

# Analysis of clinical and pathological factors in patients undergoing surgery for rectal cancer: a single-centre experience with 692 patients in China

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## Research

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# Abstract

**Background:** The management of rectal carcinoma has substantially evolved over the past two decades, so as AJCC staging and NCCN guidelines. The inherent relationships of pathologic factors warrant further study. The present study aimed to assess the associations of clinical and pathological factors in rectal cancer patients undergoing radical surgery.

**Methods:** From October 2015 to February 2019, all rectal cancer patients treated with radical surgery without neoadjuvant therapy were identified. The analysis was performed with data obtained from the prospectively collected database. Predictive factors for lymph node metastasis were analysed.

**Results:** In total, 692 patients with a median age of 61.64 years (range: 22-89) were included. There was no significant difference in onset age between male and female patients ( $61.75 \pm 11.10$  vs  $61.43 \pm 11.92$ ,  $P=0.723$ ).

Tumour location ( $P=0.004$ ), perineural invasion (PNI) ( $P=0.000$ ), lymphovascular invasion (LVI) ( $P=0.000$ ), tumour deposit (TD) ( $P=0.000$ ), and differentiation grade ( $P=0.000$ ) were significantly related to pathologic T stage in univariate analysis, while sex was not ( $p=0.192$ ).

Compared to patients with T1 disease, there was a significantly higher proportion of positive LVI in patients with stage T3 disease ( $P=0.011$ , OR=3.404, 95% CI: 1.319-8.787) but not in those with T2 ( $P=0.686$ , OR=0.804, 95% CI: 0.280-2.310) and T4 ( $P=0.063$ , OR=3.200, 95% CI: 0.941-10.886) disease. Compared to patients with T2 disease, there was a significantly higher proportion of perineural invasion in patients with stage T3 ( $P=0.000$ , OR=6.2376, 95% CI: 3.371-11.685) but not T4 ( $P=0.172$ , OR=2.309, 95% CI: 0.694-7.676) disease. Compared to patients with T1 disease, a significantly higher proportion of TDs occurred in patients with stage T3 ( $P=0.013$ , OR=6.106, 95% CI: 1.455-25.631) and stage T4 ( $P=0.019$ , OR=7.146, 95% CI: 1.378-37.044) but not stage T2 ( $P=0.435$ , OR=0.503, 95% CI: 0.089-2.824) disease. The overall incidence of lymph node metastasis was 44.9% (19.6% for T1, 23.6% for T2, 56.7% for T3, and 67.8% for T4). Patient age, sex, and tumour location did not significantly affect lymph node metastasis (LNM). The presence of LVI (OR=3.882, 95% CI=2.338-6.440,  $P=0.000$ ), TD (OR=27.645, 95% CI=9.805-77.947,  $P=0.000$ ), higher T stage (OR=1.969, 95% CI=1.471-2.635,  $P=0.000$ ), and poorly differentiated histology (OR=2.255, 95% CI=1.544-3.293,  $P=0.000$ ) were associated with a higher incidence of LNM on multivariate analysis. Perineural invasion ( $P=0.000$ ) significantly affected LNM in univariate but not multivariate analysis (OR=1.213, 95% CI=0.734-2.003,  $P=0.452$ ).

**Conclusion:** There was no significant difference between male and female patients in onset age. Tumour location, PNI, LVI, TD, and differentiation grade were significantly related to pathologic T stage. Patients with the presence of LVI and TD, higher T stage, and poorly differentiated histology have a significantly higher chance of LNM.

## Background

The management of rectal carcinoma has substantially evolved over the past two decades. Radical resection is the preferred treatment for early rectal cancer, and neoadjuvant radiochemotherapy (nRCT) followed by total mesorectal excision (TME) has been the standard recommended therapy for locally advanced rectal carcinoma (LARC)[1–7].

Surgical resection remains the most effective therapy for rectal cancers. Pathologic findings in surgical resection specimens are the best predictor of prognosis. The main postoperative pathological information includes tumour differentiation grade, macroscopic type, lymphovascular invasion (LVI), perineural invasion (PNI), tumour deposit (TD), primary tumour stage, and lymph node stage. AJCC staging and NCCN guidelines have been updated in recent decades. For example, the classification of tumour nodules as TDs versus LNs has been debated in the past. Since the AJCC 7th (2010) edition, the new nodal subclassification category N1c is used if there are TDs but no concurrent positive LNs[8]. The percentage of LN metastasis has also changed in the new classifications. Therefore, the inherent relationships of these pathologic factors warrant further study. The present study aimed to explore the correlations of clinical and pathological factors in patients undergoing surgery for rectal cancer.

