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The effect of lymph node ratio on the surgical outcomes in patients with colorectal cancer

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The current study aimed to evaluate the effect of lymph node ratio (LNR) on the short-term and long-term outcomes of colorectal cancer (CRC) patients who underwent radical CRC surgery. We retrospectively collected CRC patients who underwent radical surgery from Jan 2011 to Jan 2020 in a single-center hospital. The patients were divided into the high LNR group and the low group according to the median. The baseline information and the short-term outcomes were compared between the high group and the low group. Univariate and multivariate logistic regression was performed to analyze the independent predictors for overall survival (OS) and disease-free survival (DFS). A 1:1 proportional propensity score matching (PSM) was used to reduce the selection bias between the two groups. Kaplan–Meier method was used to estimate the OS and DFS between the two groups in different T stages. A total of 1434 CRC patients undergoing radical surgery were enrolled in this study, and there were 730 (50.9%) patients in the low LNR group and 704 (49.1%) patients in the high LNR group. After the PSM, there were 618 patients in both groups, the baseline characteristics between the two groups had no significant difference ($p > 0.05$). After comparing the Surgery-related information and The Short-term outcomes, the high LNR group had a longer hospital stay (after PSM, $p < 0.01$). In univariate and multivariate logistic regression analyses, age (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$), tumor location (univariate analysis, $p = 0.020$; multivariate analysis, $p = 0.024$), lymph-vascular space invasion (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$), cancer nodules (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$), tumor size (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$), LNR (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$), and overall complications (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$) were independent risk factors for OS, and age (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$), tumor location (univariate analysis, $p = 0.032$; multivariate analysis, $p = 0.031$), T stage (univariate analysis, $p < 0.01$; multivariate analysis, $p = 0.014$), lymph-vascular space invasion (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$), cancer nodules (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$), LNR (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$), and overall complications (univariate analysis, $p < 0.01$; multivariate analysis, $p < 0.01$) were identified as independent risk factors for DFS. The high LNR group had a worse OS in T3 ($p < 0.01$) and T4 ($p < 0.01$) as well as a worse DFS in T3 ($p < 0.01$) and T4 ($p < 0.01$). No association was found between LNR and postoperative complications, but the high LNR group had a longer hospital stay. LNR was identified as an independent predictor for OS and DFS. Furthermore, high LNR had a worse OS and DFS under T3 and T4 stages. Therefore, LNR was more prognostically significant for CRC patients under T3 and T4 stages.

Keywords Lymph node ratio, Colorectal cancer, Complications, Survival, Surgery

Colorectal cancer (CRC) is the third most common cancer in humans[1]. Although there are many therapeutic options nowadays, radical surgery is still the most important treatment for CRC[2–5]. At present, the Tumor Node Metastasis (TNM) system is the most commonly used tool to evaluate the survival results in clinical practice. The number of metastatic lymph nodes plays an important role in the TNM system. Many studies demonstrated that a higher number of lymph nodes retrieved would lead to more accurate staging and significantly improved

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survival outcomes[6–9]. However, the N-stage assessment could be influenced easily by the extent of lymph node dissection, surgeons' technique, tumor location, and the thoroughness of lymph node dissection[10–12]. It leads to an insufficient number of lymph nodes, which is not enough to accurately predict prognosis.

The survival predictive capacity of lymph node ratio (LNR, the number of metastatic lymph nodes divided by the total number of lymph nodes resected) seems to be less dependent on the number of resected nodes. In addition, previous studies reported that LNR might reduce the stage migration phenomenon and consequently, allow more accurate prediction of prognosis than using the number of metastatic lymph nodes alone[13,14]. The prognostic value of LNR had been demonstrated in many cancers including breast cancer, gastric cancer, pancreatic cancer and CRC[15–19].

There was an increasing number of studies supporting that LNR could be used as a marker for predicting CRC survival, however, most of them were small-scale studies[20–23]. In addition, the cut-off value of LNR varied among these studies, meanwhile, no consensus had been reached and no studies discussed the impact of LNR on postoperative complications. Therefore, this study aimed to investigate the effect of LNR on the short-term and long-term outcomes of patients after CRC surgery.

Materials and methods

Patients

This was a retrospective study that included 1434 patients who underwent radical CRC surgery from Jan 2011 to Jan 2020 in a single-center hospital. Ethical approval from the ethics committee of the First Affiliated Hospital of Chongqing Medical University was obtained (2022-K396), and informed consent was acquired for all patients. This study was conducted by the Declaration of Helsinki.

Inclusion and exclusion criteria

A total of 5473 CRC patients were collected. Patients who underwent radical CRC surgery in a single clinical center were included in this study. The exclusion criteria were as follows: 1, stage IV CRC patients (n = 875); 2, non-R0 CRC surgery (n = 25); 3, incomplete clinical data (n = 399); and 4, no metastatic lymph nodes were detected (n = 2740). Finally, a total of 1434 eligible CRC patients were enrolled for final analysis. The flow chart of inclusion and exclusion was shown in Fig. 1.

