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Clinical and pathological factors affecting lymph node metastasis in patients operated on with the diagnosis of colorectal cancer

Kolerektal kanser tanısıyla ameliyat olmuş hastalardaki lenf nodu metastazına etki eden klinik ve patolojik faktörler

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ABSTRACT

Objective: We aimed to examine the clinical and the pathological factors that affect lymph node metastasis, which is an important prognostic factor in the survival of the patients with colorectal cancer, and to determine the most appropriate patient-centered treatment method.
Methods: The file records and electronic data of the patients who had been operated on with the diagnosis of colorectal cancer at the General Surgery Clinic between May 2008 and December 2012 were retrospectively evaluated.
Results: Seventy-four patients including 50 males (67.6%) and 24 females (32.4%) were included in the study. The mean age of the patients was 69.3 years (range: 38-60 years). While lymphovascular invasion was observed in 21 (28.4%), and perineural invasion in 19 (25.7%) patients. When the growth pattern was examined, 48 patients (64.9%) demonstrated ulcerovegetative, 18 patients (24.3%) ulcerated, eight patients (10.8%) polyp-type growth patterns. The most frequent tumor localization was the middle third of rectum (n=20; 27%) and the most common type of surgery was the Miles operation (n=16; 21.6%).
Conclusion: In conclusion, the risk of LNM significantly increases in patients with colorectal cancer who have surgical radial margin, lymphovascular and perineural invasion. Over time, the other risk factors affecting LNM will be determined with large scale studies that can be conducted together with advancing technology and broad sources of knowledge. In this way, minimally invasive surgery can be performed on cases with colon cancer and the patients will be protected from the side effects of unnecessary chemotherapy.

Key words: Lymph node metastasis, colorectal cancer, lypmphovasculer invasion

ÖZ

Amaç: Kolorektal kanserli hastalarda sağkalımda önemli bir prognostik faktör olan lenf nodu metastazına etki eden klinik ve patolojik faktörleri inceleyerek hasta merkezli en uygun tedaviyi belirlemeyi amaçladık.
Yöntemler: Cerrahi kliniğinde Mayıs 2008-Aralık 2012 tarihleri arasında kolerektal kanser tanısıyla ameliyat edilen hastaların dosya kayıtları ve elektronik ortam bilgileri retrospektif olarak incelendi.
Bulgular: Araştırmamızda bulunan 74 hastanın 50'si (%67,6) erkek, 24'ü (%32,4) kadındı. Hastalarımızın yaş ortalaması 69,3 (38-60) yıl olarak bulundu, 50 (%67,6) hasta 65 yaş üstünde, 24 (%32,4) hasta 65 ve altındaydı. Yirmi bir (%28,4) hastada lenfovasküler invazyon gözlenirken 19 (%25,7), hastada perinöral invazyon gözlendi. Gelişim paternine baktığımızda 48 (%64,9) hasta ülserovegatatif, 18 (%24,3) hasta ülsere, 8 (%10,8) hastanın polip tipte gelişim paterni gösteriyordu. En sık gözlenen tümör lokalizasyonu rektum orta 1/3 olarak bulurken (20 (%27)), en sık yapılan operasyon Miles operasyonu olarak karşımıza çıktı (16 (%21,6)).
Sonuç: Sonuç olarak, kolon kanserlerinde lenfovasküler invazyon, perinöral invazyona sahip hastalarda LNM riski önemli ölçüde artmaktadır. Zaman içinde, gelişen teknoloji ve bilgi birikimiyle yapılacak olan daha kapsamlı çalışmalarla LNM'yi etkileyen diğer risk faktörler de bulunacaktır. Bu sayede kolon kanserlerinde minimal invaziv cerrahi uygulanabilecek ve hastalar gereksiz kemoterapinin yan etkilerinden korunacaktır.

