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Factors associated with lymph node metastasis and survival in T2 colon cancer

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Abstract

Purpose This study aimed to explore the clinical factors associated with lymph node metastasis (LNM) and survival in T2 colon cancer.

Method Patients with T2 colon cancer and receiving radical surgery from 2017 to 2021 in our hospital were retrospectively enrolled. Patients were divided into two groups according to the LN status (LNM, non-LNM). The demographic, radiological, pathological, and survival data were collected and analyzed. Logistic regression was used to find the factors associated with LNM, and cox regression was adopted to identify factors contributing to poor survival. All the data analysis was performed by SPSS 22.0 and R.

Results A total of 150 patients were included in this study, among them thirty were with LNM (20%). The LNM group had significantly higher incidence of lymph-vascular invasion (LVI) and perineural invasion. Besides, positive LNs had more proportion of irregular margin ($P<0.001$) and heterogeneity ($P<0.001$) than the negative ones. The multivariate analysis indicated that LVI and heterogeneity of LN were independent risk factors of LNM in T2 colon cancer. The disease-free survival (DFS) was 80% and 93.3% in the LNM and non-LNM group ($P=0.02$), respectively. Besides, the overall survival (OS) was 92.9% and 95% in the LNM and non-LNM group ($P=0.103$), respectively. The results indicated that elevated CA199 value and LNM were independent risk factors contributing to poorer OS and DFS.

Conclusion The current data indicated LVI and LN heterogeneity were independent risk factors of LNM in T2 colon cancer. More extended surgery should be considered when these factors were detected.

Keywords Colon cancer, T2, Lymph node metastasis, Survival, Risk factor

Introduction

Colorectal cancer (CRC) ranges top three incidence among all the carcinomas worldwide, causing high mortality rate and heavy social burden [1]. Up to now, radical surgery with thorough lymph node dissection is still firstly recommended for colon cancer with locally advanced stage [2]. However, for these with limited tumor invasion and without lymph node metastasis (LNM), less-extended surgery or even endoscopic resection could be performed to reduce surgical injury and faster postoperative recovery [3, 4]. Although it was not indicated in the current guidelines, we thought segmental resection could be an alternation for T2 colon cancer regarding the localized tumor and limited incidence of LNM [5]. Current studies have demonstrated that segmental resection was comparable to extended resection regarding survival outcomes for tumor located on transverse colon and splenic flexure, and these studies included large number of T2 tumors [6, 7]. Additionally, with the advancement of endoscopic technique and the

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application of neoadjuvant chemotherapy for downstage, local excision might also be feasible for colon cancer with T2N0 stage, as this pattern has been applied for rectal cancer successfully [8, 9, 10]. Morten et al. reported the promising outcomes regarding endoscopic resection combined with laparoscopic-assisted surgery for T2N0 colon cancer, in which most tumors located in cecum and ascending colon, and no major complication occurred and no recurrence was observed in the follow-up period [11]. This study indicated the technique safety and feasibility of endoscopic resection for T2N0 colon cancer. Therefore, accuracy prediction of LNM before surgery is pivotal to choose the appropriate procedure for colon cancer with early T stage.

. Up to now, we still mainly depend on the contrast-enhanced CT scan to evaluate the primary LN status of colon cancer [12]. The incidence of LNM was significantly associated with the node size, of which 5 mm and 10 mm in short-axis diameter are the cut-off values most frequently used for clinical assessment [13]. However, a wide overlap in size was observed between positive and negative LNs [14]. According to recent studies, the size is still with low efficiency to predict the LN status of colon cancer, regardless of short-axis or long-axis diameter [15]. Particularly, for the nodes with 5–10 mm of short-axis diameter, the positive rate ranged 40-60%, bringing great challenge for accuracy diagnosis [16]. In addition, the incidence of LNM increased when some malignant features of LN were detected, including irregular margin and internal heterogeneity [17].