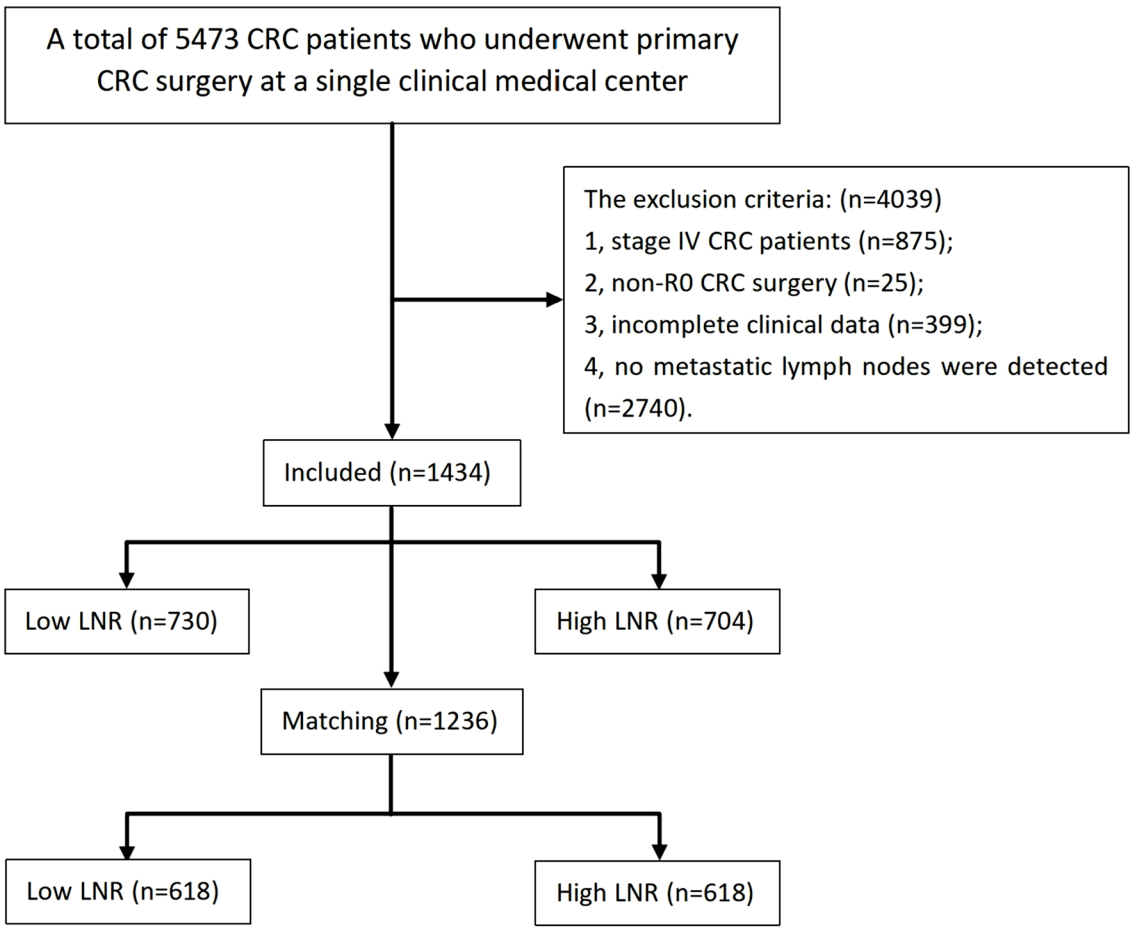

Figure 1. Flow chart of patient selection. LNR lymph nodes ratio.

Surgery management and follow-up
According to clinical guidelines, this study enrolled all patients who underwent radical resection, including total mesorectal excision or complete mesocolic excision, which was pathologically confirmed as R0 resection. Patients were followed by telephone review.

Definitions
The TNM stage was diagnosed according to the AJCC 8th Edition[24]. The complications were defined according to the Clavien-Dindo classification, and ≥ III classification complications were defined as major complications[25]. The time interval from the date of surgery to the time of last follow-up or death was defined as overall survival (OS); while the time interval from the date of surgery to the time of the last follow-up or pathological and imaging diagnosis of tumor recurrence or metastasis was defined as disease-free survival (DFS).

Data collection
The baseline information comprised age, sex, body mass index (BMI), smoking, drinking, type 2 diabetes mellitus (T2DM), tumor location, tumor size, T stage, metastatic lymph nodes, total lymph nodes and LNR. The surgery-related information included lymph-vascular space invasion, nerve invasion, cancer nodules, operation time, estimated blood loss. The short-term outcomes consisted of hospital stay, overall complications, major complications and various postoperative complications. All information was collected from the medical record system and telephone interviews.