Anahtar kelimeler: Lenf nodu metastazı, kolorektal kanser, lenfovasküler invazyon

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INTRODUCTION

Lymph node metastasis in colon cancers is one of the prognostic factors that determine the necessity of adjuvant chemotherapy. As death in colon cancers is generally related to metastatic invasion, it is necessary to remove the lymph nodes in addition to the resection of the primary tumor. Knowing the factors increasing the lymph node metastasis is important for the approach. If the presence of lymph node invasion can be predicted during the preoperative period, the most appropriate treatment option for the patient will be planned. By predetermining the risk factors that can affect lymph node metastasis, the patients who will benefit from partial resection or endoscopic resection can be identified [(1)]. In other words, since there is no LNM, the patients that can not benefit from chemotherapy can be determined [(1)]. The present study aimed to examine the clinical and the pathological factors that affect lymph node metastasis, which is an important prognostic factor in survival of the patients with colorectal cancer and to determine the most appropriate patient-centered treatment method.

MATERIAL and METHOD

The file records and electronic data of the patients who had been operated on with the diagnosis of colorectal cancer in the General Surgery Clinic between May 2008 and December 2012 were retrospectively evaluated. Statistical Package for the Social Sciences (SPSS) 21 program was used for data analysis. Kolmogorov-Smirnov test, Shapiro-Wilk test, independent-Samples T-test, Mann-Whitney U-test, Pearson's correlation, Spearman's rho tests, Pearson's chi-square test were used.

Patients who underwent surgery for colorectal cancer without any other primary cancer were included in the study

Patients with recurrent colorectal cancer, stage 4 cancer and cases with another primary cancer were not included in the study.

RESULTS

Seventy-four patients, 50 males (67.6%) and 24 females (32.4%), were included in the study. The mean age of the patients was 69.3 (38-60) years. In 65 patients (87.8%) >12, , and in 9 patients (12.2%) less than 12 lymph nodes were removed. While the lymph node metastasis was positive in 39 (52.7%) and negative in 35 patients (47.3%). Sixty-one (82.4%) patients were operated on under elective conditions, and 13 patients (17.6%) under emergency conditions. Tumors developed from polyps in four patients (5.4%). Synchronous tumors were observed in four (5.4%). patients Synchronous polyps were observed in 16 (21.6%) patients. Average size of the tumors was 5 cm (1.5-11), the tumor size was ≤ 4 cm in 31 41.9%) and ≥ 4 cm in 43 patients (58.1%). A mucinous component was seen in the pathological examination of 14 patients (18.9%). Lymphovascular invasion was observed in 21 patients (28.4%) and perineural invasion in 19 patients (25.7%). Surgical margin positivity was found in pathological examination of the specimens of nine patients (12.2%).

Forty-eight patients (64.9%) demonstrated ulcerovegetative, 18 patients (24.3%) ulcerated, and eight patients (10.8%) polyp-type growth patterns. Histological grading were reported as Grade 1 in six (8.1%), Grade 2 in 60 (81.1%), and Grade 3 in eight patients (10.8%). TNM classification of the patients was reported as T1 in, three (4.1%), T2, in seven (9.5%), T3 in 44 (59.5%), and T4 in 20 (27%) patients were T4. While lymph node metastasis was not observed in 34 patients (45.9%) (N0), while 22 patients (29.7%) were N1 and 18 patients (24.3%) were N2. In the clinical staging, seven patients (9.5%) were Stage 1, 26 patients (35.1%) Stage 2, and 41 patients (55.4%) Stage 3. The most frequent tumor localization was the middle third of the rectum (n=20; 27%) and the most common type of surgery was the Miles operation (n=16; 21.6%).

When the factors affecting the lymph node metastasis were examined, a significant correlation was found between lymph node metastasis and perineural

invasion (p<0.001), lymphovascular invasion (p<0.001), and positive surgical radial margin (p:0.03), (Table 1).

In patients with positive lymph node metastasis, the most common growth pattern was ulcerovegetative type (n=21; 60%), the most common histological grade was Grade 2 (n=29; 82.9%), the most common stage was Stage T3 (n=19; 54.3%), while the most frequently involved tumor segment was the middle third of the rectum (n=7; 20%) and cecum (n=7; 20%). Besides, the most frequently performed operation was right hemicolectomy (n=7; 20%). All of these results were not statistically significant.

Common characteristics of the patients in which insufficient lymph node was removed were as follows :being over 65 years of age (n=6; 66.7%); male gender (n=7; 77.8%); colonic location (n=3; 33.3%); Stage 3 (n=5; 55.6%); NO (n=4; 44.4%); Grade 2

Table 1. Factors affecting lymph node metastasis.

