Gazi Med J 2026;37(4):538-543

**DOI:** http://dx.doi.org/10.12996/gmj.2026.4765

# Prognostic Significance of LODDS in Right-sided Colon Cancer: A Retrospective Analysis

## Sağ Taraflı Kolon Kanserinde LODDS'nin Prognostik Önemi: Retrospektif Bir Analiz

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**ABSTRACT**

**Objective:** The conventional tumor, node, metastasis (TNM) staging system for colorectal cancer possesses inherent limitations due to its dependence on lymph node dissection completeness. This study assessed the prognostic performance of the log odds of positive lymph nodes (LODDS) and lymph node ratio (LNR) against traditional TNM staging in patients who received curative resection for right-sided colon cancer.

**Methods:** We conducted a retrospective analysis of 132 patients who underwent curative resection for right-sided colon cancer between November 2014 and January 2020. LODDS and LNR were calculated and categorized using published cut-off values. Kaplan-Meier survival analysis and multivariable Cox proportional hazards regression identified independent predictors of 5-year mortality.

**Results:** During a median follow-up of 90.2 months, the 5-year overall survival rate was 50.2%. Multivariate Cox regression confirmed LODDS category, LNR category, AJCC stage, and patient age as independent predictors of 5-year mortality. Mortality hazard was markedly elevated for the highest-risk LODDS group [LODDS 2 versus LODDS 0: hazard ratio (HR) = 22.322; $p < 0.001$] compared to the highest LNR category (LNR 2 versus LNR 0: HR = 4.356; $p = 0.001$).

**Conclusion:** Both LODDS and LNR function as robust independent prognostic markers for 5-year mortality following curative resection for right-sided colon cancer. However, LODDS demonstrates superior discriminatory power in identifying patients at highest risk.

**ÖZ**

**Amaç:** Kolorektal kanserde geleneksel tümör, lenf düğümü, metastaz (TNM) evreleme sisteminin, lenf nodu diseksiyonunun yeterliliğine bağımlı olması nedeniyle bazı kısıtlılıkları bulunmaktadır. Bu çalışmada, sağ taraflı kolon kanseri nedeniyle küratif rezeksiyon uygulanan hastalarda Pozitif lenf nodlarının logaritmik odds oranı (LODDS) ve lenf nodu oranının (LNR) prognostik performansı geleneksel TNM evreleme sistemi ile karşılaştırılarak değerlendirildi.

**Yöntemler:** Kasım 2014 ile Ocak 2020 tarihleri arasında sağ taraflı kolon kanseri nedeniyle küratif rezeksiyon uygulanan 132 hastanın retrospektif analizi gerçekleştirildi. LODDS ve LNR değerleri hesaplandı ve daha önce yayımlanmış kesim noktaları kullanılarak kategorilere ayrıldı. Beş yıllık mortalitenin bağımsız belirleyicilerini saptamak amacıyla Kaplan-Meier sağkalım analizi ve çok değişkenli Cox orantısal riskler regresyon analizi uygulandı.

**Bulgular:** Ortanca 90,2 aylık takip süresinde beş yıllık genel sağkalım oranı %50,2 olarak bulundu. Çok değişkenli Cox regresyon analizi, LODDS kategorisi, LNR kategorisi, AJCC evresi ve hasta yaşının beş yıllık mortalitenin bağımsız belirleyicileri olduğunu doğruladı. En yüksek riskli LODDS grubunda mortalite riski, en yüksek LNR kategorisine kıyasla belirgin olarak daha yüksekti [LODDS 2 ve LODDS 0 karşılaştırması: risk oranı (HR) = 22,322; $p < 0,001$; LNR 2 ve LNR 0 karşılaştırması: HR = 4,356; $p = 0,001$].