LNR optimal cut-off
The median value of LNR was 18.2%, which was divided into the high group and the low group in different T stage.

Propensity score matching
We used PSM to reduce the selection bias in baseline information between the low LNR group and the high LNR group. Patients in the low LNR group were matched to patients in the high LNR group at a 1:1 proportion, and the caliper width was 0.02 SD. Age, sex, BMI, smoking, drinking, T2DM, tumor size, tumor location and T stage were included for matching.

Statistical analysis
Continuous variables were expressed as the mean ± standard deviation (SD), and categorical variables were expressed as n (%). Chi-square tests and independent-sample t-tests were used to compare the differences between the high LNR group and the low LNR group. Univariate and multivariate logistic regression analyses were performed to identify independent predictive factors for OS and DFS. Kaplan–Meier method was used to estimate the OS and DFS between the two groups in different T stages. Data were analyzed using the SPSS (version 22.0) statistical software. And a value of $p < 0.05$ was considered statistically significant.

Ethics approval and informed consent
The study was approved by the ethics committee of the First Affiliated Hospital of Chongqing Medical University was obtained (2022-K396), and informed consent was acquired from all patients. This study was conducted by the Declaration of Helsinki.

Results
Patients
A total of 1434 eligible CRC patients were enrolled in the study according to the inclusion and exclusion criteria. The low LNR group had 730 (50.9%) patients and the high LNR group had 704 (49.1%) patients. After PSM analysis, 618 patients were included in each group. (Fig. 1) The baseline information, surgery-related information and short-term outcomes of all patients is shown in Table 1.

Comparison of baseline information before and after PSM
After comparing the baseline information, the high LNR group had more older patients ($p = 0.021$), higher BMI ($p = 0.016$), higher proportions of rectal tumors ($p < 0.01$) and large tumor size (≥ 4 cm) ($p = 0.020$) than the low LNR group. Sex, smoking, drinking, T2DM, T stage had no significant difference ($p > 0.05$). There was no significant difference in all baseline information between the two groups after the 1:1 proportion PSM ($p > 0.05$) (Table 2).

Comparison of surgery-related information and short-term outcomes before and after PSM
Before PSM, the high LNR group had a higher proportion of lymph-vascular space invasion ($p < 0.01$), more intraoperative estimated blood loss ($p < 0.01$) and 30-day death ($p = 0.035$). After PSM, the high LNR group had a longer hospital stay ($p < 0.01$). There was no significant difference in other information before and after PSM, including nerve invasion, cancer nodules, operation time, overall complications, major complications, anastomotic leakage, incision Infection, lymphatic fistula, intestinal obstruction, hypoproteinemia, cardiovascular complications, pulmonary complications, urinary complications, disturbance of water and electrolyte balance, vein thrombosis, and abdominal infection ($p > 0.05$) (Table 3).

Characteristics	No. 1434
Age, year	63.1 ± 12.5
Sex	
Male	799 (55.7%)
Female	635 (44.3%)
BMI, kg/m^2	22.6 ± 3.2
Smoking	511 (35.6%)
Drinking	406 (28.3%)
T2DM	174 (12.1%)
Tumor location	
Colon	671 (46.8%)
Rectum	763 (53.2%)
Tumor size	
< 4 cm	719 (50.1%)
≥ 4 cm	715 (49.9%)
T stage	
1	26 (1.8%)
2	132 (9.2%)
3	503 (35.1%)
4	773 (53.9%)
Metastatic lymph nodes	3.5 ± 3.4
Total lymph nodes	14.8 ± 6.9
Lymph nodes ratio (%)	
Mean ± SD	27.0 ± 24.1
Median	18.2
Lymph-Vascular Space Invasion	135 (9.4%)
Nerve invasion	74 (5.2%)
Cancer nodules	256 (17.9%)
Operation time (min)	221.6 ± 72.5
Estimated blood loss (mL)	100.6 ± 122.1
Overall complications	323 (22.5%)
Major complications	37 (2.6%)
Anastomotic leakage	27 (1.9%)
Incision Infection	49 (3.4%)
Lymphatic fistula	7 (0.5%)
Intestinal obstruction	22 (1.7%)
Hypoproteinemia	82 (5.7%)
Cardiovascular complications	17 (1.2%)
Pulmonary complications	54 (3.8%)
Urinary complications	11 (0.8%)
Disturbance of water and electrolyte balance	20 (1.4%)
Vein thrombosis	12 (0.8%)
Abdominal infection	64 (4.5%)
Hospital stay (day)	11.4 ± 8.5
30-day death	8 (0.6%)

Table 1. Clinical characteristics. Variables are expressed as the mean ± SD, n (%). *BMI* body mass index; *T2DM* type 2 diabetes mellitus; *SD* standard deviation.