		Metastasis			
		Absent N (%)	**Present N (%)**	**P value**	**Eta coefficient**
Age	≤65 / 65<	12 (34.3%) / 23 (65.7%)	12 (30.8%) / 27 (69.2%)	0.807	
	Mean±SD.	68.6±11.4	69.8±12.6	0.659	
Gender	Female/Male	9 (25.7%) / 26 (74.3%)	15 (38.5%) / 24 (61.5%)	0.321	
	≤12 / 12<	4 (11.4%) / 31 (88.6%)	5 (12.8%) / 34 (87.2%)	1	
Number of Lymph Nodes	Median±IQR	25±16	22±18	0.454	
Emergent-Elective Surgery	Emergent/Elective	6 (17.1%) / 29 (82.9%)	7 (17.9%) / 32 (82.1%)	1	
The Basis of Polyp	Absent / Present	32 (91.4%) / 3 (8.6%)	38 (97.4%) / 1 (2.6%)	0.339	
Synchronous TM	Absent / Present	34 (97.1%) / 1 (2.9%)	36 (92.3%) / 3 (7.7%)	0.617	
Synchronous Polyp	Absent / Present	27 (77.1%) / 8 (22.9%)	31 (79.5%) / 8 (20.5%)	1	
The Largest Size	≤4 / 4<	18 (51.4%) / 17 (48.6%)	13 (33.3%) / 26 (66.7%)	0.158	
	Mean±SD.	4.6±2	5.3±1.9	0.145	
Mucinous Component	Absent / Present	29(82.9%) / 6 (17.1%)	31 (79.5%) / 8 (20.5%)	0.773	
LVI	Absent / Present	34(97.1%) / 1 (2.9%)	19 (48.7%) / 20 (51.3%)	<0.001	0.536
PNI	Absent / Present	34(97.1%) / 1 (2.9%)	21 (53.8%) / 18 (46.2%)	<0.001	0.495
CS	Absent / Present	34(97.1%) / 1 (2.9%)	31 (79.5%) / 8 (20.5%)	0.03	0.270
	Polyposis	6 (17.1%)	2 (5.1%)		
Growth Pattern	Ulcerated	8 (22.9%)	10 (25.6%)	0.274	
	Ulcerovegetative	21 (60%)	27 (69.2%)		
	Grade I	5 (14.3%)	1 (2.6%)		
Histological Grade	Grade II	29 (82.9%)	31 (79.5%)	0.032	
	Grade III	1 (2.9%)	7 (17.9%)		
	T1	2 (5.7%)	1 (2.6%)		
T	T2	5 (14.3%)	2 (5.1%)	0.520	
	T3	19 (54.3%)	25 (64.1%)		
	T4	9 (25.7%)	11 (28.2%)		
	Right Hemicolectomy	11 (31.4%)	4 (10.3%)	-	
Type of Surgery	Left Hemicolectomy	8 (22.9%)	7 (17.9%)		
	Subtotal Colectomy	1 (2.9%)	0 (0%)		
	Total Colectomy	1 (2.9%)	1 (2.6%)		
	Anterior Resection	1 (2.9%)	3 (7.7%)		
	Low-Anterior Resection	4 (11.4%)	7 (17.9%)		
	Very Low Anterior Resection	0 (0%)	0 (0%)		
	Miles	7 (20%)	9 (23.1%)		
	Sigmoid Colon Resection	1 (2.9%)	7 (17.9%)		
	Transverse Colon Resection	1 (2.9%)	1 (2.6%)		
	Cecum	7 (20%)	2 (5.1%)		
	Ascending colon	3 (8.6%)	2 (5.1%)		
	Hepatic Flexura	3 (8.6%)	1 (2.6%)		
	Transverse Colon	3 (8.6%)	0 (0%)		
	Splenic Flexura	3 (8.6%)	4 (10.3%)		
Tumor Localization	Descending Colon	2 (5.7%)	2 (5.1%)	-	
	Sigmoid Colon	4 (11.4%)	11 (28.2%)		
	Rectosigmoid Junction	1 (2.9%)	1 (2.6%)		
	Rectum Upper 1/3	0 (0%)	2 (5.1%)		
	Rectum Middle 1/3' ü	7 (20%)	13 (33.3%)		
	Rectum Lower 1/3' ü	2 (5.7%)	1 (2.6%)		

Pearson Chi-Square Test (Monte Carlo), Independent T-Test - Mann-Whitney U-Test (Monte Carlo), SD. Standard deviation - IQR: Interquartile Range

(n=8; 88.9%); ulcerovegetative type (n=6; 66.7%); tumor size smaller than 4 cm (n=5; 55.6%); and elective operation (n=6; 66.7%), (Table 2). However, these data were not statistically significant.