**Sonuç:** Hem LODDS hem de LNR, sağ taraflı kolon kanserinde küratif rezeksiyon sonrasında beş yıllık mortalite açısından güçlü ve bağımsız

**Cite this article as:** Aksu E, Yavuz A, Yıldırım SC, Bostancı H, Dikmen K, Göbüt H, et al. Prognostic significance of LODDS in right-sided colon cancer: a retrospective analysis. Gazi Med J. 2026;37(4):538-543

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**Received/Geliş Tarihi:** 10.07.2026
**Accepted/Kabul Tarihi:** 28.09.2026
**Publication Date/Yayınlanma Tarihi:** 15.10.2026

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**ABSTRACT**

Incorporating LODDS into clinical assessment could enhance risk stratification and inform adjuvant treatment strategies.

**Keywords:** Right-sided colon cancer, log odds of positive lymph nodes (LODDS), lymph node ratio (LNR), prognosis, survival analysis

**ÖZ**

prognostik belirteçler olarak işlev görmektedir. Bununla birlikte, LODDS, en yüksek risk taşıyan hastaların belirlenmesinde daha üstün ayırt edici güce sahiptir. LODDS'nin klinik değerlendirmeye dahil edilmesi, risk sınıflandırmasının geliştirilmesine ve adjuvan tedavi stratejilerinin belirlenmesine katkı sağlayabilir.

**Anahtar Sözcükler:** Sağ taraflı kolon kanseri, pozitif lenf nodlarının logaritmik odds oranı (LODDS), lenf nodu oranı (LNR), prognoz, sağkalım analizi

## INTRODUCTION

Colorectal cancer (CRC) remains one of the most prevalent malignancies and a major contributor to cancer-related deaths worldwide (1,2). Precise staging forms the cornerstone of prognostic evaluation and therapeutic planning. The American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) classification serves as the internationally recognized benchmark, with regional lymph node involvement (N-stage) consistently identified as the paramount determinant of survival (3).

Despite widespread adoption, the TNM N-stage classification has inherent limitations. Its principal constraint is dependency solely on the absolute number of positive lymph nodes. When inadequate lymphadenectomy yields fewer than the AJCC-recommended 12 nodes for pathological assessment, the risk of pathological under-staging increases, potentially leading to suboptimal treatment decisions (4). Furthermore, significant prognostic heterogeneity exists among patients within the same N-stage category when total nodes examined differ.

Alternative staging systems have been proposed to address these shortcomings. The lymph node ratio (LNR) represents the simple proportion of positive nodes relative to total retrieved nodes. The Log Odds of Positive Lymph Nodes (LODDS) offers a more sophisticated measure, defined by the formula: LODDS = log [(p + 0.5) / (n + 0.5)], where p is the number of positive nodes and n is the number of negative nodes. By integrating both components of nodal harvest, LODDS demonstrates superior statistical stability and prognostic reliability, especially in cases with limited lymph node yield (5,6).

The prognostic superiority of LODDS has been established across several malignancies, including gastric, breast, and rectal cancers (7-9). CRC is increasingly recognized not as a single entity, but as two distinct diseases: Right-sided and left-sided tumors, each with unique biological and clinical profiles. Right-sided colon cancers (RCC), originating from the cecum, ascending colon, and hepatic flexure, are frequently diagnosed at more advanced stages, exhibit distinct molecular characteristics, and are associated with poorer prognosis (10,11).

While the prognostic value of LODDS has been explored in pooled CRC cohorts and specifically in rectal cancer, its comparative performance against TNM staging and LNR has not been rigorously assessed in a cohort dedicated exclusively to RCC. The primary aim of this study was to evaluate the independent prognostic value of the LODDS system for long-term survival following curative resection for RCC, comparing its performance directly with conventional TNM stage and LNR.

## MATERIALS AND METHODS

### *Study Design and Patient Cohort*

We included patients who received an initial primary diagnosis of adenocarcinoma and subsequently underwent right hemicolectomy between November 2014 and January 2020. Right-sided colon tumors were anatomically defined as those located in the cecum, ascending colon, or hepatic flexure.

**Inclusion Criteria:**

(1) Primary pathological diagnosis of adenocarcinoma;

(2) History of undergoing right hemicolectomy;

(3) Achievement of curative-intent resection (R0);

(4) Minimum of 12 lymph nodes retrieved and examined postoperatively.