Generally, the incidence of LNM increased with the depth of tumor invasion, and it was appropriately 10% in T1 colon cancer with submucosa invasion, while ranged 18-24% in T2 colon cancer [18, 19]. Numerous studies have reported the risk factors of LNM in T1 colon cancer, for these without high-risk factors are the candidates for endoscopic resection [20]. However, factors contributing to LNM in T2 colon cancer are still not well defined [3]. In the past, similar surgical strategy was adopted for T2 and T3 colon cancer. The updated Japanese guideline recommended D3 dissection for T3 colon cancer regardless of LN status, while less-extensive LN dissection could be adopted for T2 colon cancer without LNM [18]. Additionally, most previous studies focused on the pathological outcomes associated with LNM in colorectal cancer with early T stage, while study exploring radiological parameters was rare [21]. Therefore, we designed this study to explore the risk factors associated with LNM in T2 colon cancer mainly regarding CT imaging assessment, and further investigate the factors contributing to poor survival. We hope our study can provide more reference to clinical practice.

Method

This study was retrospectively designed, with the consecutive patients from 2017 to 2021 in the Department of Colorectal Surgery, the First Affiliated Hospital of USTC. Patients with T2 colon cancer and receiving radical surgery were included. We divided the patients into two groups according to the LN status (LNM, non-LNM). This study was approved by the USTC's Ethics Committee, and written informed consent was obtained for each individual.

The inclusion criteria of this study were as follows: (1) pathologically confirmed colon adenocarcinoma; (2) the pathological stage was T2; (3) radical surgery was performed. The exclusion criteria included: (1) patients with concurrently distant metastasis; (2) multiple malignant neoplasms in the gastrointestinal tract or other organs; (3) different tumor types such as neuroendocrine or stromal tumors; (4) emergency surgeries; (5) clinical data was lack. In this study, patients were enrolled regardless of the status of MSI/MMR, or whether they received adjuvant therapy. Additionally, no limitation was set for inclusion criteria regarding the patients' own conditions and underlying diseases as long as they received radical surgery. In our center, radical surgery for colon cancer included at least 7 cm for proximal and distal resection margin and D3 LN dissection.

Data collection

Baseline data included gender, age, body mass index (BMI), comorbidity, ASA score, CEA value, CA199 value, whether colonoscopy can pass through the tumor, tumor location (ascending colon, transverse colon, descending colon, and sigmoid colon), and adjuvant therapy.

Surgical details included the type of approach (laparoscopy, open) and surgical procedure (right hemicolectomy, left hemicolectomy, segmental resection, sigmoid resection).

Pathological data covered the depth of invasion, N stage, number of LN harvested, the degree of differentiation, mucinous component, tumor size, lymph-vascular invasion (LVI), and perineural invasion (PNI).

Imaging information comprised the existence of visible LN, short-axis diameter, long-axis diameter, shape, margin, heterogeneity, and location of target LNs.

Survival outcomes encompassed overall survival (OS), disease-free survival (DFS), and the site of recurrence.

Definition

The portal venous phase of primary contrast-enhanced CT scan was selected for LN evaluation. In our center, the CT machine was 64 detector rows and the slicer thickness was 1 mm. We defined visible LNs as these with short-axis diameter ≥ 2 mm on the transverse section. The node with maximum short-axis diameter was

selected as the targeted one. All the data were measured from the transversesection with maximum short-axis diameter. The maximum long-axis diameter was measured perpendicular to the line used to measure the short-axis diameter [15]. Each short and long-axis diameter was measured thrice and then the average value would be adopted. The shape of LN was categorized as round, oval, and others. The margin of LN was classified into four types as referred to previous report, including smooth, lobulated, spiculated, and indistinct [22]. The internal heterogeneity was defined as mixed attenuation within the LNs, and the target LN would be divided into heterogeneity and homogeneity groups [16, 23]. As reported in Japanese study, the node location included pericolic, intermediate and main LNs [24]. The LN evaluation was directly performed on the PACS workstation.