## Materials And Methods

### Patients

We enrolled 1061 patients with primary rectal cancer who had undergone radical resection at the First Affiliated Hospital of Nanjing Medical University between October 2015 and February 2019. The inclusion criteria for the study were as follows: (1) preoperative pathological diagnosis of rectal cancer diagnosed by endoscopy-guided biopsy; (2) inferior tumour margin located within 15 cm of the anal verge; (3) detailed postoperative pathological reports including histological differentiation grade, depth of tumour invasion, macroscopic type, number of LNs examined, LN metastasis, TD, lymphovascular invasion (LVI), and perineural invasion (PNI); (4) no evidence of distant metastasis; and (5) no history of malignancy other than nonmelanoma skin cancer. Patients were excluded if they met the following criteria: (1) received previous neoadjuvant chemoradiotherapy (CRT) or chemotherapy before surgical resection; (2) tumour located > 15 cm from the anal verge; and (3) fewer than 10 LNs removed. Among the 1061 patients, 219 received neoadjuvant CRT or chemotherapy; 116 had tumours located > 15 cm from the anal verge; and 34 had inadequate LN detection; all of these patients were excluded from the study. The remaining 692 patients were analysed (Fig. 1). This retrospective study was approved by the Institutional Research Ethics Committee of the First Affiliated Hospital of Nanjing Medical University.

### Surgery and histopathological examinations

The 692 patients underwent curative TME. Samples were obtained from opposite side of the resected specimens and fixed in formalin for 24 h after surgery. The specimens were then sliced transversely at increments of 5 mm. The slices were embedded in paraffin, sectioned, and examined histologically after haematoxylin and eosin (HE) staining. The results were evaluated by experienced pathologists. The histological grade, presence of LN metastasis, LNI and PNI were all evaluated.

# Statistical analysis

The study was designed to identify clinicopathologic variables that could be associated with the pathological T and N stages. Categorical variables such as patient demographics (such as sex) and tumour characteristics (such as tumour location, differentiation grade, PNI, LVI, TD, and pathologic T and N staging) were compared with chi-square tests, while for continuous variables such as patient age, Student's t tests and analysis of variance (ANOVA) were used. Multiple covariate analysis was performed using the stepwise regression hazards regression model. The hazard ratio (HR) and P value with the 95% confidence interval (CI) were calculated for the variable groups. All P values were 2-tailed, and P values less than 0.05 were considered statistically significant. Statistical analyses were performed with SPSS version 19.0 (SPSS, Chicago, IL).

## Results

### Patient Demographics And Clinicopathologic Data

The patient characteristics are shown in Table 1. There were 245 females (35.4%) and 447 males (64.6%), with a mean age of  $61.64 \pm 11.39$  (range: 22–89) years. The average age at the onset of rectal cancer was  $61.43 \pm 11.92$  years for female patients and  $61.75 \pm 11.10$  years for male patients. There was no significant difference in onset age between female and male patients ( $F = 0.126$ ,  $P = 0.723$ ). In total, 98 (14.2%) patients had upper-rectal cancer (10–15 cm), 346 (50%) patients had mid-rectal cancer (5–10 cm from the anal verge), and 248 (35.8%) patients had lower rectal cancer (less than 5 cm from the anal verge) (Table 1).

Table 1  
 Characteristics of the patients (n = 692)

Characteristics	Number of patients (%)	
Sex, n (%)		Age, median, years
Female	245 (35.4%)	61.43 ± 11.92
Male	447 (64.6%)	61.75 ± 11.10
Age, median ± SD (years)		61.64 ± 11.39
Tumor location (cm)		
≤ 5 cm	248 (35.8%)	
5–10 cm	346 (50%)	
> 10 cm, ≤ 15 cm	98(14.2%)	
Pathology, n (%)		
Common adenocarcinoma	639 (92.3%)	
Mucinous adenocarcinoma	34 (4.9%)	
Signet ring cell carcinoma	7 (1.0%)	
Neuroendocrine carcinoma	4 (0.6%)	
Others	8 (0.8%)	
Tumor differentiation grade, n (%)		
Moderate-high	447(64.6%)	
Low	245(35.4%)	
TD, n (%)		
Negative	597 (86.3%)	
Positive	95 (13.7%)	
LVI, n (%)		
Negative	552(79.8%)	
Positive	140(20.2%)	
PNI, n (%)		
Negative	558(80.6%)	
Positive	134(19.4%)	

TD = tumour deposit, LVI = lymphovascular invasion, PNI = perineural invasion.

Characteristics	Number of patients (%)
Pathologic T stage, n (%)	
T1	51 (7.4%)
T2	199 (28.8%)
T3	411 (59.4%)
T4	31 (4.5%)
Pathological N stage, n (%)	
N0	381 (55.1%)
N1	189 (27.3%)
N2	122 (17.6%)
TD = tumour deposit, LVI = lymphovascular invasion, PNI = perineural invasion.	

