

Prognostic Value of Log Odds of Positive Lymph Nodes (LODDS) in Gastric Cancer: A Comparative Analysis with Lymph Node Ratio and N Stage

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ABSTRACT

Objective: The present analysis sought to compare the prognostic relevance of log odds of positive lymph nodes (LODDS), lymph node ratio (LNR), and standard N-based staging in patients who received curative-intent surgical treatment for stomach cancer.

Methods: Medical records of patients who underwent curative gastrectomy between March 2019 and March 2025 were examined retrospectively. Clinicopathological characteristics, together with lymph node-related parameters, were analyzed. The Kaplan–Meier method was used to estimate survival, and differences across groups were evaluated using the log-rank test. Prognostic factors were investigated through univariate and multivariate Cox regression analyses. Separate multivariate models were constructed for LNR, LODDS, and N stage to account for potential collinearity among nodal variables. Discriminative performance was additionally examined by constructing receiver operating characteristic (ROC) plots, and findings yielding *P* values under 0.05 were taken to be statistically meaningful.

Results: The analytical cohort comprised 55 cases observed over a median surveillance duration of 29 months. Univariate analysis identified five factors significantly associated with survival: tumor (T) category, node (N) classification, tumor differentiation grade, LNR, and LODDS. Once multivariate correction was applied, the prognostic value of LODDS was preserved as an independent prognostic marker (hazard ratio: 3.159; 95% confidence interval: 1.484-6.722; *P* = 0.003), whereas LNR no longer reached significance. Although N stage retained prognostic relevance, its predictive strength was lower than that observed for LODDS. ROC analysis demonstrated favorable predictive performance for all nodal parameters, with LODDS showing the highest AUC value (0.876).

Conclusion: In gastric cancer, LODDS appears to retain prognostic relevance for overall survival and may provide superior discriminative ability compared with conventional nodal staging systems.

Keywords: Gastric cancer, lymph node ratio, LODDS, N stage, overall survival, prognosis, ROC analysis

INTRODUCTION

Despite continuous advances in diagnostic modalities and therapeutic strategies, gastric cancer remains a major global health burden and a leading cause of cancer-related mortality worldwide, particularly in patients with advanced disease.¹

Surgical resection remains the primary curative treatment; however, long-term survival is largely influenced by tumor stage and biological behavior.² Among prognostic factors, lymph node involvement plays a central role in determining oncological outcomes.



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The tumor-node-metastasis (TNM) staging system developed by the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) is currently the most widely adopted classification system for gastric cancer. Within this framework, nodal status is determined according to the number of metastatic lymph nodes identified in the surgical specimen.³ Accurate nodal staging requires the examination of at least 16 lymph nodes, as recommended by current guidelines.⁴ Nevertheless, adequate lymph node retrieval may not always be achieved in routine clinical practice, potentially resulting in stage migration and reduced prognostic accuracy. To overcome these limitations, alternative lymph node assessment methods have been proposed. Among these, the lymph node ratio (LNR), defined as the ratio of metastatic to examined lymph nodes, and the log odds of positive lymph nodes (LODDS), which incorporates both positive and negative lymph node counts, have attracted increasing attention.⁵ Several studies have demonstrated that these metrics may provide more refined prognostic information than conventional pN staging, particularly in situations where lymph node harvest is suboptimal. Previous investigations have suggested that LODDS may offer superior prognostic discrimination compared with LNR, especially among patients with limited nodal involvement or node-negative disease.⁶ Unlike LNR, which assigns all node-negative patients to the same category, LODDS incorporates information from both positive and negative lymph nodes, potentially allowing for more precise risk stratification. Furthermore, studies involving large cohorts of patients with gastrointestinal malignancies, including gastric cancer, have reported that LODDS may outperform both conventional nodal staging and LNR in predicting long-term survival outcomes.^{7,8}

The present study aimed to evaluate the prognostic significance of LNR and LODDS in patients undergoing curative surgery for gastric cancer and to compare their predictive performance with that of the conventional pN classification of the AJCC/UICC/TNM staging system.

MAIN POINTS

- Log odds of positive lymph nodes (LODDS) is an independent prognostic marker for overall survival after curative gastrectomy for gastric cancer.
- In multivariate analysis, LODDS retained its independent prognostic significance, whereas lymph node ratio (LNR) lost statistical significance.
- LODDS demonstrated the highest discriminative performance (AUC: 0.876) among LODDS, LNR, and N stage on ROC analysis.
- LODDS may serve as a valuable complementary parameter to conventional nodal staging systems, particularly when lymph node harvest is suboptimal.
- These findings support further evaluation of LODDS in prognostic nomograms and risk stratification models for gastric cancer.

