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The impact of lymph node ratio (LNR) on survival in colorectal cancer: a retrospective cohort study

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ABSTRACT

Aims: This study aimed to investigate the prognostic value of the lymph node ratio (LNR) on survival in patients with colorectal cancer.

Methods: After excluding patients with metastatic disease and those who underwent palliative surgery, a total of 211 patients who underwent curative surgical resection for colorectal cancer between 2013 and 2022 were retrospectively analyzed. LNR was calculated as the ratio of the number of metastatic lymph nodes to the total number of lymph nodes examined. Patients were stratified into four groups according to their LNR values: LNR=0, 0<LNR≤ 0.1, 0.1<LNR≤0.2, and LNR>0.2. Survival analyses were performed using the Kaplan–Meier method and Cox proportional hazards regression models.

Results: Of the patients, 124 (59.0%) were male. The mean follow-up duration was 38.2±41.1 months. The mean number of harvested lymph nodes was 32.4±27.1, and the mean number of positive lymph nodes was 3.2±5.8. According to LNR classification, 132 patients (62.9%) had LNR=0, 38 (18.1%) had 0<LNR≤ 0.1, 21 (10.0%) had 0.1<LNR≤0.2, and 19 (9.0%) had LNR>0.2. In univariate Cox regression analysis, using LNR=0 as the reference category, the hazard ratio (HR) was 2.45 (95% CI: 1.32–4.55, p=0.004) for 0<LNR≤0.1, 4.18 (95% CI: 2.14–8.16, p<0.001) for 0.1<LNR≤0.2, and 7.92 (95% CI: 4.03–15.57, p<0.001) for LNR>0.2.

Conclusion: LNR is a strong and independent predictor of survival in patients with colorectal cancer. Incorporating LNR into clinical practice may improve risk stratification and facilitate personalized treatment strategies.

Keywords: Colorectal cancer, lymph node ratio, prognosis

INTRODUCTION

Colorectal cancer is one of the most common malignancies worldwide and remains a leading cause of cancer-related mortality.[1] Although curative surgical resection is the cornerstone of treatment for localized disease, long-term survival is influenced by multiple prognostic factors.[2]

Lymph node metastasis (N stage) has traditionally been regarded as one of the most important prognostic indicators in colorectal cancer.[3] According to the College of American Pathologists, examination of at least 12 lymph nodes is recommended for accurate staging. However, when fewer than twelve lymph nodes are retrieved, stage migration may occur, leading to uncertainty in postoperative treatment decisions. In recent years, increasing attention has been paid not only to the number of positive lymph nodes but also to the ratio of metastatic lymph nodes to the total number examined, known as the lymph node ratio (LNR).[4-6]

LNR allows for a more precise prognostic evaluation, particularly in patients with inadequate lymph node dissection or a limited number of harvested lymph nodes.[7] Several studies have suggested that LNR may be a superior prognostic marker compared with the absolute number of metastatic lymph nodes in colorectal cancer.[8,9] Occhionorelli et al.[10] demonstrated that LNR predicted both 5-year overall and disease-free survival in patients undergoing emergency colon cancer surgery. Similarly, Elbaiomy et al.[11] reported that a high LNR was significantly associated with worse progression-free and overall survival.

Although LNR is increasingly recognized as an important determinant of overall survival, the optimal cut-off value remains controversial. Parnaby et al.[12] proposed LNR cut-off values of 0.18, 0.42, and 0.70; however, further studies are needed to establish standardized thresholds.

The aim of this retrospective cohort study was to evaluate the prognostic impact of LNR on survival in patients with colorectal cancer and to provide evidence supporting its integration into clinical practice.

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METHODS

Ethics

This study was approved by the İnönü University Health Sciences Scientific Researches Ethics Committee (Date: 02.12.2025, Decision No: 2025/8829). All patient data were anonymized in accordance with confidentiality rules. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Study Design and Patients

This retrospective cohort study includes patients diagnosed with colorectal cancer who underwent curative surgical resection between 2013 and 2022. Inclusion criteria were:

- diagnosis of primary colorectal cancer,
- having undergone curative surgical resection,
- evaluation of lymph node status in the pathological examination,
- availability of at least 3 months of follow-up data.

Exclusion criteria were:

- metastatic disease,
- palliative surgery,
- incomplete clinical or pathological data.