Regarding histological type, 639 (92.3%) tumours were common adenocarcinomas, 34 (4.9%) were mucinous adenocarcinomas, 7 (1.0%) were signet ring cell carcinomas, and 4 (0.6%) were neuroendocrine carcinomas. The histologic diagnoses were moderately differentiated adenocarcinoma in 447 (64.6%) patients and poorly differentiated adenocarcinoma in 245 (35.4%) patients (Table 1).

A total of 86.3% (597/692) of patients were TD negative, and 13.7% (95/692) were positive. A total of 79.8% (552/692) of the patients were LVI negative, and 20.2% (140/692) were LVI positive. PNI was found in 19.4% (134/692) of the patients, while PNI was absent in 80.6% (558/692). With regard to the pathological T and N stages, 51 (7.4%), 199 (28.8%), 411 (59.4%), 31 (4.5%) patients had T1, T2, T3 and T4 disease, while 381 (55.1%), 189 (27.3%), and 122 (17.6%) had N0, N1 and N2 disease.

## Association Between Pathological T Stage And N Stage

Table 2 and Figs. 2 and 3 show the associations between each pathological T1-4 stage and N0-3 stage. For pathologic stage T1, the percentages of N0, N1 and N2 were 80.4%, 15.7% and 3.9%, respectively. For pathologic stage T2, the percentages of N0, N1 and N2 were 76.4%, 17.1% and 6.5%, respectively. For pathologic stage T3, the percentages of N0, N1 and N2 were 43.3%, 33.3% and 23.4%, respectively. For pathologic stage T4, the percentages of N0, N1 and N2 were 32.3%, 32.3 and 35.5%, respectively (Table 2). Figure 2 shows that an increased T stage was associated with an increased percentage of N1 and N2. Goodman-Kruskal gamma statistic analysis confirmed this result (gamma = 0.579, P = 0.000).

Table 2

Distribution of T stage and N stages in 692 patients with rectal cancer.

T stage	N stage		
	N0	N1	N2
T1	80.4% (41/51)	15.7% ( 8/51)	3.9% (2/51)
T2	76.4% (152/199)	17.1% (34/199)	6.5% (13/199)
T3	43.3% (178/411)	33.3% (137/411)	23.4% (96/411)
T4	32.3% (10/31)	32.3% (10/31)	35.5% (11/31)

Figure 3 shows the average number of metastatic LNs for each pathologic T stage. The mean numbers of metastatic LNs in patients with T1, T2, T3, and T4 disease were  $0.59 \pm 2.22$ ,  $0.62 \pm 1.391$ ,  $2.41 \pm 3.796$ , and  $3.26 \pm 4.719$ , respectively. Multiple comparisons by analysis of variance (ANOVA) showed that there was no significant difference in the average number of metastatic LNs between T1 and T2 ( $P = 0.953$ ) or T3 and T4 ( $P = 0.160$ ). However, significant differences were observed between T1 and T3 ( $P = 0.000$ ), T1 and T4 ( $P = 0.000$ ), T2 and T3 ( $P = 0.000$ ), and T2 and T4 ( $P = 0.000$ ).

## Clinicopathologic variables that correlate with the T stage

We analysed the clinicopathological factors that could be correlated with the pathological T stage, as shown in Table 3. On univariate analysis, tumour location ( $P = 0.004$ ), PNI ( $P = 0.000$ ), LVI ( $P = 0.000$ ), TD ( $P = 0.000$ ), and differentiation grade ( $P = 0.000$ ) were significantly correlated with the pathological T stage, but sex was not ( $p = 0.192$ ).

Table 3

Associations between clinicopathological variables and pathological T stage

		$\chi^2$	P	Exp	95% CI	P
PNI(n)						
Negative	positive	58.728	0.000			
T1	51	0		--		
T2	187	12		1		
T3	293	118		6.2376	3.371–11.685	0.000
T4	27	4		2.309	0.694–7.676	0.172
LVI (n)						
Negative	Positive	34.053	0.000			
T1	46	5		1		
T2	183	16		0.804	0.280–2.310	0.686
T3	300	111		3.404	1.319–8.787	0.011
T4	23	8		3.200	0.941–10.886	0.063
TD (n)		42.704	0.000			
Negative	positive					
T1	49	2		1		
T2	195	4		0.503	0.089–2.824	0.435
T3	329	82		6.106	1.455–25.631	0.013
T4	24	7		7.146	1.378–37.044	0.019
Differentiation (n)		19.996	0.000			
High grade	Low grade					
T1	42	9		1		
T2	143	56		1.828	0.835–4.000	0.131
T3	248	163		3.067	1.454–6.471	0.003
T4	14	17		5.667	2.065–15.547	0.001
Sex (n)		4.741	0.192			
Male	Female					
		$\chi^2$	P	Exp	95% CI	P

