Original Article

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Comparison of the Effectiveness of Laboratory Parameters in Predicting Lymph Node Positivity in Patients with Gastric Cancer

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Abstract

Aim: We proposed that inflammation and nutrition-based laboratory indices measured at the time of initial diagnosis could predict lymph node positivity in patients with gastric adenocarcinoma. In this context, this study aimed to evaluate and compare the predictive performance of the C-reactive protein (CRP) -to-albumin ratio (CAR), CRP-to-lactate dehydrogenase ratio (CLDR), lymphocyte-to-CRP ratio (LCR), and CRP-albumin-lymphocyte index (CALLY).

Methods: This retrospective, single-center observational study included 215 consecutive patients who underwent gastrectomy for histologically confirmed gastric adenocarcinoma between January 2014 and May 2024. Preoperative laboratory parameters were used to calculate CAR, CLDR, LCR, and CALLY. Receiver operating characteristic (ROC) curve analysis assessed discriminative ability, and multivariable logistic regression was performed to identify independent predictors of lymph node positivity, adjusting for age, sex, and neoadjuvant therapy status.

Results: Lymph node metastasis was present in 173 patients (80%). CAR and CLDR were significantly higher in patients with nodal involvement (p=0.014 and p=0.017, respectively), whereas LCR and CALLY showed borderline associations (p=0.056 and p=0.052). ROC analysis revealed modest predictive ability, with area under the curve values of 0.622 for CAR and 0.618 for CLDR. In multivariable analysis, both CAR [odds ratio (OR): 1.36, p=0.026] and CLDR (OR: 19.93, p=0.018) remained independent predictors of lymph node positivity.

Conclusion: CAR and CLDR are inexpensive and widely accessible indices that independently predict lymph node metastasis in gastric cancer at diagnosis. Although their discriminative performance is modest, they may provide complementary value when combined with imaging and clinicopathological data to improve preoperative risk stratification.

Keywords: Gastric cancer, lymph node metastasis, C-reactive protein, albumin, lymphocytes, lactate dehydrogenase, biomarkers

Introduction

Gastric cancer remains a major global health challenge, ranking as the fifth most common malignancy and the third leading cause of cancer-related mortality worldwide (1). Its prevalence is particularly high in East Asian countries, including China, Japan, and South Korea. The disease is most frequently diagnosed between the ages of 40 and 65 and occurs nearly twice as often in men as in women (2).

Lymph node metastasis is one of the most critical prognostic factors in gastric cancer, as it strongly influences tumor, node, metastasis staging, surgical strategies, and the selection of neoadjuvant or adjuvant therapy (3). Accurate prediction of nodal involvement

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at the time of initial diagnosis is therefore essential for guiding treatment planning and improving outcomes. Despite the widespread use of computed tomography, magnetic resonance imaging, and endoscopic ultrasound for preoperative staging, these modalities have limited sensitivity in distinguishing reactive from metastatic lymph nodes (4,5). Recently, systemic inflammation has been recognized as a key driver of tumor progression and metastasis. Several inflammation-based and nutrition-based indices derived from routine blood tests, such as the C-reactive protein (CRP) -to-albumin ratio (CAR), lymphocyte-to-CRP ratio (LCR), and systemic immune-inflammation index, have been extensively investigated for their prognostic significance (6,7). However, newer indices, including the CRP-to-lactate dehydrogenase (LDH) ratio (CLDR) and the CRP-albumin-lymphocyte index (CALLY), remain underexplored, particularly in relation to predicting lymph node metastasis in gastric cancer (8-10).

We hypothesized that preoperative inflammation and nutrition-based indices measured at the time of diagnosis could predict lymph node positivity in patients with gastric adenocarcinoma. Accordingly, this single-center study aimed to evaluate and compare the predictive performance of four indices-CAR, CLDR, LCR, and CALLY-in estimating lymph node status at baseline. By identifying cost-effective and widely available biomarkers, this approach may provide additional value in clinical practice by supporting more accurate preoperative risk stratification and personalized treatment planning.