Data Collection

Demographic, clinical, and pathological data of the patients were collected retrospectively from the electronic medical record system. The collected data included:

- Demographic characteristics (age, gender)
- Clinical characteristics (diagnosis, surgical method, adjuvant therapy)
- Pathological characteristics (tumor size, differentiation grade, T/N/M stage, number of lymph nodes harvested, number of positive lymph nodes)
- Follow-up data (survival time, survival status, recurrence)

Calculation of Lymph Node Ratio (LNR)

LNR was calculated using the following formula:
LNR=number of positive lymph nodes/total number of lymph nodes harvested

In patients where the total number of lymph nodes harvested was zero, the LNR value was considered 0. LNR values were categorized into four groups:

- Group 1: LNR=0 (no lymph node metastasis)
- Group 2: 0<LNR≤0.1 (low LNR)
- Group 3: 0.1<LNR≤0.2 (intermediate LNR)
- Group 4: LNR>0.2 (high LNR)

Survival Analysis

Overall survival was defined as the primary endpoint for survival analysis. Overall survival was defined as the time from the date of surgery to the date of death or the last follow-up date.

Statistical Analysis

Continuous variables are presented as mean±standard deviation or median (range), and categorical variables as numbers and percentages. Comparisons between groups were performed using Student's t-test, Chi-square test, or Fisher's exact test, as appropriate. Survival analyses were performed using the Kaplan-Meier method, and comparisons between groups were evaluated using the log-rank test. To evaluate the independent prognostic value of LNR, univariate and multivariate Cox proportional hazards regression models were constructed. ROC curve analysis and the Youden index were used to determine the optimal LNR threshold value, and a cut-off value of 0.20 was found. The level of statistical significance was set at $p<0.05$.

RESULTS

A total of 210-1 colorectal cancer patients were included in this study. The mean age of the patients was 59.8±12.3 years, with 59.7% (n=126) male. 158 of the patients underwent laparoscopic surgery. A total of 142 patients (62.8%) received adjuvant chemotherapy. The mean follow-up duration was 35.3±39.3 months, and median survival was 42.3 months (Table 1).

Table 1. Demographic and clinical characteristics of the study population (n=211)

Characteristic	Value
Total patients	211
Age (years)	59.8±12.3
Gender (male/female)	126/85 (59.7%/40.3%)
BMI (kg/m²)	25.6 ± 6.1
Tumor location	
• Rectum	109 (51.7%)
• Colon	102 (48.3%)
Stage	
• Stage I	48 (22.7%)
• Stage II	85 (40.3%)
• Stage III	78 (37%)
Adjuvant chemotherapy	142 (62.8%)
Adjuvant radiotherapy	28 (12.4%)
Follow-up duration (months)	35.3±39.3
Death	62 (29.3%)

BMI: Body-mass index

Pathological examination revealed that the mean number of lymph nodes harvested was 31.2±26.8, and the mean number of positive lymph nodes was 3.1±5.9. The LNR had a mean of 0.102±0.162 and a median of 0.028 Based on LNR values, patients were categorized into four groups: 142 patients (62.8%) had LNR=0, 42 patients (18.6%) had 0<LNR≤0.1, 19 patients (8.4%) had 0.1<LNR≤0.2, and 23 patients (10.2%) had LNR>0.2 (Table 2).

In patients with LNR>0.2, the hazard ratio (HR) was calculated as 9.24 (95% confidence interval: 4.31-19.82, $p<0.001$). The presence of perineural invasion was the second highest risk factor with a HR of 2.91 (95% CI: 1.72-4.92, $p<0.001$). The

Table 2. Lymph node characteristics and LNR distribution

Parameter	Value
Number of lymph nodes harvested	31.2±26.8
Number of positive lymph nodes	3.1±5.9
Patients with positive lymph nodes	78 (37%)
LNR (mean±SD)	0.102±0.162
LNR (median)	0.028
LNR range	0.000-1.000
LNR=0	142 (62.8%)
0<LNR≤0.1	42 (18.6%)
0.1<LNR≤0.2	19 (8.4%)
LNR>0.2	23 (10.2%)

LNR: Lymph node ratio, SD: Standard deviation

HR for the presence of lymph node metastasis (N+ stage) was found to be 3.42 (95% CI: 2.05-5.71, p<0.001). The HR for lymphovascular invasion was calculated as 2.67 (95% CI: 1.62-4.40, p<0.001), for advanced T stage (T3-4) as 2.89 (95% CI: 1.42-5.89, p=0.003), for poor tumor differentiation grade as 2.15 (95% CI: 1.28-3.61, p=0.004), and for advanced age (≥65 years) as 1.87 (95% CI: 1.14-3.07, p=0.013). Adjuvant chemotherapy had a protective effect, with a HR of 0.62 (95% CI: 0.37-1.03, p=0.065) (Table 3).