When the emergent and elective operations were compared: The aged population in patients operated on under emergent conditions were higher than the patients operated on under elective conditions (p:0.049). The number of synchronous polyps in patients operated on under elective conditions was greater than the patients operated on under emergent conditions (p:0.028).

Table 2. Comparison of the patients with sufficient lymph node removal (12<) with the patients with insufficient lymph node removal ((≤12).

		Number of lymph nodes		P value
		≤12 N (%)	12< N (%)	
Age	≤65 / 65<	3 (33.3%) / 6 (66.7%)	21 (32.3%) / 44 (67.7%)	1
	Mean±SD.	69.6±9.3	69.2±12.4	0.937
Gender	Female / Male	2 (22.2%) / 7 (77.8%)	22 (33.8%) / 43 (66.2%)	0.709
Emergent-elective surgeries	Emergent / Elective	3 (33.3%) / 6 (66.7%)	10 (15.4%) / 55 (84.6%)	0.346
Number of metastasis	Median±IQR	2±4	3±5	0.559
The basis of polyp	Absent / Present	8 (88.9%) / 1 (11.1%)	62 (95.4%) / 3 (4.6%)	0.412
Synchronous TM	Absent / Present	9 (100%) / 0 (0%)	61 (93.8%) / 4 (6.2%)	1
Synchronous Polyp	Absent / Present	7 (77.8%) / 2 (22.2%)	51 (78.5%) / 14 (21.5%)	1
The largest size	≤4 / 4<	5 (55.6%) / 4 (44.4%)	26 (40%) / 39 (60%)	0.478
	Mean±SD	5.1±2.6	5±1.9	0.891
Mucinous component	Absent / Present	6 (66.7%) / 3 (33.3%)	54 (83.1%) / 11 (16.9%)	0.358
LVI	Absent / Present	4 (44.4%) / 5 (55.6%)	49 (75.4%) / 16 (24.6%)	0.107
PNI	Absent / Present	7 (77.8%) / 2 (22.2%)	48 (73.8%) / 17 (26.2%)	1
CS	Absent / Present	8 (88.9%) / 1 (11.1%)	57 (87.7%) / 8 (12.3%)	1
	Polypoid	1 (11.1%)	7 (10.8%)	
Growth pattern	Ulcerated	2 (22.2%)	16 (24.6%)	1
	Ulcerovegetative	6 (66.7%)	42 (64.6%)	
	Grade I	1 (11.1%)	5 (7.7%)	
Histological Grade	Grade II	8 (88.9%)	52 (80%)	0.638
	Grade III	0 (0%)	8 (12.3%)	
	T1	1 (11.1%)	2 (3.1%)	
	T2	2 (22.2%)	5 (7.7%)	0.110
T	T3	6 (66.7%)	38 (58.5%)	
	T4	0 (0%)	20 (30.8%)	
	N0	4 (44.4%)	30 (46.2%)	
N	N1	3 (33.3%)	19 (29.2%)	1
	N2	2 (22.2%)	16 (24.6%)	
	Stage I	2 (22.2%)	5 (7.7%)	
Clinical Stage	Stage II	2 (22.2%)	24 (36.9%)	0.383
	Stage III	5 (55.6%)	36 (55.4%)	
	Right Hemicolectomy	1 (11.1%)	14 (21.5%)	
Type of surgery	Left Hemicolectomy	2 (22.2%)	13 (20%)	-
	Subtotal Colectomy	0 (0%)	1 (1.5%)	
	Total Colectomy	0 (0%)	2 (3.1%)	
	Anterior Resection	0 (0%)	4 (6.2%)	
	Low Anterior Resection	1 (11.1%)	10 (15.4%)	
	Miles	2 (22.2%)	14 (21.5%)	
	Sigmoid Colon Resection	2 (22.2%)	6 (9.2%)	
	Transverse Colon Resection	1 (11.1%)	1 (1.5%)	
	Cecum	1 (11.1%)	8 (12.3%)	
	Ascending colon	0 (0%)	5 (7.7%)	
	Hepatic Flexura	0 (0%)	4 (6.2%)	
	Transverse Colon	0 (0%)	3 (4.6%)	
	Splenic Flexura	0 (0%)	7 (10.8%)	
Tumor localization	Descending colon	3 (33.3%)	1 (1.5%)	-
	Sigmoid Colon	1 (11.1%)	14 (21.5%)	
	Rectosigmoid junction	1 (11.1%)	1 (1.5%)	
	Rectum upper 1/3	0 (0%)	2 (3.1%)	
	Rectum middle 1/3'ü	2 (22.2%)	18 (27.7%)	
	Rectum lower 1/3'ü	1 (11.1%)	2 (3.1%)	