Materials and Methods

Compliance with Ethical Standards

This retrospective, single-center observational study was conducted in accordance with the principles of the Declaration of Helsinki and its later amendments. Approval was obtained from the Bolu Abant Izzet Baysal University Non-Interventional Clinical Research Ethics Committee (approval no.: 2024/300; date: 19.11.2024).

Study Design

Medical records of consecutive adult patients who underwent gastrectomy for histologically confirmed gastric adenocarcinoma between January 2014 and May 2024 were reviewed. Of 270 initially screened patients, 43 who underwent emergency surgery for complications (e.g., perforation or bleeding) and 12 with incomplete records were excluded. The final cohort consisted of 215 patients.

Demographic characteristics (age, sex), clinical information, preoperative laboratory results, operative notes, and postoperative histopathological findings were collected. All blood samples were obtained at the time of initial diagnosis, before any treatment, after at least 8 hours of fasting, and within 7 days prior to surgery. Patients who subsequently received neoadjuvant therapy were not excluded; however, their laboratory results reflected pretreatment baseline status, and neoadjuvant therapy was prespecified as an adjustment covariate in the analyses.

Laboratory Assessment

Based on routine laboratory measurements, four preoperative indices were calculated:

- C-reactive protein-to-albumin ratio: CRP/Albumin
- CRP-to-lactate dehydrogenase ratio: CRP/LDH
- Lymphocyte-to-CRP ratio: Lymphocyte/CRP
- CRP-albumin-lymphocyte index: (Albumin × Lymphocyte)/(CRP × 10^4)

No additional composite scores were analyzed to maintain focus on these a priori selected indices.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics for Windows, version 27.0 (Armonk, NY, USA). Normality of continuous variables was tested using the Kolmogorov-Smirnov test. Group comparisons between lymph node-negative and lymph node-positive patients were performed using the Independent Samples t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables.

Diagnostic performance of the indices was assessed using receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC), 95% confidence intervals (CIs), and optimal cut-off values determined by the Youden index were reported, along with corresponding sensitivity and specificity.

Independent predictors of lymph node positivity were identified using multivariable logistic regression, which included age, sex, neoadjuvant therapy status, and the four indices (CAR, CLDR, LCR, CALLY). Odds ratios (ORs) with 95% CIs were calculated. A two-tailed p-value <0.05 was considered statistically significant.

Results

A total of 215 patients met the inclusion criteria and were included in the final analysis. The mean age of the cohort was 65.8±12.3 years, and 160 patients (74.4%) were male. Lymph node metastasis was confirmed in 173 patients (80%) based on postoperative histopathological examination.

Comparison of inflammation and nutrition-based indices between patients with and without lymph node metastasis revealed significant differences (Table 1). CAR and CLDR values were significantly higher in the lymph node positive group (p=0.014 and p=0.017, respectively), whereas LCR (p=0.056) and CALLY (p=0.052) demonstrated borderline significance. These findings

suggest that patients with nodal involvement exhibit a heightened systemic inflammatory response and impaired nutritional status compared with those without lymph node metastasis.

Receiver operating characteristic curve analysis demonstrated modest diagnostic performance for all indices (Table 2, Figure 1). CAR had the highest discriminative ability (AUC: 0.622, 95% CI: 0.540-0.704, p=0.014), followed closely by CLDR (AUC: 0.618, 95% CI: 0.535-0.698, p=0.017). LCR (AUC: 0.585, p=0.056) and CALLY (AUC: 0.573, p=0.052) exhibited only borderline predictive performance.

Multivariable logistic regression was performed to identify independent predictors of lymph node metastasis (Table 3). After adjusting for age, sex, and neoadjuvant therapy status, both CAR (OR: 1.36, 95% CI: 1.04-1.78, p=0.026) and CLDR (OR: 19.93, 95% CI: 1.69-235.31, p=0.018) remained statistically significant. In contrast, LCR and CALLY were not significant (p>0.05). Importantly, inclusion of neoadjuvant therapy status in the regression model did not alter the predictive value of CAR and CLDR, indicating that their associations reflect baseline inflammatory and metabolic status rather than treatment-related effects.