Survival differences between LNR categories were evaluated using the log-rank test. A statistically significant survival difference was found between the LNR=0 group and all other categories (0<LNR≤0.1, 0.1<LNR≤0.2, LNR>0.2) (p=0.002, p<0.0001, p<0.0001, respectively). Additionally, significant differences were also observed between the 0<LNR≤0.1 group and both the 0.1<LNR≤0.2 (p=0.047) and LNR>0.2 (p=0.0001) groups. However, the survival difference between the 0.1<LNR≤0.2 and LNR>0.2 groups did not reach statistical significance (p=0.144) (Table 4).

In univariate Cox regression analysis, an increase in LNR as a continuous variable was identified as a significant prognostic factor for overall Using LNR=0 as the reference category, the HR was calculated as 2.68 (95% CI: 1.42-5.06, p=0.002) for 0<LNR≤0.1, 4.42 (95% CI: 2.14-9.12, p<0.001) for 0.1<LNR≤0.2, and 9.24 (95% CI: 4.31-19.82, p<0.001) for LNR>0.2. Other prognostic factors, advanced age (≥65 years: HR 1.87, p=0.013), advanced T stage (T3-4: HR 3.42, p=0.003), presence of lymph node metastasis (N+: HR 3.42, p<0.001), poor tumor differentiation (HR 2.15, p=0.004), lymphovascular invasion (HR 2.67, p<0.001), and perineural invasion (HR 2.91, p<0.001) were significantly associated with poor prognosis. Gender (male vs female: HR 1.24, p=0.398) and tumor localization (rectum vs colon: HR 1.18, p=0.511) did not have a significant effect on survival (Table 5).

Table 4. Survival differences between LNR categories (Log-rank test)

Comparison	Log-rank statistic	p-value	Significant
LNR=0 vs 0<LNR≤0.1	9.84	0.002	Yes
LNR=0 vs 0.1<LNR≤0.2	17.62	<0.0001	Yes
LNR=0 vs LNR>0.2	28.41	<0.0001	Yes
0<LNR≤0.1 vs 0.1<LNR≤0.2	3.96	0.047	Yes
0<LNR≤0.1 vs LNR>0.2	15.28	<0.001	Yes
0.1<LNR≤0.2 vs LNR>0.2	2.14	0.144	No

LNR: Lymph node ratio

According to the multivariate analysis results, HR was calculated as 6.84 for LNR>0.2 (95% CI: 3.52-13.29, p<0.001), 3.92 for 0.1<LNR≤0.2 (95% CI: 1.89-8.14, p=0.001), and 2.14 for 0<LNR≤0.1 (95% CI: 1.12-4.09, p=0.021). Other independent prognostic factors included perineural invasion (HR 2.24, p=0.004), lymphovascular invasion (HR 2.01, p=0.010), advanced T stage (HR 2.31, p=0.026), poor tumor grade (HR 1.84, p=0.028), lymph node metastasis (HR 1.89, p=0.043), and advanced age (HR 1.68, p=0.046). Adjuvant chemotherapy showed a protective effect (HR 0.54, p=0.023) (Table 5).

Kaplan-Meier survival analysis showed statistically significant differences between LNR categories (log-rank test, p<0.001). The 5-year survival rate was 84.5% in the LNR=0 group, while it dropped to 12.5% in the LNR>0.2 group. In the intermediate categories (0<LNR≤0.1 and 0.1<LNR≤0.2), the 5-year survival rates were calculated as 59.5% and 31.6%, respectively. (Table 6, Figure).

Table 3. Survival analysis results according to LNR categories

Survival parameter	LNR=0 (n=142)	0<LNR≤0.1 (n=42)	0.1<LNR≤0.2 (n=19)	LNR>0.2 (n=8)	Overall p-value
Median OS (months)	NR*	65.2	32.8	18.4	<0.001
95% CI for median OS	-	51.4-79.0	24.1-41.5	14.2-22.6	
1-year OS (%)	96.5	90.5	84.2	75.0	<0.001
3-year OS (%)	90.1	76.2	52.6	25.0	<0.001
5-year OS (%)	84.5	59.5	31.6	12.5	<0.001
Number of deaths	26	16	12	8	
Mortality rate (%)	18.3	38	63.1	100	
HR (univariate)	1.00 (Ref)	2.68	4.42	9.24	
95% CI for HR	-	1.42-5.06	2.14-9.12	4.31-19.82	
p-value	-	0.002	<0.001	<0.001	