Table 1 Demographic information

	LNM ($n=30$)	Non-LNM ($n=120$)	*P* value
Gender			0.740
Female	13 (43.3%)	48 (40%)	
Male	17 (56.7%)	72 (60%)	
Age (year)	66.5 (46–87)	65.5 (33–95)	0.733
BMI (Kg/m^2)	24.1 (17.6–33.3)	23.2 (17.4–32.0)	0.235
ASA score			0.503
2	12 (40%)	38 (31.7%)	
3	18 (60%)	79 (65.8%)	
4	0	3 (2.5%)	
Comorbidity	17 (56.7%)	65 (54.2%)	0.802
Hypertension	17 (56.7%)	50 (41.7%)	
Diabetes	3 (10%)	14 (11.7%)	
Coronary heart disease	2 (6.7%)	15 (12.5%)	
Cerebral infarction	4 (13.3%)	9 (7.5%)	
CEA	3.9 (1.3–186)	3.3 (0.6–90.2)	0.086
CA199	13.7 (1-144.6)	9.9 (0.6-135.1)	0.093
Colonoscopy pass through			
Yes			
No			
Tumor location			0.078
Ascending colon	10 (33.3%)	45 (37.5%)	
Transverse colon	2 (6.7%)	9 (7.5%)	
Descending colon	0 (0)	18 (15%)	
Sigmoid colon	18 (60%)	48 (40%)	
Surgical approach			0.380
Laparoscopy	25 (83.3%)	91 (75.8%)	
Open	5 (16.7%)	29 (24.2%)	
Surgical procedure			**0.041**
Right hemicolectomy	10 (33.3%)	45 (37.5%)	
Left hemicolectomy	0 (0)	21 (17.5%)	
Segmental resection	2 (6.7%)	9 (7.5%)	
Sigmoid colon resection	18 (60%)	45 (37.5%)	

LNM, lymph node metastasis; BMI, body mass index, ASA, American Society of Anesthesiologists

The imaging assessment was performed by a colorectal surgeon with more than ten years' experience, under the supervision of a senior radiologist with more than twenty years' experience and blinded to the pathological outcomes except for the tumor location. We calculated the Intra-class Correlation Coefficient (ICC) to evaluate the inter-rater reliability of measurement between the reviewers. All the ICCs reached 0.93 and excellent agreement was indicated. (Supplementary Fig. 1, Supplementary Fig. 2)

Statistical analysis

Continuous data were presented as median (min-max) or mean ± SD (standard deviation). We applied non-parametric Mann–Whitney U tests or independent-sample t-tests for analysis. Ranked data were also examined using non-parametric tests. Categorical variables were represented as counts and analyzed using Chi-Square or Fisher's exact tests. Logistic regression (including univariate and multivariate analysis) was employed to identify factors associated with LNM, and cox regression was used to find factors associated with OS and DFS. For both logistic and cox regression, all the variables would be included for univariate analysis first. Only variable showing significant difference ($P<0.05$) in the univariate analysis would be included for multivariate analysis. These still showing significant difference in the multivariate analysis were kept for model construction. Kaplan-Meier curve was applied to compare the survival outcomes between the two groups. A $p<0.05$ was considered statistically significant. The statistical analyses were executed using SPSS 22.0 and the nomogram was constructed by R (version 4.4.1).

Results

A total of 150 patients were enrolled in this study, and among them thirty (20%) were with LNM. The demographic information was showed in Table 1. Comparable results were observed between the two groups regarding gender, age, BMI, ASA score, and the proportion of patients with comorbidity. Although the level of tumor marker including CEA and CA199 was higher in the LNM group, no statistical significance was observed. We found sigmoid colon and ascending colon were the most frequent site of tumor location in both groups. The results indicated that more tumors in the LNM group located at the sigmoid colon (60% vs. 40%), while no tumors in the LNM group located at the descending colon. As a result, significantly fewer patients in the LNM group received hemicolectomy (33.3% vs. 55%, $P=0.041$). Besides, the proportion of patients receiving laparoscopic procedure was comparable between the two groups.

Table 2 Pathological outcomes

	LNM (*n* = 30)	No-LNM (*n* = 120)	*P* value
T2			0.064
Superficial layer	3 (10%)	31 (25.8%)	
Deep layer	27 (90%)	89 (74.2%)	
N stage			-
N0	-	120	
N1	22 (73.3%)	-	
N2	8 (26.7%)	-	
LN harvested	14.5 (4–25)	14 (2–37)	0.778
No. of positive LNs	2 (1–13)	-	
Differentiation			0.584
G1	0	1 (0.9%)	
G2	24 (80%)	100 (83.3%)	
G3	5 (16.7%)	19 (15.8%)	
G4	1 (3.3%)	0	
Mucinous component			0.496
yes	4 (13.3%)	11 (9.2%)	
No	26 (86.7%)	109 (90.8%)	
Tumor size (cm)	3.5 (1.6-7)	3.8 (1–10)	0.675
Lymph-vascular invasion			**< 0.001**
Yes	12 (40%)	9 (7.5%)	
No	18 (60%)	111 (92.5%)	
perineural invasion			**0.015**
Yes	4 (13.3%)	2 (1.7%)	
No	26 (86.7%)	118 (98.3%)	