MATERIALS AND METHODS

Study Design and Patient Selection

Records of individuals who received operative management of stomach cancer at a tertiary referral institution from March 2019 through March 2025 were examined in this retrospective study. Among the 140 cases reviewed during the study period, 70 were excluded because of missing clinical data, and 15 were excluded due to peritoneal carcinomatosis detected intraoperatively. The study included 55 patients with complete clinical and pathological data.

Ethics Approval

Authorization for the present work was obtained from the Koşuyolu High Specialization Training and Research Hospital Institutional Review Board prior to initiation (approval date: 03.06.2025, decision no: 2025/109/11/43). All phases of this work adhered closely to the ethical standards outlined in the Helsinki Declaration. Written informed consent for the surgical procedure was obtained from all patients at the time of hospital admission. As this was a retrospective review of existing medical records, separate informed consent specific to the study was not obtained; the study protocol was approved by the Institutional Review Board.

Data Collection

Patient demographic information and clinicopathological characteristics were retrospectively reviewed. Variables evaluated included age, gender, tumor stage, histological grade, histopathological subtype, gastrectomy type, neoadjuvant treatment status, and lymph node-related parameters. Indices related to nodal status included both the total number of harvested nodes and the number found to harbor metastases. Patient outcomes, including follow-up duration, mortality rate, recurrence, and site of recurrence, were evaluated retrospectively.

Definitions

Overall survival was defined as the interval between the date of surgery and either death or the last documented follow-up. The LNR was calculated by dividing the number of metastatic lymph nodes by the total number of examined lymph nodes; patients were categorized into three groups: LNR1 (0), LNR2 (>0-0.1), and LNR3 (>0.1). The LODDS was calculated as the natural logarithm of the ratio between positive and negative lymph nodes, and patients were further stratified into five categories: LODDS1 (≤ -4), LODDS2 (-4 to -2.5), LODDS3 (-2.5 to -2), LODDS4 (-2 to -0.5), and LODDS5 (> -0.5). The cut-off values used for both the LNR and LODDS classifications were adopted from previously published and validated studies in the gastric cancer literature to facilitate comparison with existing evidence.⁹

Statistical Analysis

Data processing for all statistical procedures was carried out with SPSS (version 27). For continuous data, results were reported using either mean $\pm$ standard deviation or median (with min

and max), depending on whether the variable followed a normal distribution. Qualitative variables were expressed as counts and percentages. Survival curves were constructed using the Kaplan-Meier method, and subgroup comparisons were performed using the log-rank test. To identify variables associated with overall survival, Cox proportional hazards modeling was subsequently performed using both single-variable and multivariable models. Given the risk of collinearity among the nodal parameters, the N category, LNR, and LODDS were each assessed in separate multivariate models. The results of the survival analysis were expressed as hazard ratios (HRs) with 95% confidence intervals. The discriminative capacity of nodal indicators for overall survival was examined by plotting receiver operating characteristic (ROC) curves, and the corresponding area under the curves (AUCs) were computed. A *P* value below 0.05 was accepted as the threshold for statistical significance.

RESULTS

The cohort ultimately included in the present study consisted of fifty-five individuals. Their mean age stood at 64.60 ± 12.01 years, with male subjects accounting for 60% of the sample. Total gastrectomy was performed in 54.5% of cases, whereas subtotal gastrectomy was performed in the remaining 45.5%, 43.6% of the patients received neoadjuvant therapy. Overall, 49.1% of the patients had grade 3 tumors, and the most common stage was T3(43.6%). Among the N-stage cases, 43.6% were N0, while the remainder had varying degrees of lymph node involvement. Histopathological evaluation revealed that the vast majority of cases (83.6%) were adenocarcinomas (NOS) (Table 1).