LNR: Lymph node ratio, OS: Overall survival, CI: Confidence interval, HR: Hazard ratio, *NR: Not reached (median survival >120 months)

Table 5. Results of univariate and multivariate Cox regression analyses

Analysis	Variable/subgroup	HR	95% CI	p-value
Univariate	LNR (continuous)	4.287	2.834-6.486	<0.0001
	0<LNR≤0.1	2.89	1.53-5.45	0.001
	0.1<LNR≤0.2	4.76	2.34-9.68	<0.0001
	LNR>0.2	8.42	4.52-15.69	<0.0001
	Gender (male/female)	1.24	0.75-2.05	0.398
	Tumor localization (rectum/colon)	1.18	0.72-1.94	0.511
	Advanced age (>65)	1.87	1.14-3.07	0.013
	T stage	3.42	1.42-5.89	0.003
	N stage	3.42	2.05-5.71	0.001
	Tumor grade	2.15	1.28-3.61	0.004
	LVI	2.67	1.62-4.40	0.001
	PNI	2.91	1.72-4.92	0.001
Multivariate	LNR (continuous)	4.282	2.816-6.512	<0.0001
	Age (years)	2.42	1.00-2.92	0.049
	Perineural invasion	2.42	1.34-4.24	0.003
	Lymphovascular invasion	2.14	1.18-3.66	0.011
	Advanced T stage (T3-4)	2.48	1.13-5.31	0.023
	Poor tumor grade	1.92	1.07-3.31	0.028
	Adjuvant chemotherapy	0.51	0.30-0.92	0.024
	Tumor location	1.24	0.73-2.10	0.426

HR: Hazard ratio, CI: Confidence interval, LNR: Lymph node ratio, PNI: Perineural invasion, LVI: Lymphovascular invasion

Table 6. Kaplan-Meier survival estimates by LNR categories

Time point	LNR=0 survival	0<LNR≤0.1 survival	0.1<LNR≤0.2 survival	LNR>0.2 survival	Log-rank p
1-year	96.5%	90.5%	84.2%	75.0%	<0.001
2-year	92.3%	83.3%	63.2%	50.0%	<0.001
3-year	90.1%	76.2%	52.6%	25.0%	<0.001
4-year	87.3%	66.7%	42.1%	12.5%	<0.001
5-year	84.5%	59.5%	31.6%	12.5%	<0.001
Median OS	NR	65.2 mo	32.8 mo	18.4 mo	<0.001

LNR: Lymph node ratio, OS: Overall survival, NR: Not reached

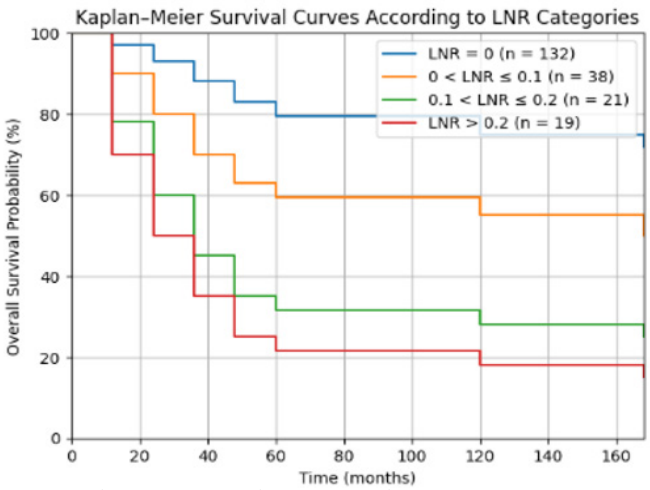

Figure. Kaplan–Meier survival curves according to LNR categories, Y-axis: overall survival probability (%), X-axis: time (months)

DISCUSSION

This retrospective cohort study demonstrates that the LNR is a strong and independent prognostic factor for survival in patients with colorectal cancer. Our findings indicate that LNR provides significant prognostic information beyond traditional nodal staging and is closely associated with overall survival. In particular, patients with higher LNR values exhibited a markedly increased risk of mortality, with the most pronounced effect observed in those with LNR>0.2.

In our cohort, LNR showed a substantial impact on survival outcomes. The calculated HR for LNR as a prognostic variable underscores its strong association with colorectal cancer mortality. These findings are consistent with previous studies reporting LNR as an independent predictor of survival. Chen et al.[13] reported a hazard ratio of 1.24–5.12 for LNR, while a meta-analysis by Wang et al.[14] confirmed that elevated LNR values are significantly associated with poorer survival outcomes in colorectal cancer patients. Our results not only support these findings but also demonstrate an even stronger effect size, emphasizing the clinical relevance of LNR in prognostic assessment.