Univariate and multivariate logistic regression analyses of the OS

Through using univariate and multivariate logistic regression analyses, we found that age ($p < 0.01$, HR = 1.026, 95% CI 1.016–1.035), tumor location ($p = 0.024$, HR = 1.289, 95% CI 1.034–1.607), lymph-vascular space invasion ($p < 0.01$, HR = 1.942, 95% CI 1.402–2.689), cancer nodules ($p < 0.01$, HR = 1.660, 95% CI 1.289–2.139), tumor size ($p < 0.01$, HR = 1.357, 95% CI 1.085–1.696), LNR ($p < 0.01$, HR = 2.035, 95% CI 1.609–2.573), and overall complications ($p < 0.01$, HR = 1.704, 95% CI 1.358–2.139) were independent risk factors for OS. The other factors including sex, BMI, T2DM, T stage, nerve invasion, smoking and drinking had no predictive value for OS (Table 4).

Characteristics	Before PSM			After PSM		
	Low LNR (730)	High LNR (704)	*p* value	Low LNR (618)	High LNR (618)	*p* value
Age (year)	62.3 ± 12.3	63.8 ± 12.5	0.021*	63.6 ± 11.7	63.0 ± 12.7	0.436
Sex			0.894			0.864
Male	408 (55.9%)	391 (55.5%)		343 (55.5%)	346 (56.0%)	
Female	322 (44.1%)	313 (44.5%)		275 (44.5%)	272 (44.0%)	
BMI (kg/m^2)	22.4 ± 3.1	22.8 ± 3.3	0.016*	22.7 ± 3.1	22.6 ± 3.2	0.788
Smoking	270 (37.0%)	241 (34.2%)	0.276	216 (35.0%)	223 (36.1%)	0.429
Drinking	212 (29.0%)	194 (27.6%)	0.533	175 (28.3%)	175 (28.3%)	1.000
T2DM	90 (12.3%)	84 (11.9%)	0.818	75 (12.1%)	60 (9.7%)	0.171
Tumor size			0.020*			0.649
< 4 cm	344 (47.1%)	375 (53.3%)		308 (49.8%)	316 (51.1%)	
≥ 4 cm	386 (52.9%)	329 (46.7%)		310 (50.2%)	302 (48.9%)	
Tumor location			< 0.01*			0.458
Colon	384 (52.6%)	287 (40.8%)		331 (53.6%)	344 (55.7%)	
Rectum	346 (47.4%)	417 (59.2%)		287 (46.4%)	274 (44.3%)	
T stage			0.074			0.088
1	14 (1.9%)	12 (1.7%)		14 (2.3%)	11 (1.8%)	
2	67 (9.2%)	65 (9.2%)		64 (10.4%)	50 (8.1%)	
3	233 (31.9%)	270 (38.4%)		198 (32.0%)	238 (38.5%)	
4	416 (57.0%)	357 (50.7%)		342 (55.3%)	319 (51.6%)	

Table 2. Comparison baseline characteristics between the high LNR group and the low LNR group before and after PSM. Variables are expressed as the mean ± SD, n (%). *BMI* body mass index; *T2DM* type 2 diabetes mellitus. *P value < 0.05.

Characteristics	Before PSM			After PSM		
	Low LNR (730)	High LNR (704)	*p* value	Low LNR (618)	High LNR (618)	*p* value
Surgery-related information						
Lymph-vascular space invasion	49 (6.7%)	86 (12.2%)	< 0.01*	39 (6.3%)	39 (6.3%)	1.000
Nerve invasion	34 (4.7%)	40 (5.7%)	0.381	24 (3.9%)	37 (6.0%)	0.088
Cancer nodules	118 (16.2%)	138 (19.6%)	0.089	103 (16.7%)	125 (20.2%)	0.107
Operation time (min)	218.5 ± 71.8	224.9 ± 73.1	0.099	217.7 ± 72.5	224.9 ± 72.4	0.082
Estimated blood loss (mL)	87.9 ± 102.8	101.1 ± 161.6	< 0.01*	83.9 ± 95.8	114.7 ± 137.7	0.057
Short-term outcomes						
Overall complications	150 (20.5%)	173 (24.6%)	0.068	129 (20.9%)	153 (24.8%)	0.755
Major complications	19 (2.6%)	18 (2.6%)	0.956	18 (2.9%)	14 (2.3%)	0.474
Anastomotic leakage	16 (2.2%)	11 (1.6%)	0.381	15 (2.4%)	10 (1.6%)	0.312
Incision infection	21 (2.9%)	28 (4.0%)	0.251	19 (3.1%)	26 (4.2%)	0.288
Lymphatic fistula	6 (0.8%)	1 (0.1%)	0.125	4 (0.6%)	1 (0.2%)	0.374
Intestinal obstruction	13 (1.8%)	12 (1.7%)	0.912	10 (1.6%)	10 (1.6%)	1.000
Hypoproteinemia	38 (5.2%)	44 (6.3%)	0.394	34 (5.5%)	41 (6.6%)	0.404
Cardiovascular complications	8 (1.1%)	9 (1.3%)	0.750	8 (1.3%)	7 (1.1%)	0.795
Pulmonary complications	24 (3.3%)	30 (4.3%)	0.333	21 (3.4%)	29 (4.7%)	0.248
Urinary complications	4 (0.5%)	7 (1.0%)	0.333	4 (0.6%)	6 (1.0%)	0.525
Disturbance of water and electrolyte balance	8 (1.1%)	12 (1.7%)	0.326	7 (1.1%)	11 (1.8%)	0.342
Vein thrombosis	5 (0.7%)	7 (1.0%)	0.520	5 (0.8%)	6 (1.0%)	0.762
Abdominal infection	30 (4.1%)	34 (4.8%)	0.509	25 (4.0%)	31 (5.0%)	0.412
Hospital stay (day)	11.1 ± 9.6	11.6 ± 7.2	0.288	11.3 ± 10.2	11.5 ± 6.3	< 0.01*
30-day death	1 (0.1%)	7 (1.0%)	0.035*	1 (0.2%)	5 (0.8%)	0.218

