly differentiated GC and that its prognostic value surpasses that of the pN, LNR, NPLN, and NTLN staging systems. Integrating LODDS with tumor differentiation into the GC staging system provides clinicians with a more accurate tool for survival risk stratification for patients undergoing surgical treatment and lymph node dissection, thereby providing stronger support for personalized treatment and prognostic assessment.

CONCLUSION

LODDS has been shown to be a reliable independent prognostic risk factor for patients with GC, providing a more precise risk stratification in patients with moderately and poorly differentiated GC compared to pN, LNR, NPLN and NTLN. The study showed that LODDS values were significantly associated with several clinical characteristics, including age, pathologic type, degree of differentiation, nerve invasion, vascular tumor thrombosis, recurrence or metastasis, and pTNM staging. In addition, the LODDS was significantly and positively correlated with tumor markers of the CA family. Prognostic models constructed based on the LODDS with other key clinical indicators (*e.g.*, age, tumor differentiation, CEA, CA125) had predictive power beyond the traditional pTNM staging system, showing higher accuracy and potential for clinical application. This finding emphasizes the significant value of LODDS in the prognostic assessment of GC.

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