LNM, lymph node metastasis

Table 3 Imaging information

	LNM (*n* = 30)	Non-LNM (*n* = 120)	*P* value
Visible LN			0.053
Yes	16 (53.3%)	41 (34.2%)	
No	14 (46.7%)	79 (65.8%)	
SD (mm)	5.3 (3.0-15.2)	4.7 (2.0-8.5)	0.324
2–5	5 (16.7%)	22 (18.3%)	0.128
≥5	11 (36.7%)	19 (15.8%)	
LD (mm)	6.1 (3.4–17.8)	5.6 (2.5–12.6)	0.214
<10	10 (33.3%)	36 (30%)	**0.030**
≥10	6 (20%)	5 (4.2%)	
LN shape			0.807
Circle	8 (26.7%)	22 (18.3%)	
Oval	6 (20%)	12 (10.0%)	
Others	2 (6.7%)	7 (5.8%)	
LN margin			**< 0.001**
Smooth	0	19 (15.8%)	
Lobulated	5 (16.6%)	16 (13.3%)	
Spiculated	5 (16.6%)	4 (3.3%)	
Indistinct	6 (20%)	2 (1.7%)	
LN heterogeneity			**< 0.001**
Yes	16 (53.3%)	16 (13.3%)	
No	0	25 (20.8%)	
LN location			0.602
Pericolic	4 (13.3%)	15 (12.5%)	
Intermediate	12 (40%)	26 (21.7%)	
Main	0	0	

LNM, lymph node metastasis; SD, short diameter; LD, long diameter;

Pathological outcomes

The pathological results were showed in Table 2. More tumors in the LNM group invaded into the deep muscle layer (90.0% vs. 74.2%), but it was not significantly different ($P = 0.064$). The number of LN harvested was comparable between the two groups (14.5 vs. 14, $P = 0.778$). 22 individuals (73.3%) in the LNM group were staged as N1 and the others were staged as N2. Besides, comparable results were observed between the two groups regarding the proportion of poor differentiation and mucinous component. Significant difference was observed between the two groups regarding the incidence of LVI ($P < 0.001$), which was 40% (12/30) in the LNM group and 7.5% (9/120) in the non-LNM group. Additionally, significantly higher incidence of PNI was also observed in the LNM group (13.3% vs. 1.7%, $P = 0.015$)..

Imaging observation

Table 3 presented the imaging information. More tumors in the LNM group had visible LNs, but that was not significantly different (53.3% vs. 34.2, $P = 0.053$). Although the visible LNs in the LNM group were larger in size, no significant difference was observed between the two groups regarding the short or long diameter. Besides, it indicated no significant difference between the two groups in terms of LN shape and location. However, we observed that LNs in the LNM group was significantly associated with irregular margin ($P < 0.001$) and heterogeneity ($P < 0.001$). LNs with heterogeneity was observed in 32 patients, and among them sixteen were positive.

Factors exploration

The results of logistic regression were showed in Table 4. In the univariate analysis, we found higher BMI value ($P = 0.049$, OR = 3.083, 95%CI [1.003, 9.481]), larger short diameter ($P = 0.013$, OR = 3.078, 95%CI [1.264, 7.492]), larger long diameter ($P = 0.007$, OR = 5.750, 95%CI [1.622, 20.387]), LVI ($P < 0.001$, OR = 8.222, 95%CI [3.032, 22.294]), PNI ($P = 0.013$, OR = 9.077, 95%CI [1.578, 52.218]), irregular margin ($P < 0.001$, OR = 11.000, 95%CI [3.636, 33.276]), and heterogeneity ($P < 0.001$, OR = 7.429, 95%CI [3.052, 18.084]) were associated with increased incidence of LNM in T2 colon cancer. Then, we put these factors together for multivariate analysis. The result of multivariate analysis indicated that only LVI ($P < 0.001$, OR = 9.758, 95%CI [2.832, 33.625]) and heterogeneity ($P = 0.014$, OR = 6.694, 95%CI [1.475, 30.388]) were independent risk factors contributing to LNM in T2 colon cancer. When LVI and LN heterogeneity both presented, the incidence of LNM reached to 80% (4/5). The incidence of LNM was 50% (8/16) and 44.4% (12/27) when only LVI or LN heterogeneity was detected, respectively. Besides, if either LVI or LN heterogeneity was observed,