Table 3. Summary of outcomes between the high LNR group and the low LNR group before and after PSM. Variables are expressed as the mean ± SD, n (%). *LNR* lymph nodes ratio, *PSM* propensity score matching. **p* value < 0.05.

Risk factors	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age (years)	1.030 (1.020–1.039)	< 0.01*	1.026 (1.016–1.035)	< 0.01*
Sex (male/female)	0.898 (0.723–1.116)	0.333		
BMI (kg/m^2)	0.983 (0.950–1.017)	0.330		
T2DM (yes/no)	1.020 (0.727–1.430)	0.909		
Tumor location (colon/ rectum)	1.290 (1.041–1.599)	0.020*	1.289 (1.034–1.607)	0.024*
T stage (4/3/2/1)	1.215 (1.041–1.418)	0.014*	1.128 (0.958–1.328)	0.149
Lymph-vascular space invasion	2.223 (1.610–3.068)	< 0.01*	1.942 (1.402–2.689)	< 0.01*
Nerve invasion	1.405 (0.835–2.366)	0.201		
Cancer nodules	1.631 (1.268–2.098)	< 0.01*	1.660 (1.289–2.139)	< 0.01*
Smoking (yes/no)	1.026 (0.822–1.282)	0.819		
Drinking (yes/no)	0.983 (0.775–1.248)	0.889		
Tumor size (≥ 4 cm/ < 4 cm)	1.378 (1.109–1.714)	< 0.01*	1.357 (1.085–1.696)	< 0.01*
LNR (high/low)	2.099 (1.669–2.641)	< 0.01*	2.035 (1.609–2.573)	< 0.01*
Overall complications (yes/no)	1.843 (1.470–2.309)	< 0.01*	1.704 (1.358–2.139)	< 0.01*

Table 4. Univariate and multivariate analysis of overall survival. *HR* hazard ratio; *CI* confidence interval; *BMI* body mass index; *T2DM* type 2 diabetes mellitus, *LNR* lymph nodes ratio. *P value < 0.05.

Univariate and multivariate logistic regression analyses of the DFS

Univariate and multivariate logistic regression analyses were used to find out independent predictors for DFS. We found that age ($p < 0.01$, HR = 1.018, 95% CI 1.010–1.027), tumor location ($p = 0.031$, HR = 1.250, 95% CI 1.021–1.531), T stage ($p = 0.014$, HR = 1.212, 95% CI 1.040–1.412), lymph-vascular space invasion ($p < 0.01$, HR = 1.666, 95% CI 1.204–2.304), cancer nodules ($p < 0.01$, HR = 1.575, 95% CI 1.247–2.990), LNR ($p < 0.01$, HR = 1.996, 95% CI 1.613–2.471), and overall complications ($p < 0.01$, HR = 1.478, 95% CI 1.192–1.832) were identified as independent risk factors for DFS. The other factors including sex, BMI, T2DM, nerve invasion, smoking drinking and tumor size had no predictive value for DFS (Table 5).

Comparison between the high LNR group and the low LNR group in patients with rectal or colon cancer

After comparing the baseline characteristics between the high LNR group and the low LNR group in rectal cancer patients, the high LNR group had a higher BMI ($p = 0.033$), more intraoperative estimated blood loss ($p < 0.01$). In colon cancer patients, the high LNR group had more older patients ($p = 0.039$), more intraoperative estimated blood loss ($p = 0.030$) and a higher proportion of overall complications ($p = 0.020$). The other baseline characteristics had no significant differences ($p > 0.05$). (Table S1, S2).