			$\chi^2$	P	Exp	95% CI	P
T1	26	25					
T2	128	71					
T3	273	138					
T4	20	11					
Tumor location (n)			13.065	0.004			
$\leq 5$ cm		$> 5$ cm					
T1	13	38			1.196	0.440–3.247	0.726
T2	91	108			0.486	0.213–1.107	0.486
T3	135	276			0.836	0.375–1.866	0.836
T4	9	22			1		

Logistic regression analysis revealed relationships between T stage and these significant pathologic factors. Regarding LVI, compared to T1 patients, a significantly higher proportion of T3 patients were positive for LVI (OR = 3.404, 95% CI: 1.319–8.787, P = 0.011); however, the same result was not observed in T2 patients (P = 0.686, OR = 0.804, 95% CI: 0.280–2.310). T4 patients had a tendency towards a greater probability of positive LVI, but the difference was not significant (P = 0.063, OR = 3.200, 95% CI: 0.941–10.886).

Regarding PNI, compared to T2 patients, a significantly higher proportion of T3 patients had PNI (OR = 6.2376, 95% CI: 3.371–11.685, P = 0.000); however, the same result was not observed in T4 patients (OR = 2.309, 95% CI: 0.694–7.676, P = 0.172).

Regarding TD, compared to T1 patients, there was a significantly higher proportion of T3 and T4 but not T2 patients with TD (OR = 6.106, 95% CI: 1.455–25.631, P = 0.013; OR = 7.146, 95% CI: 1.378–37.044, P = 0.019; OR = 0.503, 95% CI: 0.089–2.824, P = 0.435, respectively).

Regarding tumour differentiation grade, compared to T1 patients, a significantly higher chance of T3 and T4 but not T2 patients had poorly differentiated disease (OR = 3.067, 95% CI: 1.454–6.471, P = 0.003; OR = 5.667, 95% CI: 2.065–15.547, P = 0.001; OR = 1.828, 95% CI: 0.835–4.000, P = 0.131).

Regarding tumour location, there were no differences between patients with T4 disease and those with T1 (P = 0.726), T2 (P = 0.486) and T3 (P = 0.836) disease.

## Clinicopathologic variables that may be correlated with LNM

We also analysed the clinicopathologic factors that could be correlated with pathologic lymph node metastasis (LNM), as shown in Table 4. Based on univariate analysis, patient age, sex, and tumour location did not significantly affect LNM. However, LVI, PNI, pathologic T stage, tumour differentiation grade, and TD (all P = 0.000) were significantly correlated with LNM. When these factors were entered into a multivariate

analysis using a logistic regression model, LVI (OR = 3.882, 95% CI = 2.338–6.440, P = 0.000), pathological T stage (OR = 1.969, 95% CI = 1.471–2.635, P = 0.00), tumour differentiation grade (OR = 2.255, 95% CI = 1.544–3.293, P = 0.000), and TD (OR = 27.645, 95% CI = 9.805–77.947, P = 0.000) retained significance as risk factors for LNM. However, PNI (P = 0.452, OR = 1.213, 95% CI = 0.734–2.003) was not a risk factor for LNM based on the multivariate analysis.

Table 4

Associations between clinicopathologic variables and lymph node metastasis (LNM)

	LNM Negative (381)	LNM positive (311)		Univariate analysis (P)	Exp	Adjusted odds ratio (95% CI)	Multivariate analysis (P)
Sex			$\chi^2=0.886$	0.380			
Male	252	195					
Female	129	116					
Age	61.92 ± 11.25 (381)	61.29 ± 11.57 (311)	F = 0.078	0.780			
Tumor location			$\chi^2=1.445$	0.229			
≤ 5 cm	129	119					
> 5cm	252	192					
PNI			$\chi^2=28.859$	0.000	1.213	0.734– 2.003	0.452
Negative	335	223					
Positive	46	88					
LVI			$\chi^2=83.659$	0.000	3.882	2.338– 6.440	0.000
Negative	352	200					
Positive	29	111					
Pathological T stage			$\chi^2=79.238$	0.000	1.969	1.471– 2.635	0.000
T1	41	10			1		
T2	152	47			1.309	0.559– 3.065	0.535
T3	178	233			3.126	1.380– 7.082	0.006
T4	10	21			4.730	1.499– 14.927	0.008
Differentiation			$\chi^2=42.700$	0.000	2.255	1.544– 3.293	0.000
High	287	160					