**Exclusion Criteria:**

(1) Familial adenomatous polyposis or Lynch syndrome;

(2) Age under 18 years;

(3) Synchronous tumors, peritoneal dissemination, or distant metastatic disease at diagnosis (Stage IV);

(4) Emergent surgery for perforation or obstruction;

(5) Death within the immediate postoperative period (first 30 days);

(6) Fewer than 12 lymph nodes harvested.

### *Parameters Investigated*

We collected demographic information (gender, age), tumor-specific characteristics (location, size, differentiation grade, lymphovascular and perineural invasion), surgical details, and long-term survival outcomes.

### *Staging Systems Evaluated*

Three distinct lymph node staging systems were compared:

**1. TNM stage:** Patients were staged according to AJCC 8$^{th}$ edition criteria (N0, N1a, N1b, N2a, N2b).

**2. LNR:** Calculated by dividing positive lymph nodes by total retrieved nodes. LNR values were stratified into three categories: LNR 0 (≤0.05), LNR 1 (>0.05 to ≤0.2), and LNR 2 (>0.2) (8).

**3. Log odds of positive nodes (LODDS):** Computed using the formula: log [(pnod + 0.5) / (tnod + 0.5)]. LODDS values were categorized into three groups: LODDS 0 (≤-1.36), LODDS 1 (>-1.36 to ≤-0.53), and LODDS 2 (>-0.53). These cut-off points were selected based on values demonstrated to hold prognostic significance in large-scale studies (5,8).

This single-center, retrospective cohort study was conducted at Gazi University, Faculty of Medicine Hospital. The study protocol adhered to the principles outlined in the Declaration of Helsinki and received approval from the Local Ethics Committee of Gazi University (approval number: E-77082166-604.01-1451101, date: 13/01/2026). Informed consent was obtained from all individual participants included in the study.

### *Statistical Analysis*

Statistical analyses were performed using IBM SPSS Statistics 27. Continuous data are presented as mean ± standard deviation or median (range); categorical variables as frequencies (%). Normality was assessed with the Kolmogorov-Smirnov test. Group comparisons used the Independent Sample t-test (normal distribution) or the Mann-Whitney U test (non-normal). Pearson's $\chi^2$ test analyzed qualitative variable associations. Survival was analyzed via Kaplan-Meier with Log-Rank test comparison. Independent prognostic factors were identified using Cox proportional hazards regression (Backward:LR method). The prognostic efficacy of TNM N-stage, LNR, and LODDS was compared using ROC curve analysis, calculating the AUC for each. A p-value < 0.05 was considered statistically significant.

## RESULTS

The study cohort comprised 132 patients who underwent curative resection for right-sided colon cancer, consisting of 70 (53.0%) male and 62 (47.0%) female patients. Mean age at surgery was 64.11 ± 12.92 years. Most tumors were classified as moderately (55.3%) or well-differentiated (26.5%). According to AJCC staging, 43.9% were Stage 2 and 40.9% were Stage 3. The mean number of lymph nodes retrieved per patient was 35.36 ± 15.99, with a mean of 1.46 ± 3.09 metastatic lymph nodes identified. Median follow-up duration was 90.2 months, and the 5-year overall survival rate was 50.2%. The demographic and clinical characteristics of this patient population are detailed in Table 1.