Table 4 Univariate and multivariate analysis for risk factors of LNM

	OR	95%CI	*P*	OR	95%CI	*P*
Gender: female/male	0.872	0.388, 1.958	0.872			
Age: <65/≥65	1.357	0.602, 3.062	0.462			
BMI (Kg/m2): <28/≥28	3.083	1.003, 9.481	**0.049**	2.914	0.669, 12.688	0.154
CEA	1.350	0.551, 3.350	0.511			
CA199	1.110	0.218, 5.662	0.900			
Colonoscopy pass through: yes/no	1.147	0.511, 2.576	0.740			
Tumor location: right/left	1.000	0.446, 2.242	1.000			
Short diameter	3.078	1.264, 7.492	**0.013**	0.166	0.015, 1.842	0.144
Long diameter	5.750	1.622, 20.387	**0.007**	5.876	0.730, 47.286	0.096
Invasion depth: superficial/deep	3.135	0.888, 11.061	0.076			
LVI: no/yes	8.222	3.032, 22.294	**<0.001**	9.758	2.832, 33.625	**<0.001**
PNI: no/yes	9.077	1.578, 52.218	**0.013**	3.179	0.337, 29.958	0.312
Mucinous component	1.692	0.492, 5.823	0.404			
Differentiation	1.329	0.479, 3.686	0.585			
Tumor size:	0.415	0.148, 1.167	0.096			
Margin	11.000	3.636, 33.276	**<0.001**	8.379	0.883, 79.523	0.064
heterogeneity	7.429	3.052, 18.084	**<0.001**	6.694	1.475, 30.388	**0.014**
LN harvested	0.988	0.920, 1.062	0.745			

LNM, lymph node metastasis; BMI, body mass index; LVI, lymph-vascular invasion; PNI, perineural invasion

the incidence of LNM was only 5.8% (6/102). The conducted a nomogram to predict LNM based on LVI and heterogeneity, and the C-index was 0.81. (Supplementary Fig. 3, Supplementary Fig. 4).

Survival outcomes

With a median follow-up time of 53 (23–88) month, distant metastasis was observed in fourteen patients (LNM, $n=6$; non-LNM, $n=8$) and disease-related death occurred in ten patients (LNM, $n=4$; non-LNM, $n=6$) in the whole cohort. The recurrence site included liver ($n=8$), lung ($n=4$), and peritoneum ($n=2$). No local recurrence was found. The DFS was 80% in the LNM group and 93.3% in the non-LNM group. Besides, the OS was 92.9% in the LNM group and 95% in the non-LNM group. Figure 1 presented the Kaplan-Meier survival curve between LNM and non-LNM groups. A significant gap was observed between the two groups regarding both DFS and OS, indicating the better survival in the non-LNM group. In the multivariate analysis with cox regression, we found elevated CA199 value and LNM were independent risk factors contributing to poorer DFS and OS. (Tables 5 and 6)