Table 1. Clinicopathological Characteristics of Patients with Gastric Cancer (n = 55)

Variable	Overall (n = 55)
Age (years), mean $\pm$ SD	64.60 $\pm$ 12.01
Sex, n (%)	
Male	33 (60.0)
Female	22 (40.0)
Type of surgery, n (%)	
Total gastrectomy	30 (54.5)
Subtotal gastrectomy	25 (45.5)
Neoadjuvant therapy, n (%)	
Yes	24 (43.6)
No	31 (56.4)
Tumor grade, n (%)	
G1	9 (16.3)
G2	19 (34.5)
G3	27 (49.1)

Table 1. Continued

Variable	Overall (n = 55)
T stage, n (%)	
1a	1 (1.8)
1b	11 (20.0)
2	5 (9.1)
3	24 (43.6)
4a	11 (20.0)
4b	3 (5.5)
N stage, n (%)	
0	24 (43.6)
1	10 (18.2)
2	8 (14.5)
3a	7 (12.7)
3b	6 (10.9)
Final pathology, n (%)	
Adenocarcinoma (NOS)	46 (83.6)
Adenocarcinoma with mucinous component	2 (3.6)
Signet ring cell carcinoma	5 (9.1)
Gastric carcinoma with lymphoid stroma	2 (3.6)
Total lymph nodes retrieved, median (min-max)	28 (7-61)
Positive lymph nodes, median (min-max)	1 (0-41)
LNR stage, n (%)	
LNR1	36 (65.4)
LNR2	15 (27.3)
LNR3	4 (7.3)
LODDS stage, n (%)	
LODDS1	6 (10.9)
LODDS2	27 (49.1)
LODDS3	3 (5.5)
LODDS4	12 (21.8)
LODDS5	7 (12.7)
Distant metastasis, n (%)	
Yes	13 (23.6)
No	42 (76.4)
Site of recurrence, n	
Lung	2
Peritoneum	8
Liver	2
Anastomotic site	1
Follow-up (months), median (min-max)	29 (2-75)
Overall survival (months), mean (95% CI)	52.2 (44.1-60.3)

SD, standard deviation; NOS, not otherwise specified; LNR, lymph node ratio; LODDS, log odds of positive lymph nodes; CI, confidence interval; Min, minimum; Max, maximum.

Lymph node evaluation demonstrated a median of 28 retrieved lymph nodes (range, 7-61) and a median of 1 metastatic lymph node (range, 0-41). According to the LNR classification, 65.4% of patients were LNR1. In the LODDS system, LODDS2 represented the largest subgroup, accounting for 49% of the cohort. Median surveillance was 29 months (range, 2-75 months); distant metastatic disease developed in 23.6% of patients during this interval. Peritoneal dissemination, observed in 8 cases, was the most common recurrence pattern, followed by pulmonary and systemic metastases. A median survival of 52.2 months was estimated for the cohort (95% CI: 44.1-60.3) (Table 1). Variables potentially affecting overall survival were assessed by univariate Cox proportional hazards regression. On univariate analysis, several variables were significantly associated with overall survival: T category (HR 1.689; 95% CI 1.172–2.434; $P=0.005$), nodal category (HR 1.624; 95% CI 1.236–2.134; $P<0.001$), and tumor grade (HR 5.711; 95% CI 1.382–23.608; $P=0.016$). Likewise, both LNR (HR 3.262; 95% CI 1.735–6.135; $P<0.001$) and LODDS (HR 2.409; 95% CI 1.516–3.827; $P<0.001$) showed strong prognostic associations with survival. No meaningful association between overall survival and age ($P=0.172$), sex ($P=0.991$), or end outcome status ($p=0.998$) was detected (Table 2).

To minimize the potential impact of multicollinearity among lymph node parameters, separate multivariate Cox regression models were constructed for LNR, LODDS, and N stage.

Table 2. Univariate Cox Regression Analysis for Overall Survival			
Variable	HR	95% CI	P value
Age	0.978	0.947-1.010	0.172
Sex	1.006	0.342-2.958	0.991
T stage	1.689	1.172-2.434	0.005
N stage	1.624	1.236-2.134	< 0.001
Tumor grade	5.711	1.382-23.608	0.016
Final pathology	0.999	0.592-1.688	0.998
LNR stage	3.262	1.735-6.135	< 0.001
LODDS stage	2.409	1.516-3.827	< 0.001

HR, hazard ratio; CI, confidence interval; LNR, lymph node ratio; LODDS, log odds of positive lymph nodes.

Following multivariable adjustment, the association between LNR and overall survival approached but did not reach statistical significance (HR 3.491; 95% CI 0.967-12.593; $p=0.056$), whereas LODDS remained an independent predictor (HR 3.159; 95% CI 1.484-6.722; $p=0.003$). After adjustment, the N category likewise emerged as a significant correlate of survival (HR 1.694; 95% CI 1.011-2.840; $p=0.045$); nonetheless, the magnitude of its prognostic effect remained below that demonstrated by LODDS (Table 3).