	LNM Negative (381)	LNM positive (311)		Univariate analysis (P)	Exp	Adjusted odds ratio (95% CI)	Multivariate analysis (P)
Low	94	151					
TD			$\chi^2=131.791$	0.000	27.645	9.805– 77.947	0.000
Negative	377	220					
Positive	0	95					

As shown in Table 2, Fig. 2 and Fig. 3, we further confirmed the correlation between the primary tumour (T) and nodule status (N) by a binary logistic regression model. Compared with T1, the HRs of LNM for T2, T3, and T4 patients were 1.309 (95% CI: 0.559–3.065, P = 0.535), 3.126 (95% CI: 1.380–7.082, P = 0.006) and 4.730 (95% CI: 1.499–14.927, P = 0.008), respectively. More advanced T stages (T3 and T4) were significantly associated with a higher incidence of LNM.

## Discussion

The results of the present study demonstrated the relationships among clinical and pathological factors in patients undergoing surgery for rectal cancer. These clinicopathological factors included sex, age, tumour location, differentiation grade, LVI, PNI, TD, and pathological T and N stages.

Our study demonstrated that the number of male rectal cancer patients was approximately 1.8 times that of female patients. However, no significant difference in age at onset was observed between female and male rectal cancer patients.

LVI is defined as the involvement of tumours in vascular and lymphatic structures [9–10]. In our study, 20.2% of 692 patients had LVI, which was in agreement with previous studies that reported that the incidence of LVI in rectal cancer patients who underwent curative surgery was 20–30% based on pathological evaluation[11–14].

The regional LN is the most common site of tumour metastasis. To accurately evaluate LNM, as many LNs as possible should be assessed to determine the N stage. Both the total number of regional LNs removed and the number of positive LNs involved should be reported. The AJCC 7th and 8th editions state that it is important to obtain and examine at least 12 LNs[8]. The prior 6th edition suggested obtaining a range from 7 to 14 LNs. In this study, an average of  $18.56 \pm 5.68$  (from 10–49) LNs were obtained and examined.

We determined that LVI, pathological T stage, differentiation grade, and TD were significantly related to N based on univariate and multivariate analyses. The presence of LVI and TD, poor differentiation and advanced T stage (T3 and T4) were significantly associated with LNM. PNI was also an independent risk factor for N in univariate analysis but not multivariate analysis. The HRs were calculated for every risk factor

in our study and are shown in Table 4. The strongest risk factor was TD (hazard ratio (HR) = 27.645; 95% CI 9.805–77.947; P = 0.000), partly resulting from TD accounting for a small portion of the N stage. From the AJCC 7th (2010) edition to the 8th edition, the new nodal subclassification category N1c is used if there is TD but no concurrent positive LNs. In our study, 13.7% (95/692) of patients had TDs, including 4.5% (18/400) of patients who lacked positive LNs and 26.4% (77/292) of patients who had positive LNs. Similar to Chen`s report[15] (approximately 10% of colorectal cancers have TDs, and 2.5% of colon cancer and 3.3% of rectal cancer have TDs without positive LNs). Our finding was slightly lower than the 14.8% in stage III colorectal cancer previously reported[16].

We also found that the higher the T stage was, the higher the probability of TD. Compared with T1 stage, stage T3 (OR = 6.106, 95% CI = 1.455–25.631, P = 0.013) and T4 (OR = 7.146, 95% CI = 1.378–37.044, P = 0.019) were more likely to have positive TDs; the same result was not observed for stage T2 (P = 0.435, OR = 0.503, 95% CI = 0.089–2.824). Many studies have shown that the presence of TDs is associated with advanced tumour growth and reduced disease-free and overall survival[17–21].

Our study explored the relationships between pathological T and N stages in 692 patients receiving surgery and not neoadjuvant therapy. In our study, the overall LN involvement was 44.9%. The percentage of LNI at each pathologic T stage was as follows: 19.6% in T1, 23.6% in T2, 56.7% in T3, and 67.8% in T4. A previous study showed that the percentage of LNI at each tumour depth was as follows: 5.7% for T1; 19.6% for T2; 65.7% for T3; 78.8% for T4[22]. Another study reported that the overall incidence of LNM was 12.7% for colorectal cancer (5.6% for T1 and 14.5% for T2; p = 0.021)[23]. In Patel`s study[24], no patients with stage T1/2 N0 rectal adenocarcinoma who underwent resection without neoadjuvant or adjuvant CRT had LNM. The lower rate of LNM in patients with T1 disease in these previous studies could be due to positive TDs not being categorized as N1c before the AJCC 7th edition or selection bias. Compared to stage T1, there is a slight increase in the LNM rate in T2, although it is not significant; however, there are significant increases in T3 and T4 compared with T1 (Table 2, Fig. 2 and Fig. 3). This conclusion was confirmed by univariate and multivariate analyses (Table 4). Compared with T1, the hazard ratios of LNM for T3 and T4 were 3.126 (95% CI: 1.380–7.082, P = 0.006) and 4.730 (95% CI: 1.499–14.927, P = 0.008), respectively, but a significantly increased risk was not observed for T2 patients (HR = 1.309, 95% CI: 0.559–3.065, P = 0.535). Therefore, increased depths of tumour penetration are associated with a greater incidence of LNM.