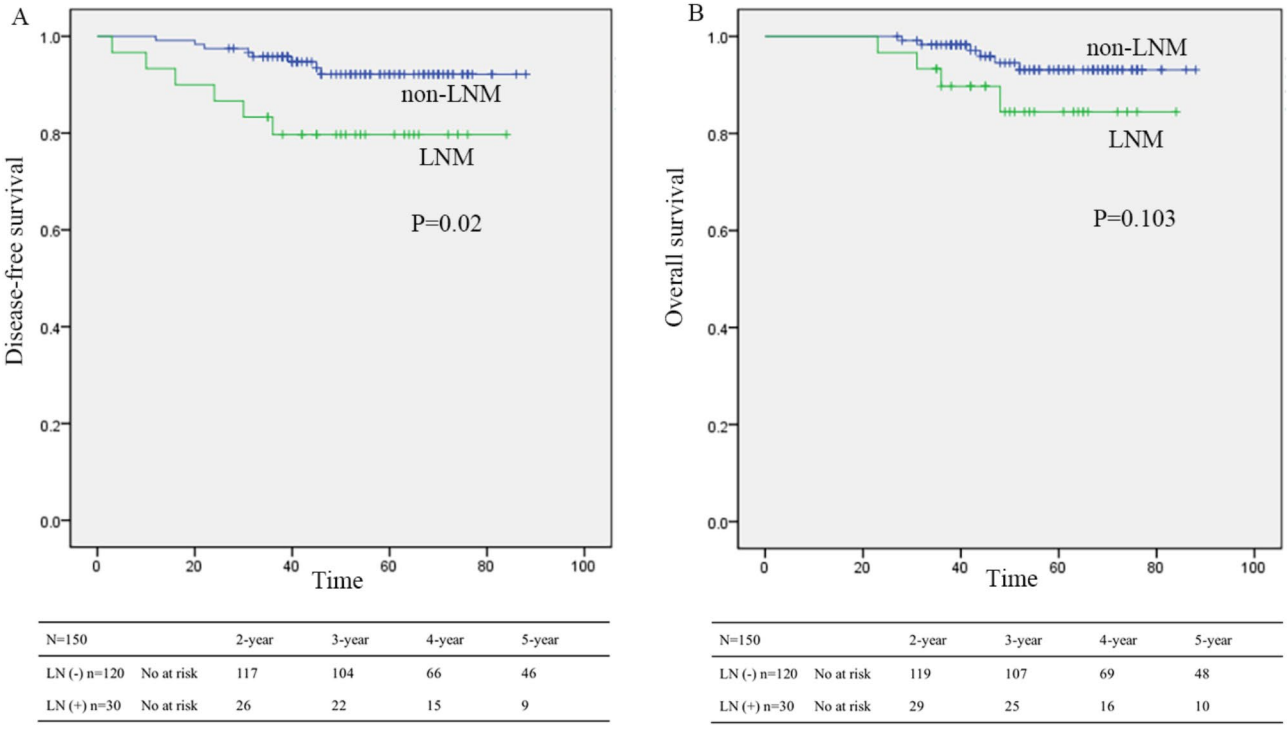
Discussion

In this study, we systematically explored the potential factors associated with LNM in T2 colon cancer, especially the radiological parameters, and further investigated the risk factors contributing to poor survival.

Consistent to previous reports, we found LVI was one independent risk factor of LNM in T2 colon cancer [25, 26]. The incidence of LVI was 40% and 7.5% in the LNM and non-LNM group, respectively. Although PNI was also significantly associated with higher incidence of LNM in the univariate analysis, the significance was not indicated in the multivariate analysis. This was different from the result in the previous study [25]. Our result demonstrated that LVI is superior to PNI in predicting LNM in T2 colon cancer. As high-risk factors supplemental to TNM system of CRC, both LVI and PNI could contribute to poorer survival outcomes [27]. However, in this cohort, the association between LVI/PNI and survival was not indicated. We thought the early T stage might help decrease the survival gap. Some studies demonstrated the poor differentiation could contribute to LNM in CRC, but this was not indicated in our study [21]. We thought this might because over 80% individuals were with moderate differentiation.

Generally, the incidence of LNM increased with the depth of tumor invasion [28]. Some previous studies indicated that invasion into the deep muscular layer was associated with higher incidence of LNM when compared with these in the superficial layer [3]. In our study, the similar trend was also observed, in which LNM group had more tumors invading into the deep muscle layer. However, that was not statistically significant. We thought the limited sample size could contribute to this negative outcome.

Radiological parameters were rarely mentioned in the published literatures to predict LNM in T2 colon cancer. We thought this might because most imaging had no visible LNs. Even though, we still found LN heterogeneity, one of the malignant features of LNs, was independent risk factor of LNM. This could provide more reference to



N=150		2-year	3-year	4-year	5-year
LN (-) n=120	No at risk	117	104	66	46
LN (+) n=30	No at risk	26	22	15	9

N=150		2-year	3-year	4-year	5-year
LN (-) n=120	No at risk	119	107	69	48
LN (+) n=30	No at risk	29	25	16	10

Fig. 1 Survival outcomes; **A**, disease-free survival; **B**, overall survival. LNM, lymph node metastasis