The capacity of each nodal measure to differentiate survival outcomes was investigated by means of ROC curve analysis. High AUC values were obtained for all three measures, including LODDS (AUC: 0.876), LNR (AUC: 0.874), and N category (AUC: 0.861), indicating strong predictive ability for overall survival. Among these parameters, LODDS had the highest AUC, indicating superior discriminatory capacity compared with other lymph-node parameters (Figure 1).

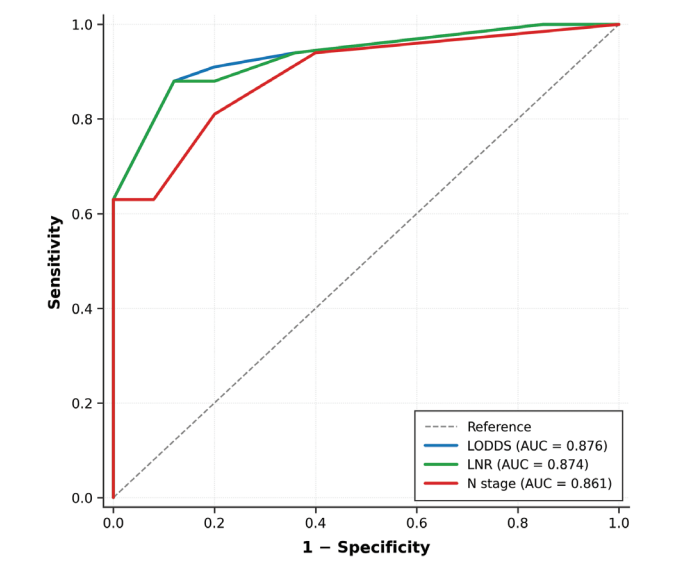


Figure 1. ROC curves for LODDS, LNR, and N stage in predicting overall survival in gastric cancer. AUC values: LODDS = 0.876, LNR = 0.874, N stage = 0.861. LODDS demonstrated the highest discriminative capacity among the three nodal staging systems. LODDS, log odds of positive lymph nodes; LNR, lymph node ratio; ROC, receiver operating characteristic.

Table 3. Multivariate Cox Regression Analysis for Overall Survival

Variable	Model 1 (LNR)		Model 2 (LODDS)		Model 3 (N stage)	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
Age	1.002 (0.966-1.040)	0.909	0.996 (0.964-1.030)	0.820	1.012 (0.974-1.051)	0.546
T stage	0.768 (0.378-1.563)	0.467	0.581 (0.300-1.126)	0.108	0.801 (0.421-1.527)	0.501
Tumor grade	3.628 (0.725-18.169)	0.117	3.834 (0.779-18.865)	0.098	3.487 (0.725-16.775)	0.119
LNR	3.491 (0.967-12.593)	0.056	-	-	-	-
LODDS	-	-	3.159 (1.484-6.722)	0.003	-	-
N stage	-	-	-	-	1.694 (1.011-2.840)	0.045

Model 1 includes LNR; Model 2 includes LODDS; Model 3 includes N stage. Each model was adjusted for age, T stage, and tumor grade. Statistically significant P values are shown in bold. HR, hazard ratio; CI, confidence interval; LNR, lymph node ratio (ratio of metastatic to examined lymph nodes); LODDS, log odds of positive lymph nodes.

DISCUSSION

The results of our analysis show that LODDS retains prognostic significance for survival, while the conventional N classification maintains prognostic value. LNR was significant in univariate analysis, but this effect was not preserved after multivariate adjustment. No lymph node parameter demonstrated significant superiority, and LODDS could be used as a complementary approach for prognostic assessment.

Over the past decade, LODDS has attracted increasing attention in gastric cancer research, and findings from large patient cohorts have particularly emphasized its clinical relevance. Drawing on a sample of 10,748 individuals, Xia et al.¹⁰ found that prognostic models built around LODDS outperformed conventional nodal staging schemes in predicting overall survival. In a comparable vein, Gu et al.⁹ reported, drawing on a multi-institutional cohort of 7,620 individuals, that LODDS-driven stratification outperformed both standard pN staging and LNR in prognostic terms. Although our study demonstrates that LODDS is independently associated with overall survival, LODDS did not show a significant advantage compared with other lymph node parameters. Such findings imply that the prognostic utility of LODDS may vary depending on patient characteristics, the size of the analyzed cohort, and the degree to which surgical procedures are standardized. In particular, it may be difficult to demonstrate significant differences among lymph node parameters in case series comprising a limited number of patients reflecting real-world data. Therefore, we believe that, rather than replacing current lymph node assessment systems, LODDS can be used in clinical practice as a complementary parameter.