## Conclusion

The present study indicated that the presence of LVI, PNI, TD, low pathological differentiation grade, and advanced pathological T stage (T3 and T4) were independent factors associated with a higher incidence of LNM on univariate and multivariate analyses.

## Abbreviations

PNI  
perineural invasion  
LVI

lymphovascular invasion  
TD  
tumour deposit  
LNM  
lymph node metastasis  
nRCT  
neoadjuvant radiochemotherapy  
TME  
total mesorectal excision  
LARC  
locally advanced rectal carcinoma  
LNs  
lymph nodes  
HR  
The hazard ratio  
CI  
confidence interval  
LNM  
lymph node metastasis

## **Declarations**

### **Ethical Approval and Consent to participate**

This retrospective study was approved by the Institutional Research Ethics Committee of the First Affiliated Hospital of Nanjing Medical University (No:2019-SR-316).

### **Consent for publication**

All authors of this paper have read and and complied with author guidelines. The contents of this manuscript have not been copyrighted or published previously. The contents of this manuscript are not under consideration for publication elsewhere. The contents of this manuscript will not be copyrighted, submitted, or published elsewhere while acceptance by the manuscript is under consideration. All authors approve to publish this article in Journal of Experimental & Clinical Cancer Research.

### **Availability of supporting data**

Not applicable

### **Competing interests**

The authors have declared that no competing interests exist.

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### Authors' contributions

Liping Xu, Chi Zhang and Zhaoyue Zhang contributed equally to this work as first authors.

**Liping Xu, Chi Zhang, Zhaoyue Zhang** and **Xinyu Tang** carried out the data collection, data analysis and drafted the manuscript; **Xinchen Sun** and **Qin Qin** supervised the research program and edited the manuscript; **Xinchen Sun** and **Qin Qin** had significant roles in the study design and manuscript review. All authors read and approved the final manuscript.