**Table 1.** Baseline patient demographics and clinical characteristics.

| Variable (n = 132) | n | | % | |
|---|---|---|---|---|
| **Gender** | | | | |
| Female | 62 | | 47.0 | |
| Male | 70 | | 53.0 | |
| **Differentiation** | | | | |
| Poor | 24 | | 18.2 | |
| Moderate | 73 | | 55.3 | |
| Well | 35 | | 26.5 | |
| **Dukes category** | | | | |
| A | 20 | | 15.2 | |
| B1 | 52 | | 39.4 | |
| B2 | 6 | | 4.5 | |
| C1 | 36 | | 27.3 | |
| C2 | 18 | | 13.6 | |
| **Stage** | | | | |
| 1 | 20 | | 15.2 | |
| 2 | 58 | | 43.9 | |
| 3 | 54 | | 40.9 | |
| **LODDS** | | | | |
| 0 | 86 | | 65.2 | |
| 1 | 41 | | 31.1 | |
| 2 | 5 | | 3.7 | |
| **LNR** | | | | |
| 0 | 103 | | 78.0 | |
| 1 | 19 | | 14.4 | |
| 2 | 9 | | 6.8 | |
| **Quantitative variables** | | **Median** | **Min.** | **Max.** |
| Age at operation | 64.11 ± 12.92 | 66.0 | 28.0 | 89.0 |
| Number of resected lymph nodes | 35.36 ± 15.99 | 31.0 | 12.0 | 91.0 |
| Number of metastatic lymph nodes | 1.46 ± 3.09 | 0.0 | 0.0 | 20.0 |
| Tumor diameter (mm) | 55.80 ± 25.36 | 50.0 | 2.0 | 130.0 |

LNR: Lymph node ratio, LODDS: Log odds of positive lymph nodes, Min.: Minimum, Max.: Maximum.

### *Univariate Analysis*

Univariate analysis revealed no significant association between survival and gender or tumor differentiation ($p > 0.05$). However, survival was strongly correlated with Dukes Category ($\chi^2 = 25.955$; $p < 0.001$) and AJCC Stage ($\chi^2 = 21.435$; $p < 0.001$). Significant relationships were also found for LODDS Category ($\chi^2 = 12.426$; $p = 0.002$), with LODDS 0 showing higher survival than categories 1-2, and for LNR Category ($\chi^2 = 12.525$; $p = 0.002$). Deceased patients had significantly more metastatic lymph nodes ($p < 0.001$) and were older at surgery ($p = 0.041$) compared to survivors. No significant differences were observed in total retrieved lymph nodes or tumor size ($p > 0.05$). These results are summarized in Table 2.

### *Multivariate Analysis*

In multivariate analysis, LODDS category, LNR category, AJCC Stage, and age at operation emerged as independent predictors of 5-year mortality ($p < 0.05$). After adjustment, LODDS category remained a significant prognostic factor. Compared to LODDS 0, the mortality hazard was 2.319 times higher for LODDS 1 [95% confidence interval (CI): 1.225-4.390; $p = 0.010$] and 22.322 times higher for LODDS 2 (95% CI: 6.552-76.052; $p < 0.001$). Similarly, LNR category was an independent prognostic factor, with LNR 1 [hazard ratio (HR) = 2.977; 95% CI: 1.463-6.060; $p = 0.003$] and LNR 2 (HR = 4.356; 95% CI: 1.774-10.693; $p = 0.001$) associated with increased risk versus LNR 0. AJCC stage also retained significance: Stage 2 (HR = 1.955; 95% CI: 1.235-3.095; $p = 0.004$) and Stage 3 (HR = 2.963; 95% CI: 1.952-4.497; $p < 0.001$) showed elevated mortality risk relative to Stage 1 (Table 3).

## DISCUSSION

Accurate prognostic stratification is essential for adjuvant therapy decisions following resection for CRC. Our findings underscore a key limitation of conventional TNM N-stage: Its dependence on the absolute count of positive nodes, which renders it unreliable when lymph node retrieval is suboptimal (4). In contrast, this study