Risk factors	Univariate analysis		Multivariate analysis	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age (years)	1.022 (1.013–1.030)	< 0.01*	1.018 (1.010–1.027)	< 0.01*
Sex (male/female)	0.906 (0.742–1.107)	0.334		
BMI (kg/m^2)	0.993 (0.962–1.025)	0.657		
T2DM (yes/no)	0.878 (0.636–1.214)	0.432		
Tumor location (colon/ rectum)	1.241 (1.018–1.512)	0.032*	1.250 (1.021–1.531)	0.031*
T stage (4/3/2/1)	1.280 (1.107–1.480)	< 0.01*	1.212 (1.040–1.412)	0.014*
Lymph-vascular space invasion	2.080 (1.547–2.795)	< 0.01*	1.666 (1.204–2.304)	< 0.01*
Nerve invasion	1.885 (1.254–2.834)	< 0.01*	1.400 (0.896–2.189)	0.139
Cancer nodules	1.580 (1.253–1.993)	< 0.01*	1.575 (1.247–1.990)	< 0.01*
Smoking (yes/no)	1.110 (0.906–1.359)	0.315		
Drinking (yes/no)	1.039 (0.836–1.291)	0.728		
Tumor size (≥ 5 cm/ < 5 cm)	1.248 (1.023–1.523)	0.029*	1.211 (0.987–1.485)	0.066
LNR (high/low)	2.027 (1.645–2.497)	< 0.01*	1.996 (1.613–2.471)	< 0.01*
Overall complications (yes/no)	1.597 (1.290–1.976)	< 0.01*	1.478 (1.192–1.832)	< 0.01*

Table 5. Univariate and multivariate analysis of disease-free survival. *HR* hazard ratio; *CI* confidence interval; *BMI* body mass index; *T2DM* type 2 diabetes mellitus, *LNR* lymph nodes ratio. *p value < 0.05.

Kaplan–Meier curves in different T stages

Kaplan–Meier method was used to estimate the OS and DFS between the two groups in different T stages. We found that the high LNR group had a worse OS (Fig. 2) in T3 ($p < 0.01$) and T4 ($p < 0.01$) as well as a worse DFS (Fig. 3) in T3 ($p < 0.01$) and T4 ($p < 0.01$).

Discussion

A total of 1434 CRC patients who underwent radical CRC surgery were included in this study. And there were 618 patients in the low LNR group and the high LNR group after PSM. In multivariate logistic regression analyses, we found that age, tumor location, lymph-vascular space invasion, cancer nodules, tumor size, LNR, and overall complications were independent risk factors for OS. Age, tumor location, T stage, lymph-vascular space invasion, cancer nodules, LNR, and overall complications were identified as independent risk factors for DFS. Furthermore, it was worth noting that the high LNR group had a worse OS and DFS in T3 and T4 stages.

Many previous studies confirmed the role of LNR in predicting the survival of CRC. Jiang K et al. divided LNR into four groups based on quartiles and found that the value of LNR at 0.167–0.562 were significant prognostic factors for OS and DFS[26]. Shumacher et al. reported that an LNR of 0.18 was an important prognostic factor for DFS, but not for OS[27]. In terms of the best cut-off value, Schumacher's results were consistent with the current study. However, there was no agreement on the cut-off value of LNR and no studies discussed the impact of LNR on postoperative complications. Therefore, this study aimed to investigate the effect of LNR on the short-term and long-term outcomes of patients after CRC surgery.

In our research, we found that LNR was a very powerful prognostic factor for OS and DFS in CRC, which was consistent with previous studies. Furthermore, we expect to explore the effect of LNR on prognosis in different T stages. Thus, we divided LNR into the high group and low group according to the median, and we found that high LNR had a worse OS and DFS under T3 and T4 stages. This meant that LNR was more prognostically significant under T3 and T4 stages for CRC patients.

Lymph node metastasis was the most important way of metastasis in CRC[28,29]. More lymph node metastasis would require lymph node dissection, which not only increases the difficulty of surgery, but also increases the length of hospital stay. In our research, we divided LNR values into high and low groups according to the median