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## Figures

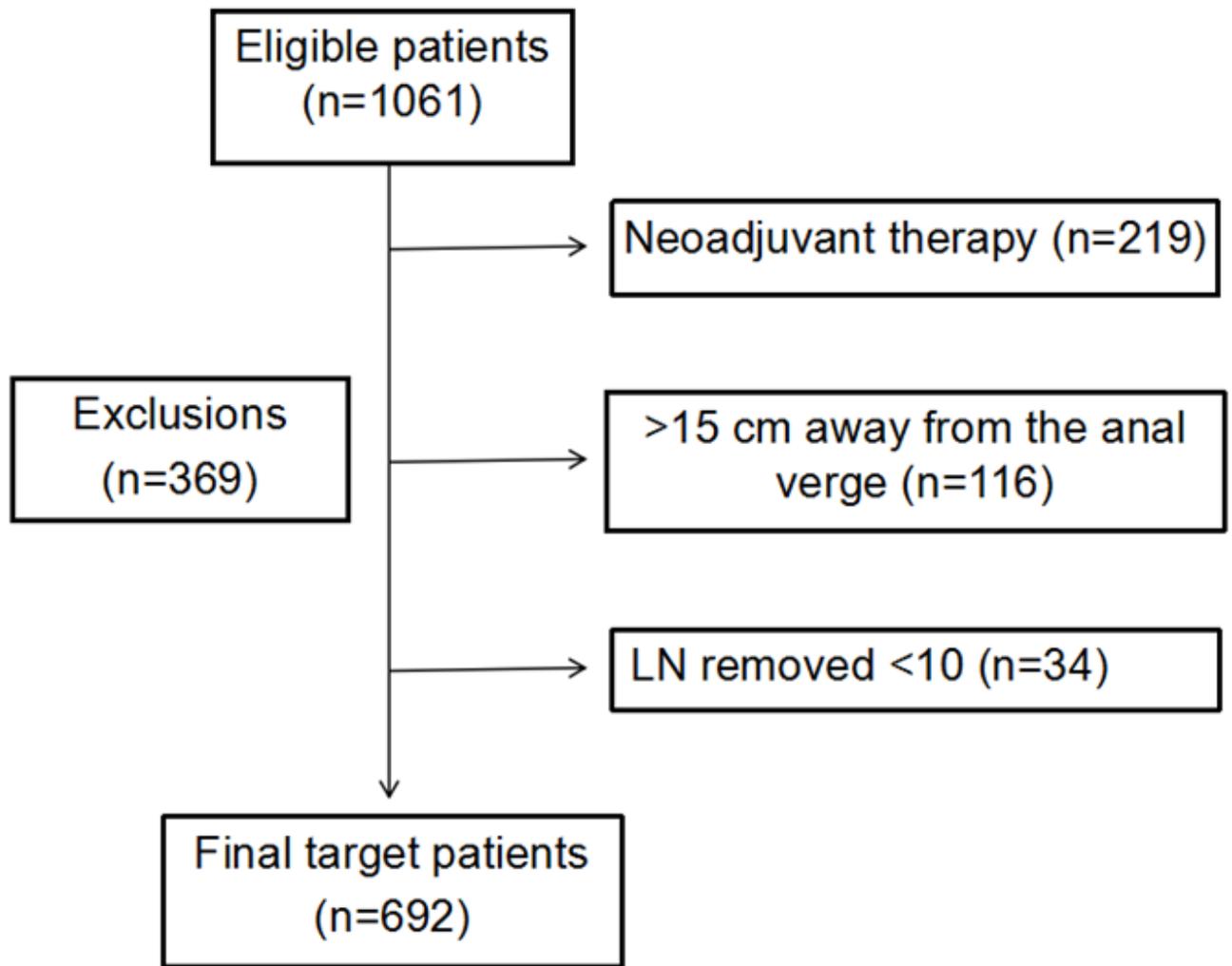


Figure 1

Flow chart for screening eligible patients.