**Table 2.** Investigation of the relationship between general characteristics and survival status.

| Survival variable | Survived (n = 85) | | EX (n = 47) | | Statistical analysis* |
|---|---|---|---|---|---|
| | n | % | n | % | |
| **Gender** | | | | | |
| Female | 38 | 44.7 | 24 | 51.1 | $\chi^2 = 0.491$ |
| Male | 47 | 55.3 | 23 | 48.9 | p = 0.483 |
| **Differentiation** | | | | | |
| Poor | 15 | 17.6 | 9 | 19.1 | $\chi^2 = 3.478$ |
| Moderate | 43 | 50.6 | 30 | 63.9 | p = 0.176 |
| Well | 27 | 31.8 | 8 | 17.0 | |
| **Dukes category** | | | | | |
| A | 20 | 23.5 | - | - | $\chi^2 = 25.955$ |
| B1 | 38 | 44.7 | 14 | 29.8 | **p < 0.001** |
| B2 | 3 | 3.5 | 3 | 6.4 | |
| C1 | 19 | 22.4 | 17 | 36.2 | |
| C2 | 5 | 5.9 | 13 | 27.6 | |
| **Stage** | | | | | |
| 1 | 20 | 23.6 | - | - | $\chi^2 = 21.435$ |
| 2 | 41 | 48.2 | 17 | 36.2 | **p < 0.001** |
| 3 | 24 | 28.2 | 30 | 63.8 | |
| **LODDS** | | | | | |
| 0 | 64 | 75.3 | 22 | 46.8 | $\chi^2 = 12.426$ |
| 1 | 20 | 23.5 | 21 | 44.7 | **p = 0.002** |
| 2 | 1 | 1.2 | 4 | 8.5 | |
| **LNR** | | | | | |
| 0 | 74 | 88.1 | 29 | 61.7 | $\chi^2 = 12.525$ |
| 1 | 7 | 8.3 | 12 | 25.5 | **p = 0.002** |
| 2 | 3 | 3.6 | 6 | 12.8 | |

*Statistical analysis: Pearson-$\chi^2$ (chi-square) cross tabulation was used to examine the relationship between two categorical variables. LNR: Lymph node ratio, LODDS: Log odds of positive lymph nodes.

demonstrates that both LNR and, more powerfully, LODDS provide robust independent prognostic value in right-sided colon cancer.

Multivariate Cox regression confirmed that LODDS category, LNR category, and AJCC stage are all independent predictors of 5-year mortality in RCC. This finding robustly supports our hypothesis that ratio-based staging systems, particularly LODDS and LNR, provide prognostic information comparable to—and potentially more robust than—traditional N-stage for right-sided colon cancers (5,6,12).

The principal finding of this study is the superior prognostic stratification offered by LODDS compared to LNR. The hazard for mortality in the highest LODDS category was 22.322 times greater than the lowest category, whereas the corresponding hazard for the highest LNR category was 4.356-fold. This enhanced performance is explained by the mathematical properties of the LODDS formula, which incorporates both positive and negative nodal counts into a continuous logarithmic metric, conferring greater stability against variations in total lymph node yield (5,6). Consequently, LODDS maintains prognostic accuracy in cohorts with heterogeneous lymphadenectomy, an advantage documented in colorectal and gastric cancers where it provides superior survival curve discrimination versus traditional N-staging (5,6,12). Its robustness as a prognostic indicator has been replicated in breast and other solid tumors (8,9,13,14). Our findings extend this evidence by specifically validating the high discriminatory capacity of LODDS in right-sided colon cancer.

Our analysis confirmed LNR as an independent prognostic factor, with significantly increased mortality hazard in its highest category. A critical limitation, however, is its inability to stratify the substantial subset of lymph node-negative patients, for whom LNR is uniformly zero. LODDS addresses this deficit by incorporating the denominator of negative nodes into a continuous variable, thereby unmasking prognostic heterogeneity within node-negative cohorts and offering more granular risk assessment than either N-stage or LNR (7,15,16). Although some reports suggest prognostic equivalence between LNR and LODDS (15,16), the broader literature, including larger series, indicates that LODDS provides superior discrimination, particularly for high-risk stratification (5,13,14).

**Table 3.** Independent risk factors associated with 5-year mortality (Cox regression analysis).

| Variables | B | S.H. | Wald | SD | p | HR | 95% confidence interval (HR) | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower | Higher |
| **LODDS 0*** | | | 26.511 | 2 | **<0.001** | | | |
| **LODDS 1** | 0.841 | 0.326 | 6.668 | 1 | **0.010** | 2.319 | 1.225 | 4.390 |
| **LODDS 2** | 3.106 | 0.625 | 24.654 | 1 | **<0.001** | 22.322 | 6.552 | 76.052 |
| **LNR 0*** | | | 15.535 | 2 | **<0.001** | | | |
| **LNR 1** | 1.091 | 0.363 | 9.054 | 1 | **0.003** | 2.977 | 1.463 | 6.060 |
| **LNR 2** | 1.471 | 0.458 | 10.311 | 1 | **0,001** | 4.356 | 1.774 | 10.693 |
| **Stage 1*** | | | 13.818 | 2 | **<0.001** | | | |
| **Stage 2** | 0.671 | 0.234 | 8.184 | 1 | **0.004** | 1.955 | 1.235 | 3.095 |
| **Stage 3** | 1.086 | 0.213 | 26.040 | 1 | **<0.001** | 2.963 | 1.952 | 4.497 |
| Age at operation | 0.065 | 0.015 | 18.122 | 1 | **<0.001** | 1.067 | 1.036 | 1.100 |