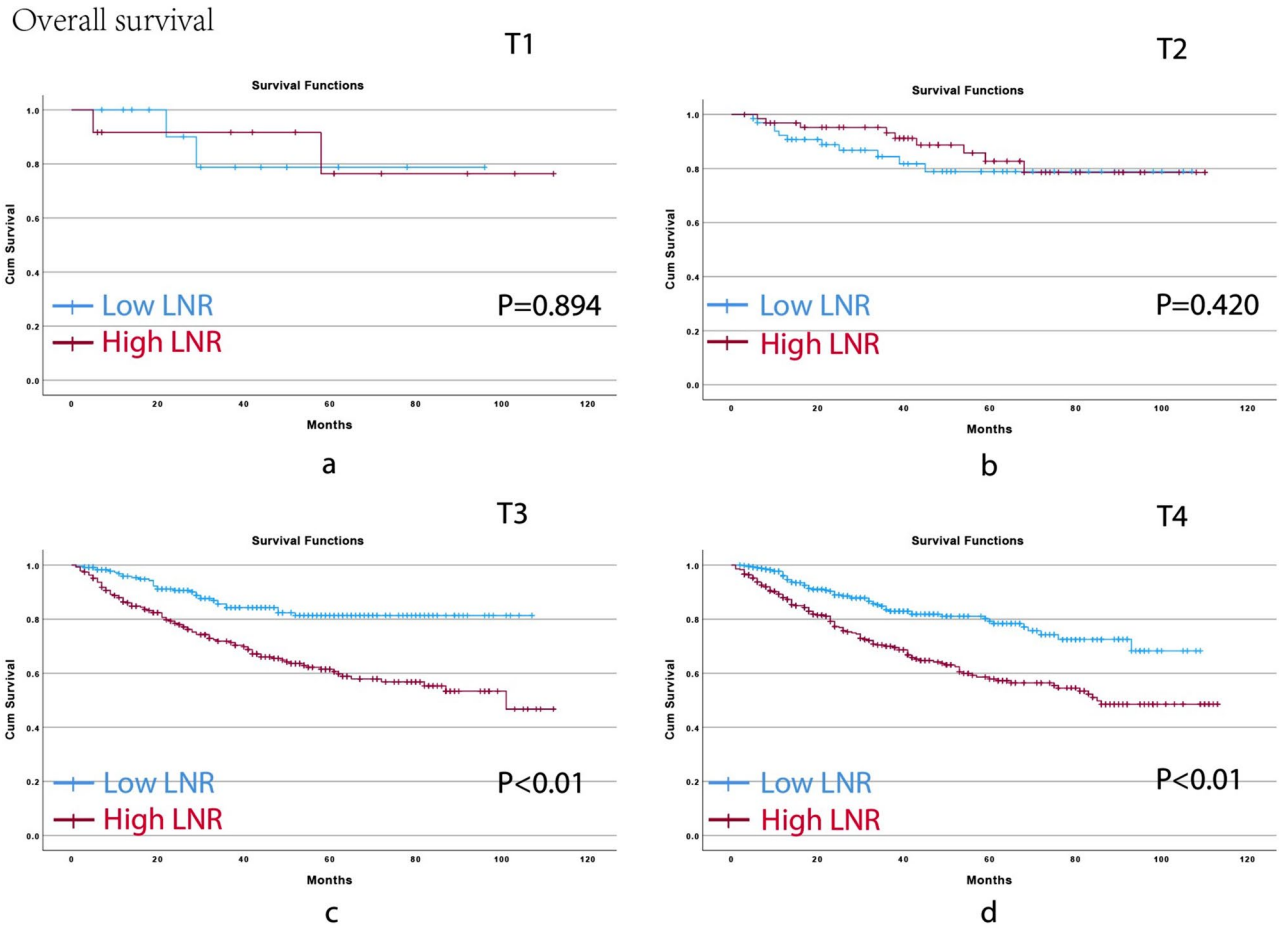

Figure 2. Kaplan–Meier survival curve for the impact of high LNR group and low LNR group on the OS of patients in T stage I–IV. (**a**) OS of T1 stage CRC patients (**b**) OS of T2 stage CRC patients (**c**) OS of T3 stage CRC patients (**d**) OS of T4 stage CRC patients. *LNR* lymph nodes ratio; *OS* overall survival.