Overall, CAR and CLDR emerged as statistically significant and independent predictors of lymph node positivity. However, their modest AUC values indicate that these indices should not be used as standalone diagnostic tools. Instead, they may serve as complementary markers alongside imaging and clinicopathological parameters to improve preoperative risk stratification.

Discussion

Neoadjuvant therapy has become an established strategy for patients with locally advanced gastric carcinoma, as it can reduce primary tumor burden and lymph node involvement, occasionally achieving pathological downstaging before surgery (11). Reliable preoperative prediction of nodal status remains essential because it strongly influences the surgical approach, the extent of lymphadenectomy, and the overall oncological treatment plan (12). Previous studies have also shown that successful downstaging correlates with improved long-term survival (13), underscoring the importance of cost-effective and widely accessible tools to complement imaging techniques.

Although D2 lymphadenectomy remains the standard surgical approach, it is associated with increased morbidity compared with less extensive procedures (14). In selected early-stage cases, limited lymphadenectomy or endoscopic resection may be appropriate alternatives (15,16). Therefore, accurate risk stratification before surgery is critical for tailoring operative strategies and optimizing treatment outcomes. Despite advances in cross-sectional imaging and endoscopic ultrasonography, these modalities still show limited sensitivity and specificity in identifying metastatic lymph nodes during initial staging, and restaging accuracy after neoadjuvant therapy also remains suboptimal (17,18). This diagnostic gap has driven growing interest in inflammation and nutrition-based biomarkers, which are inexpensive, reproducible, and reflect tumor biology at baseline.

Table 1. Comparison of inflammation and nutrition-based indices between patients with and without lymph node metastasis

Index	LN Negative (Median, IQR)	LN Positive (Median, IQR)	p-value
CAR	0.33 (0.20-0.51)	0.56 (0.34-0.88)	**0.014**
CLDR	0.057 (0.041-0.069)	0.084 (0.062-0.110)	**0.017**
LCR	0.117 (0.085-0.146)	0.068 (0.042-0.098)	0.056
CALLY	0.487 (0.310-0.682)	0.221 (0.150-0.362)	0.052

The Mann-Whitney U test was applied. Significant p-values are shown in bold.
CAR: C-reactive protein-to-albumin ratio, CLDR: C-reactive protein-to-lactate dehydrogenase ratio, LCR: Lymphocyte-to-C-reactive protein ratio, CALLY: C-reactive protein-albumin-lymphocyte index

Table 2. ROC analysis of laboratory indices for predicting lymph node positivity

Index	AUC (95% CI)	Cut-off	Sensitivity (%)	Specificity (%)	p-value
CAR	0.622 (0.540-0.704)	0.375	58.0	58.0	0.014
CLDR	0.618 (0.535-0.698)	0.064	57.0	58.0	0.017
LCR	0.585 (0.502-0.662)	3.20	55.0	56.0	0.056
CALLY	0.573 (0.489-0.651)	4.10	55.0	54.0	0.052

ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval, CAR: C-reactive protein-to-albumin ratio, CLDR: C-reactive protein-to-lactate dehydrogenase ratio, LCR: Lymphocyte-to-C-reactive protein ratio, CALLY: C-reactive protein-albumin-lymphocyte index