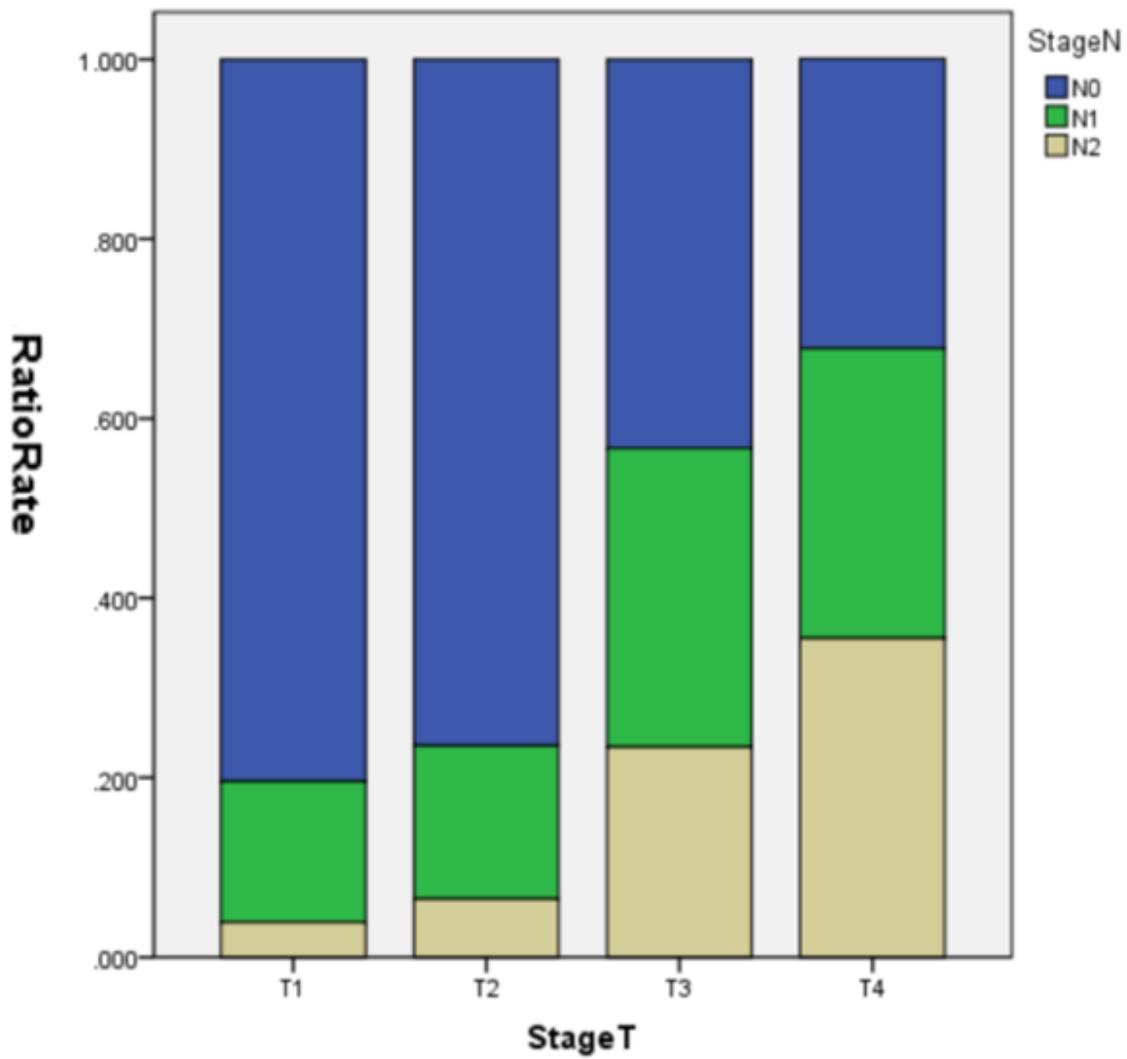
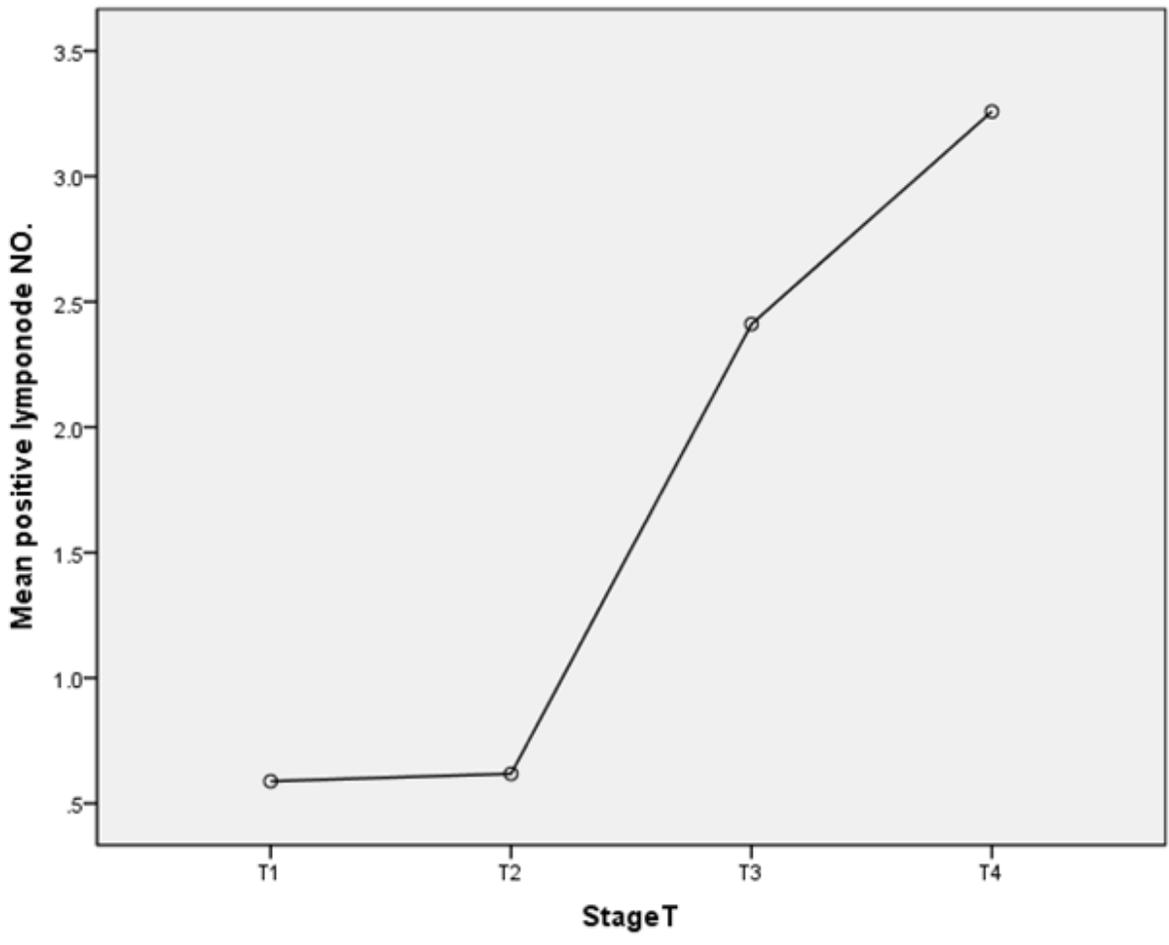


Figure 2

Stacked bar chart of N0-2 ratio for each T stage in 692 patients with rectal cancer.  $G=0.579$ ,  $P=0.000$



**Figure 3**

The mean number of positive lymph nodes for each T stage.