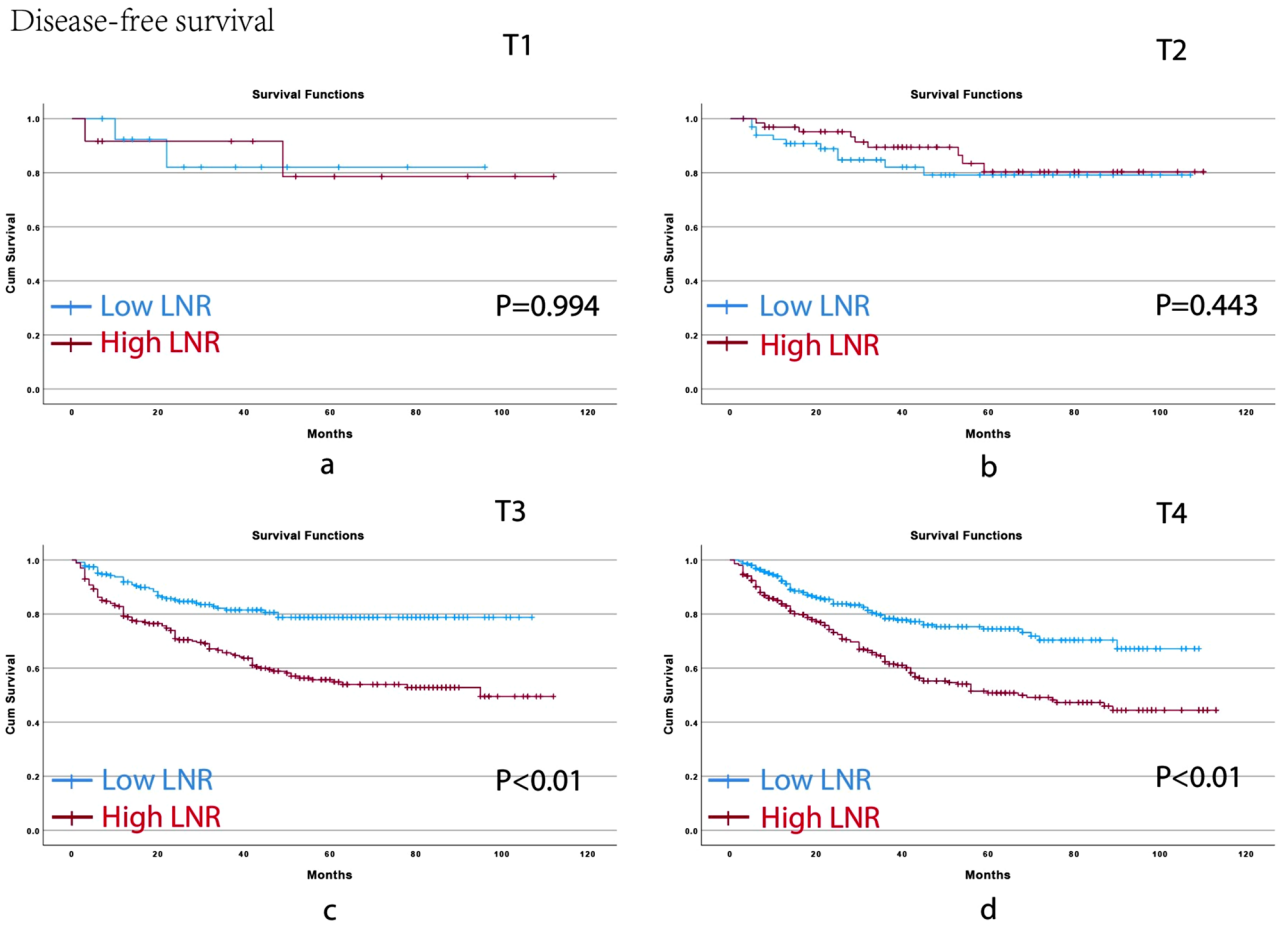

Figure 3. Kaplan–Meier survival curve for the impact of high LNR group and low LNR on the DFS survival of patients in T stage I-IV. (**a**) DFS of T1 stage CRC patients (**b**) DFS of T2 stage CRC patients (**c**) DFS of T3 stage CRC patients d. DFS of T4 stage CRC patients. *LNR* lymph nodes ratio; *DFS* disease-free survival.

and found that high LNR was associated with a longer hospital stay. Previous studies had shown that lymph node metastasis increases the risk of postoperative complications[30]. However, we just found a longer hospital stay in the high LNR group, the other postoperative complications had no statistical significance. The specific reasons might need further research to explain.

To our knowledge, this current study had the largest sample size in western China, and for the first time revealed the relationship between LNR and short-term complications in CRC patients. However, some limitations existed in this current study as well. First, the number of patients in the T1 and T2 stages were small, which might lead to data bias. Second, there was a lack of chemotherapy information in our study, which might affect the reliability of the survival analysis. Third, we suggeated further prognostic analysis more focused on the collinearity between LNR and other classic prognostic indicators. Finally, this study was a retrospective study conducted in a single center in western China, thus, the current results applied to restricted regions. Therefore, multicenter prospective randomized controlled trial studies should be conducted further to verify the applicability of our findings.

In conclusion, we found that the relationship between LNR and postoperative complications was not statistically significant, however, LNR was identified as an independent predictor for OS and DFS. Furthermore, high LNR had a worse OS and DFS under T3 and T4 stages. Therefore, LNR was more prognostically significant under T3 and T4 stages for CRC patients.

Data availability

The datasets generated and/or analysed during the current study are not publicly available due ethical limitations but are available from the corresponding author on reasonable request.

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Author contributions

L. Z. and W.C.Y. contributed to the conception and design of the study. P.D. and H.Z.X. performed the statistical analysis. L.Z.W. and L.X.R. wrote the first draft of the manuscript. L.F. and H.Z.X. wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version. During the revision of the manuscript, H.Z.X. made significant contributions.

Competing interests

The authors declare no competing interests.

Additional information

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