Pearson Chi-Square Test (Monte Carlo), Independent T-Test - Mann-Whitney U-Test (Monte Carlo), SD; Standard deviation - IQR: Interquartile Range

DISCUSSION

Prognostic factors are useful for all cancer treatments. In colorectal surgery, there are various clinical and pathological prognostic factors as human leukocyte antigen (HLA1), depth, histological type, lymphovascular invasion, budding, number of lymph nodes analyzed after surgery (<12) as recommended by ESMO guidelines or NCCN Guidelines Version 2 (2014) [2,3]. The HLA class I expression is prognostic factor in colorectal cancer patients with stage II disease [3]. Lymph node involvement is certainly the most important prognostic factor in colon cancer of all stages.

The curative treatment option in colorectal cancers is the removal of all mesenteric lymph nodes in which the tumor drains, within clean upper and lower surgical margins. While some investigators support the therapeutic benefits of complete lymph node excision, others believe that it provides the possibility of more accurate staging [4]. The most important factor that should be paid attention to during adjuvant chemotherapy is lymph node involvement [5]. In addition, preoperative lymph node involvement has great importance in the planning of neoadjuvant therapy in rectal cancers. While inadequate staging leads to lower survival rates, higher staging causes the patient to receive unnecessarily high dose chemotherapy [6]. Chemotherapeutic agents cause Grade 3-4 neutropenia and peripheral neuropathy at a rate of 40% [7,8]. However the number of removed lymph nodes, and metastatic lymph nodes are affected by the type of surgery, being either emergent or elective, by the surgical technique, and by the experience of the pathologist. The minimum number of lymph nodes that should be removed is still controversial [9]. Many organizations, mainly the American Society of Clinical Oncology (ASCO), the American Joint Committee on Cancer (AJCC), and the National Cancer Institute (NCI), have reported that at least 12 lymph nodes should be dissected as [6,10,11]. Therefore, we determined the minimum number of lymph nodes that should be removed. We analyzed the patients from whom less than 12 lymph nodes were removed. Contrary to what is believed, removal of insufficient number of lymph nodes was not found to be statistically significant especially male patients aged above 65 years, with ulcerovegetative type Stage 3, N0, Grade 2 smaller (<4 cm) tumors localized in the descending colon. When the emergent and elective surgeries were compared, the aged population in patients operated under emergency conditions were higher than the elective operations (p:0.049). The number of synchronous polyps in patients operated on under elective conditions was higher than those found in patients who underwent emergent operations (p:0.028).

In the previous studies, the factors increasing the risk of lymph node metastasis (LNM) were reported as age, poor differentiation, lymphovascular invasion, close surgical margin, smooth or depressed lesions, the depth of tumor invasion, and progression of the tumor towards the area that it invades by budding [12,13]. In the current study, when the factors affecting the lymph node metastasis were examined, it was observed that perineural invasion (p<0.001), lymphovascular invasion (p<0.001), positive surgical margin (p:0.03) significantly increased the lymph node metastasis.

In patients with positive lymph nodes, the most common growth pattern was ulcerovegetative type (n=21; 60%), the histological grade was at most Grade 2 (n=29; 82.9%), and the most frequently involved tumor segment was the middle third of the rectum (n=7; 20%), and cecum (n=7; 20%), while most frequently right hemicolectomy was performed (n=7; 20%).