*: Reference category, SD: Standard deviation, HR: Hazard ratio, LNR: Lymph node ratio, LODDS: Log odds of positive lymph nodes.

Right- and left-sided colon cancers are now recognized as biologically and clinically distinct entities. Right-sided colon cancers are frequently diagnosed at more advanced stages, harbor distinct molecular profiles, and portend poorer prognosis (10,11). Much of the existing literature on LODDS has evaluated CRC as a homogeneous group or focused on rectal cohorts (14,15,17). A primary strength of this study is its exclusive focus on RCC, enabling precise assessment of LODDS and LNR within this specific anatomical subset. This approach is supported by work suggesting lymph node-related metrics are particularly influential for survival outcomes in right-sided tumors (11). Consequently, our findings indicate that LODDS can offer clinicians critical adjunctive data to personalize adjuvant therapy and identify high-risk patients within the RCC population.

Our finding that age at operation is an independent prognostic variable aligns with the established association between advanced age and inferior survival in RCC. This relationship may be mediated by higher prevalence of comorbidities, physiological frailty, and reduced tolerance to adjuvant regimens. Although the number of positive nodes retained its expected prognostic significance in univariate analysis, both LODDS and LNR demonstrated enhanced capacity for refined risk classification. Therefore, these results argue for clinical implementation of LODDS and LNR as complementary or alternative tools to N-stage, facilitating a more nuanced approach to adjuvant therapy planning and surveillance in RCC.

### *Study Limitations*

This study has several limitations. Its retrospective, single-center design carries inherent biases and may limit generalizability. The statistical power for the highest-risk categories (LODDS 2 and LNR 2) is constrained by their small subgroup sizes. Although overall survival was the primary endpoint, disease-free survival data would have better assessed recurrence risk. Furthermore, our model did not incorporate established clinicopathological and molecular prognostic factors, such as microsatellite instability (MSI) status.

## CONCLUSION

This study confirms that both LODDS and LNR are independent prognostic factors for 5-year mortality after curative resection of right-sided colon cancer, independent of AJCC Stage. Notably, LODDS demonstrated a superior ability to identify the highest-risk subgroup (LODDS 2), with a HR of 22.322. These results suggest that LODDS may serve as a valuable complement, or even a superior alternative, to the TNM system for prognostic assessment and personalization of adjuvant therapy. Incorporating LODDS into routine clinical practice could refine risk stratification and optimize treatment. Prospective multicenter studies are needed to validate these findings and integrate LODDS into standard decision-making algorithms and should incorporate disease-free survival as a primary endpoint alongside molecular markers such as MSI and KRAS mutation status, which were not assessed in the present study.

### *Ethics*

**Ethics Committee Approval:** The study protocol adhered to the principles outlined in the Declaration of Helsinki and received approval from the Local Ethics Committee of Gazi University (approval number: E-77082166-604.01-1451101, date: 13/01/2026).

**Informed Consent:** Informed consent was obtained from all individual participants included in the study.

### *Footnotes*

Preliminary results from this study were presented as a oral presentation at TSCRS, Antalya, Türkiye, May 16-20, 2025.

### *Authorship Contributions*

Surgical and Medical Practice: K.D., O.Y., Concept: S.A., H.B., Design: E.A., O.Y., Data Collection or Processing: S.C.Y., K.D., Analysis or İnterpretation: E.A., A.Ç.B., Literature Search: S.C.Y., A.Y., Wrighting: E.A., S.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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