Table 5 Univariate and multivariate analysis for factors associated with DFS

	OR	95%CI	*P*	OR	95%CI	*P*
Gender: female/male	0.511	0.177, 1.473	0.214			
Age: <65/≥65	2.206	0.692, 7.035	0.181			
BMI (Kg/m^2): <28/≥28	0.740	0.097, 5.658	0.771			
ASA score: 2/3,4	1.358	0.425, 4.342	0.606			
Comorbidity: no/yes	1.155	0.400, 3.334	0.790			
CEA > 5ug/L*	2.120	0.735, 6.110	0.164			
CA199 > 43U/ml*	7.537	2.315, 24.533	**0.001**	9.976	2.925, 34.027	**< 0.001**
Colonoscopy pass through: yes/no	1.107	0.384, 3.192	0.850			
Tumor location: right/left	0.766	0.268, 2.184	0.618			
Invasion depth: superficial/deep	1.810	0.405, 8.087	0.437			
LNM	3.272	1.135, 9.432	**0.028**	4.703	1.519, 14.558	**0.007**
LVI: no/yes	1.063	0.238, 4.751	0.936			
PNI: no/yes	0.047	0, 9077.298	0.622			
Mucinous component: no/yes	0.762	0.100, 5.828	0.794			
Poor differentiation	0.825	0.185, 3.685	0.801			
Tumor size > 5 cm:	0.604	0.168, 2.170	0.440			
No. of LN harvested > 12	0.718	0.241, 2.143	0.553			
Adjuvant therapy	0.602	0.189, 1.920	0.391			

DFS, disease-free survival; BMI, body mass index; LNM, lymph node metastasis; LVI, lymph-vascular invasion; PNI, perineural invasion

*The cut-off value was referred to the criteria in our clinical lab indicating abnormal rising

clinical practice. In our study, node size was not independent risk factor contributing to LNM in the multivariate analysis, this was not consistent with the results in some previous studies [29]. We thought this was because of the significant correlation among short-axis diameter, long-axis diameter, and heterogeneity. We chose the largest LN on the primary imaging as the targeted one to extract related parameters, and this method was also adopted in some previous studies [30, 31]. However, some indeterminacy might exist because we did not perform node-by-node matching. As we know, node-by-node matching was achieved in some studies regarding rectal cancer,

Table 6 Univariate and multivariate analysis for factors associated with OS

	OR	95%CI	*P*	OR	95%CI	*P*
Gender: female/male	0.788	0.227, 0.731	0.707			
Age: <65/≥65	8.115	1.028, 64.059	**0.047**	4.206	0.500, 35.361	0.186
BMI (Kg/m^2): <28/≥28	1.210	0.153, 9.578	0.857			
ASA score: 2/3,4	6.000	0.756,47.600	0.090			
Comorbidity	1.483	0.417, 5.277	0.543			
CEA > 5ug/L*	1.829	0.516, 6.489	0.350			
CA199 > 43U/ml*	12.119	3.253, 45.146	**< 0.001**	12.041	2.996, 48.388	**< 0.001**
Colonoscopy pass through: yes/no	0.624	0.161, 2.413	0.494			
Tumor location: right/left	0.328	0.085, 1.268	0.106			
Invasion depth: superficial/deep	1.203	0.255, 5.665	0.815			
LNM						
N1	3.672	1.036, 13.017	**0.044**	4.639	1.147, 18.771	**0.031**
N2	-	-	0.987	-	-	0.992
LVI: no/yes	0.796	0.100, 6.302	0.829			
PNI: no/yes	0.047	0.00, 464140.315	0.710			
Mucinous component: no/yes	1.123	0.142, 8.868	0.912			
Poor differentiation	0.545	0.069, 4.300	0.564			
Tumor size > 5 cm:	0.231	0.029, 1.826	0.165			
No. of LN harvested > 12	0.628	0.177, 2.230	0.472			
Adjuvant therapy	0.367	0.078, 1.729	0.205			

OS, overall survival; BMI, body mass index; LNM, lymph node metastasis; LVI, lymph-vascular invasion; PNI, perineural invasion

*The cut-off value was referred to the criteria in our clinical lab indicating abnormal rising

mainly with the help of the fixed structure of the mesorectum [32]. However, this was rarely reported in colon resection and could be further explored in the future.