LNR is widely used as a marker of nodal tumor burden in stomach cancer, and several studies have demonstrated its prognostic relevance. Earlier work has documented a significant association between elevated LNR and poorer survival. Miciak et al.¹¹, in a cohort of 194 patients, identified LNR as an important prognostic indicator associated with tumor stage and survival. Similarly, Peng et al.¹² demonstrated that LNR retains its prognostic significance, particularly when combined with factors related to the tumor microenvironment. However, Liu et al.¹³ demonstrated that LNR-based classification may provide more homogeneous prognostic stratification than both LODDS and conventional N stage in patients with extensive lymph node dissection. Within our cohort, a link between LNR and overall survival emerged on univariate testing, yet this association did not hold once multivariate adjustment was applied. This observation might imply that LNR's predictive power is shaped by factors such as the number of nodes obtained, the extent of nodal dissection, and patient-specific attributes. Moreover, classifying all node-negative patients within the LNR0 category may limit the ability of LNR to adequately reflect prognostic heterogeneity in this subgroup. Although LNR reflects lymph node burden, its partial overlap with N stage and LODDS may have reduced its independent effect in multivariate analysis. Even so, the LNR-derived AUC of 0.874 from ROC analysis suggests that this metric retains robust discriminative power for predicting overall survival. It slightly exceeds the AUC for the N category and aligns closely with the value observed for

LODDS. This value is slightly higher than that for the N stage, and is quite similar to that for LODDS. These findings suggest that LNR is a clinically valuable prognostic parameter, but it may not be sufficient on its own, particularly in situations requiring a more detailed lymph node assessment.

Beyond its prognostic significance, LODDS may have applications in future prognostic models and risk stratification systems for gastric cancer. By incorporating information from both positive and negative lymph nodes, LODDS may provide a more comprehensive assessment of nodal status than conventional pN staging alone, particularly in patients with limited lymph node retrieval. Integration of LODDS into prognostic nomograms and clinical decision-making algorithms may contribute to more individualized postoperative surveillance and treatment planning. Nevertheless, further large-scale prospective studies are required before routine clinical implementation can be recommended.

Study Limitations

This study has several limitations. First, the retrospective, single-center design of the study limits the generalizability of the findings. Second, the relatively small sample size ($n=55$) and limited number of events (mortality) may have affected the stability of the multivariate Cox regression models and led to wide confidence intervals for the calculated HR; indeed, the result obtained for LNR remained at the threshold of statistical significance. Another factor that could lead to selection bias is the exclusion of 70 of the 140 patients initially included in the study due to missing clinical data, and 15 due to peritoneal carcinomatosis detected during surgery. Furthermore, the cut-off values used for the LNR and LODDS classifications were adapted from previously published literature rather than being specifically determined for this study; this means that the results may not reflect the optimal cut-off values for the patient population in question. Patient-specific variations in the extent of lymph node dissection and the number of lymph nodes removed may also have influenced the performance of the LNR and LODDS classifications. Finally, the fact that the findings have not been validated in an external dataset limits the assessment of the results' reproducibility across different patient groups. Therefore, the findings need to be validated in larger, multicenter, and prospective cohorts.

CONCLUSION

In gastric cancer, LODDS appears to function as an independent prognostic indicator and may provide additional value in nodal assessment when combined with established staging systems.

Ethics

Ethics Committee Approval: This retrospective study was approved by the Institutional Ethics Committee of Koşuyolu High Specialization Training and Research Hospital (decision no: 2025/109/11/43, date: 03.06.2025). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Informed Consent: Written informed consent for the surgical procedure was obtained from all patients at the time of hospital admission. As this was a retrospective review of existing medical records, separate informed consent specific to the study was not obtained; the study protocol was approved by the Institutional Review Board.

Footnotes

Author Contributions: Concept Design – V.A., M.İ.A., A.O.S.; Data Collection or Processing – V.A., M.İ.A., A.O.S., N.B.; Analysis or Interpretation – V.A., M.İ.A., Ö.F.K., Ö.Ö., S.G., A.S.S., E.P.; Literature Review – V.A., M.İ.A., M.D.; Writing, Reviewing and Editing – V.A., M.İ.A., A.O.S., E.P., M.D.

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