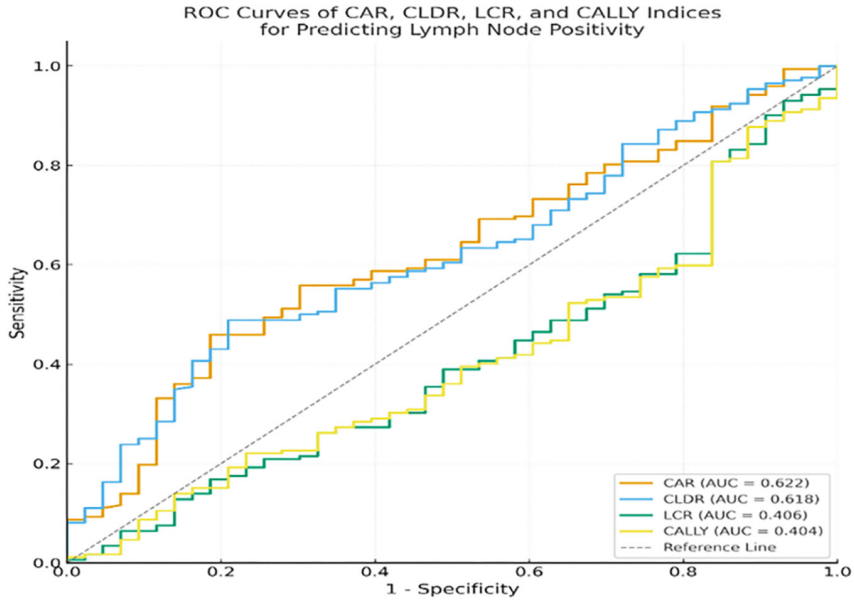

Figure 1. ROC curves of CAR, CLDR, LCR, and CALLY indices for predicting lymph node positivity
ROC: Receiver operating characteristic, CAR: C-reactive protein-to-albumin ratio, CLDR: C-reactive protein-to-lactate dehydrogenase ratio, LCR: Lymphocyte-to-C-reactive protein ratio, CALLY: C-reactive protein- albumin-lymphocyte index, AUC: Area under the curve

Table 3. Multivariate logistic regression analysis of predictors for lymph node positivity				
Variable		**OR**	**95% CI**	**p-value**
Age	-0.027	0.973	0.944-1.004	0.084
Sex (male)	0.051	1.052	0.467-2.370	0.903
Neoadjuvant therapy	-1.566	0.209	0.070-0.619	0.005
CAR	0.306	1.358	1.037-1.778	0.026
CLDR	2.992	19.931	1.688-235.309	0.018
LCR	0.054	1.055	0.824-1.351	0.634
CALLY	0.084	1.087	0.913-1.285	0.351
Model summary: χ^2=18.72, df=7, p<0.01, Nagelkerke R^2=0.286 OR: Odds ratio, CI: Confidence interval, CAR: C-reactive protein-to-albumin ratio, CLDR: C-reactive protein-to-lactate dehydrogenase ratio, LCR: Lymphocyte-to-C-reactive protein ratio, CALLY: C-reactive protein-albumin-lymphocyte index				

In the present study, four such indices were evaluated preoperatively to predict lymph node positivity. Among these, CAR and CLDR showed significant associations with nodal metastasis and remained independent predictors in multivariable analysis, even after adjusting for age, sex, and neoadjuvant therapy status. These findings highlight the importance of systemic inflammation and metabolic alterations in lymphatic spread. In contrast, LCR and CALLY demonstrated only borderline associations, suggesting weaker utility for preoperative assessment.

Our ROC analysis showed that CAR (AUC: 0.622) and CLDR (AUC: 0.618) had statistically significant but modest discriminative ability, with sensitivity and specificity around 58%. These results indicate that neither index alone is sufficient for reliable diagnosis, but that they may provide incremental value when combined with imaging and clinicopathological parameters.

The prognostic role of CAR has been consistently reported in gastric cancer, where it correlates with advanced stage, nodal involvement, and poor survival outcomes (18,19). As CRP reflects systemic inflammation and albumin indicates nutritional and functional status, CAR integrates two clinically relevant dimensions of host response. Importantly, our findings expand the evidence by identifying CLDR-a novel index incorporating CRP and LDH-as an independent predictor of nodal metastasis. LDH reflects tissue injury and tumor metabolism, and its integration with CRP may enhance risk stratification. To the best of our knowledge, this is one of the first studies to demonstrate the clinical relevance of CLDR in predicting lymph node involvement

in gastric cancer. These findings expand the current evidence by identifying CLDR as a promising biomarker and supporting its potential integration into predictive models for individualized clinical decision-making.