Regarding LNR categorization, our study revealed that patients with LNR>0.2 had a 9.24-fold higher risk of death compared with patients without lymph node metastasis. This observation aligns with previously published data. Yang et al.[15] reported a 5-year overall survival rate of 35% in patients with LNR > 0.25, while Derici et al.[16] similarly demonstrated significantly reduced survival rates among patients with high LNR values. These results suggest that, beyond conventional N staging, a high LNR reflects a more aggressive disease biology and a substantially worse prognosis.

The LNR categorization scheme used in this study (LNR=0, ≤0.1, ≤0.2, >0.2) offers a simple, reproducible, and clinically applicable stratification method. The presence of statistically significant survival differences between these categories supports the robustness of this classification. Of particular note is the prognostic importance of the 0.1 LNR cut-off value. Similar thresholds have been reported in previous studies as clinically meaningful.[17] In our analysis, patients with LNR>0.1 experienced a significantly higher risk of mortality compared with those with LNR≤0.1, suggesting that this cut-off may be useful for identifying high-risk patient subgroups. Furthermore, our findings clearly demonstrate that overall survival decreases rapidly as LNR increases, reinforcing the dose–response relationship between LNR and prognosis.

In the traditional TNM staging system, nodal status is determined solely by the absolute number of metastatic lymph nodes. However, this approach may lead to inaccurate prognostic stratification, particularly in patients who undergo inadequate lymph node dissection.[18] An insufficient number of lymph nodes retrieved during surgery may result in stage migration, thereby creating uncertainty in postoperative treatment decisions.[19] The LNR concept addresses this limitation by incorporating both the number of positive lymph nodes and the total number of examined lymph nodes, allowing for a more comprehensive and reliable prognostic

assessment. This finding is consistent with the study by Vather et al.,[20] who demonstrated that LNR has greater prognostic value than the absolute number of positive lymph nodes.

Accurate calculation of LNR depends on the harvesting and pathological examination of an adequate number of lymph nodes. In our study, the mean number of harvested lymph nodes was 31.2±26.8, exceeding the minimum threshold of 12 lymph nodes recommended by international guidelines.[22] Despite this, previous reports indicate that inadequate lymph node dissection remains a common issue in clinical practice.[23] In such cases, LNR may serve as a particularly valuable prognostic tool, enabling more accurate risk stratification even when optimal lymph node counts are not achieved.

Limitations

The major strengths of this study include the relatively large sample size, the long study period, and the comprehensive pathological evaluation of lymph node status. The inclusion of detailed clinicopathological variables and the use of both univariate and multivariate Cox proportional hazards models allowed for robust assessment of the independent prognostic value of LNR. In addition, the relatively high mean number of harvested lymph nodes strengthens the reliability of LNR calculation and reduces the potential bias related to inadequate lymph node sampling.

Nevertheless, several limitations should be acknowledged. First, the retrospective and single-center design of the study may limit the generalizability of the findings and introduce selection bias. Second, overall survival was used as the primary endpoint due to incomplete availability of disease-specific survival data, which may have influenced survival estimates. Third, molecular prognostic factors such as microsatellite instability status and KRAS/BRAF mutation profiles were not routinely assessed during the study period and therefore could not be incorporated into the analysis. Finally, although an optimal LNR cut-off value was identified using ROC curve analysis, the lack of external validation represents another limitation. Future prospective, multicenter studies incorporating molecular data and external validation cohorts are warranted to confirm the prognostic utility of LNR and to establish standardized cut-off values.

CONCLUSION

This study demonstrates that LNR is a strong and independent prognostic factor in patients with colorectal cancer. Our findings suggest that LNR can add prognostic value to the current TNM staging system and can be considered in clinical decision-making processes. More aggressive treatment approaches and strict follow-up protocols should be considered, especially for patients with high LNR values. Integrating these findings into clinical practice will contribute to better risk stratification of colorectal cancer patients and the development of personalized treatment approaches.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was approved by the İnönü University Health Sciences Scientific Researches Ethics Committee (Date: 02.12.2025, Decision No: 2025/8829).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Concept: H.K.; Desing: H.K.; Control: F.S.; Data Collection and/or Processing: H.K., F.S.; Literature Review: F.S.; Article Writing: H.K.; Critical Review: All authors.

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