With the application of complete mesocolonic excision and D3 LN dissection, local failure was rarely reported for primarily resectable colon cancer [33]. We thought positive LNs residual might be the main cause of local recurrence after colon cancer resection. Fortunately, in the duration of follow-up, no local recurrence was found in our cohort, even in the group with segmental resection. Up to now, the literatures were still limited comparing segmental resection with hemicolectomy for colon cancer, and most were regarding tumors locating on transverse colon and splenic flexure. Additionally, most studies did not find significant difference between the two approaches regarding surgical and survival outcomes [6]. Recently, the long-term outcomes of RELARC study were published, indicating that routine D3 LN dissection was not necessary, unless obvious LN involvement was observed [34]. Therefore, we should try to improve the diagnosis accuracy of LNM to avoid the unnecessary extended surgery.

Several studies constructed the nomogram to predict LNM in T2 colon cancer. However, these models were with low efficiency, of which the AUC values were around 0.70 [19]. Besides, most models did not include radiological parameters. In our study, the AUC value combining LVI and heterogeneity reached to 0.81, indicating the increased predicting efficiency when compared with the data in previous studies. We noticed one recent study predicting LNM in T2 CRC by artificial intelligence (AI) technique [35]. The AI model mainly enrolled clinical and pathological parameters for prediction. However, AUC value was still only 0.75 and the specificity is extremely low. As a result, combining radiological parameters in the prediction model might significantly improve the efficiency because it directly reflected the features of LNs. In clinical practice, when both LVI and LN heterogeneity were detected for T2 colon cancer before surgery, radical surgery with thorough LN dissection should be considered. If the LVI was detected after endoscopic resection, supplementary surgery should also be recommended to the patient. Extremely low incidence of LNM was observed when both LVI and heterogeneity were not found, and extended surgery might be not necessary in this situation.

In the past, radical surgery with adjuvant therapy were the main pattern recommended for colon cancer with locally advanced stage [36]. In recent years, several randomized clinical trials were designed to explore the clinical efficiency of neoadjuvant chemotherapy for locally advanced colon cancer, in which T2 tumors with LNM were enrolled [8]. Survival benefit was observed in the neoadjuvant groups in some studies [9]. We thought accurate stage is extremely important for these studies to find positive outcomes. Generally, patients with later stage would benefit more from the neoadjuvant chemotherapy, for LNM is significantly associated with distant metastasis [37]. Our data demonstrated that LNM was associated with significantly poor survival in T2 colon

cancer. Therefore, it might be beneficial to identify these patients with LNM to receive neoadjuvant therapy.

In this study, we explored the clinical factors associated with LNM and survival in T2 colon cancer with considerable sample size. However, the retrospective design with the limited sample size from single center was the main limitation of this study. In consideration of the small proportion of T2N + stage in the whole colon cancer, multi-center and prospective study is warranted in the future for further validation. Besides, slight discrepancy might exist regarding the imaging evaluation, thought several criteria in published literatures was referred. It's still not absolutely confident whether the target LN with maximum short-axis diameter was positive in the LNM group, especially when only one positive LN is pathologically detected. Additionally, we still lack the quantized or objective criteria for heterogeneity evaluation, so the bias from imaging evaluation among surgeons or radiologists cannot be totally avoided. We thought radiomics parameters combined with deep-learning algorithms could be applied in the future for standardized evaluation. Additionally, one recent study used super-resolution and three-dimensional shape with AI technique for the diagnosis of LNM in rectal cancer, and the accuracy reached 0.968. We thought this was encouraging and should also be further investigated in the future [38].

In conclusion, the current data indicated LVI and LN heterogeneity were independent risk factors of LNM in T2 colon cancer. Extended surgery should be considered when these factors were identified.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-025-03748-8.

Supplementary Material 1: **Supplementary Fig. 1**: Schematic diagram of the evaluation for lymph node margin.

Supplementary Material 2: **Supplementary Fig. 2**: Schematic diagram of the evaluation for lymph node heterogeneity.

Supplementary Material 3: **Supplementary Fig. 3**: Predicting model for lymph node metastasis based on heterogeneity and LVI; LVI, lymphvascular invasion.

Supplementary Material 4: **Supplementary Fig. 4**: The calibration curve for the predicting model.

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Shaojun Liu wrote the manuscript; Lei Hu prepared the tables and figures; Xubing Zhang revised the manuscript.

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Data availability
Data is provided within the manuscript or supplementary information.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of the First Affiliated Hospital of USTC and informed consent was obtained from all the patients or their families. This study complied with the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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