In contrast, prior research has suggested possible roles for LCR and CALLY in predicting prognosis and treatment response in gastrointestinal malignancies (20-22). However, our study indicates limited value for these indices in preoperative nodal assessment. Further large-scale, multicenter studies are warranted to confirm whether LCR and CALLY retain clinical significance in specific subgroups or when integrated into multi-parameter models.

Another strength of this study is that all laboratory parameters were obtained at diagnosis, before any therapy was initiated. This minimized the potential confounding effect of neoadjuvant treatment on biomarker levels. Subgroup analyses confirmed that including neoadjuvant therapy status in regression models did not alter the predictive significance of CAR and CLDR, reinforcing their role as baseline markers of disease biology.

Overall, our results demonstrate that CAR and CLDR are practical, inexpensive, and widely available biomarkers that can complement existing staging modalities. However, due to their modest accuracy, they should not be regarded as standalone diagnostic tools. Instead, integration of these indices into multimodal predictive strategies that combine imaging, histopathology, and clinical variables may offer improved accuracy and clinical applicability.

Study Limitations

This study has several limitations. First, its retrospective and single-center design may limit the generalizability of the findings. Although 215 patients were included, the sample size may still be insufficient to fully capture population heterogeneity, and larger multicenter cohorts are needed for validation. Second, while multivariable models adjusted for age, sex, and neoadjuvant therapy, other potentially relevant clinicopathological factors-such as tumor size, histology, or lymphovascular invasion-were unavailable and could not be included. Third, the diagnostic performance of the evaluated indices was modest, with AUC values below 0.70, restricting their role as standalone diagnostic tools. Finally, although some patients received neoadjuvant therapy, all laboratory measurements were obtained prior to treatment, minimizing confounding.

Despite these limitations, the study has notable strengths. It evaluated four easily obtainable, cost-effective laboratory indices in a relatively homogeneous cohort, and all measurements were performed before any therapy, ensuring reflection of baseline disease biology. Moreover, by demonstrating that both CAR and the novel CLDR independently predict lymph node positivity, this work contributes original evidence that may support the development of integrated predictive models in gastric cancer.

Conclusion

In this retrospective study, four inflammation- and nutrition-based indices were evaluated for their ability to predict lymph node positivity at the time of initial diagnosis in patients with gastric cancer. Among these, the CAR and the CLDR emerged as independent predictors, even after adjustment for age, sex, and neoadjuvant therapy. However, their modest diagnostic accuracy indicates that they should not be used as standalone tools. Instead, CAR and CLDR may provide complementary value when integrated with imaging and clinicopathological assessments to refine preoperative risk stratification.

As both indices are inexpensive, widely available, and based on routine laboratory parameters, their use may support more individualized surgical and treatment planning. Nevertheless, prospective multicenter studies with larger cohorts are required to validate these findings and to incorporate such biomarkers into clinically applicable predictive models.

Ethics

Ethics Committee Approval: Approval was obtained from the Bolu Abant Izzet Baysal University Non-Interventional Clinical Research Ethics Committee (approval no.: 2024/300, date: 19.11.2024).

Informed Consent: Retrospective, single-center observational study.

Footnotes

Authorship Contributions

Concept: M.F.K., F.B., M.S., Design: M.F.K., F.B., S.P.O., Data Collection or Processing: M.F.K., F.B., O.C., Analysis or Interpretation: M.F.K., F.B., B.O., Literature Search: M.F.K., F.B., S.P.O., M.S., Writing: M.F.K., F.B.

Conflicts of Interest: No conflict of interest were declared by the authors.

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