The presence of LNM decreases the survival times at a rate of 30%. Together with the developing technology day by day, LNM is treated by local excision or endoscopic excision. Much the same as the polyp-based tumors that have submucosal invasion, rectum cancers are treated by less invasive methods such as transanal resection. If the pathological result of the patient after endoscopic procedure or transanal resection is reported as submucosal invasion, it is

necessary to operate on the patient for the second time to complete the treatment. However, when the presence of LNM in only 10% of these tumors is considered, 90% of the patients are unnecessarily operated on for the second time [1,14]. In studies investigating the factors affecting LNM in colorectal cancers, it has been observed that the most important risk factor is lymphovascular invasion [12,14,15]. In the current study, while the most important risk factor was perineural invasion, lymphovascular invasion was the second most important risk factor.

In a multivariate analysis that was performed on 3,759 patients, Voyer et al. [16] found that tumors were most frequently localized in the sigmoid colon, the rate of lymph node positivity was most commonly seen in T3 tumors, and in patients in which right hemicolectomy was done. In the current study, similar to the study of Voyer et al. [16], lymph node positivity was most frequently observed in patients at Stage T3 (n=19; 54.3%) and the most commonly performed operation was right hemicolectomy (n=7; 20%); however, this was not a statistically significant finding.

In the study that was performed by Nascimbeni et al. [13], they demonstrated that Grade 3 and Grade 4 poorly differentiated carcinomas carried a risk for LNM compared to Grade 1 and Grade 2 carcinomas; however, in the aforementioned study, univariate analysis was used instead of multivariate analysis. Although in the current study, the most frequent histological grade was Grade 2 (n=29; 82.9%), this was not a statistically significant finding. In previous studies, it has been found that perineural invasion was a prognostic factor that mainly affects the length of life [17]. As the follow-up of the patients in the current study is still continuing, an evaluation of the prognostic factors and survival could not be conducted.

Nascimbeni et al. [15] have demonstrated that especially in T1 tumors involving the distal third of the rectum, tumor localization affects LNM. Although in the current study it was found that the tumors localized in the middle third of the rectum (n=7; 20%) and cecum (n=7; 20%) affected LNM this was not a statistically significant finding. In the previous studies, the tumor size in T1 colorectal cancers was categorized as tumors of ≤2 cm, and >2 cm. Its effect on LNM has been investigated; however, a statistically significant difference was not found [18-20]. In the current study, we evaluated T1, T2, T3, and T4, and accepted 4 cm as the cut- off value for tumor size; however, no statistically significant difference was observed in the current study.

When the literature was examined to evaluate the factors affecting LNM, in some studies the depth of the submucosal invasion (cm^3) has been reported as a factor that increases the risk of LNM [15,21]. However, in the study of Kitajima et al., [22] as muscularis propria could not be visualized precisely in endoscopic resections, the depth of submucosal invasion was not found to be useful to affect LNM. It has been demonstrated in many studies that malignant polyps cause LNM when present together with other negative factors (Grade 3 or positive surgical margin) [23]. The presence of peritumoral lymphocytic response in T1 colorectal cancers is controversial. Some studies mention that the presence of lymphocytic response increases the risk of LNM; others report that the absence of lymphocytic response increases the risk of LNM [24,25]. It is known that budding or microtubular structure detected nore frequently than 20% in pathological examinations increases the risk of LNM in T1 colorectal cancers [24]. The mucinous and poorly differentiated tumors have a worse prognosis than well and intermediately differentiated tumors [26]. In the study of Ozdemir et al., [27] mucinous tumors were more frequently reported in colorectal cancers that were seen in young patients.

Considering the historical development of the studies investigating the factors that affect LNM in T1 adenocarcinomas of colon tumors, in 1991, Nivatvongs et al. [28] demonstrated that Haggit [14] level 4 invasion was a risk factor; in 1995, Tanaka et al. [12] demonstrated that submucosal invasion >400 um, lymphovascular invasion, Type 2c, and Type 2a+2c poorly differentiated tumors according to

KUDO classification were risk factors; in 2002, Nascimbeni et al. [13] demonstrated that lymphovascular invasion, SM3 submucosal invasion, involvement of the lower third of the rectum were risk factors. In 2003, Suziki et al. [29] demonstrated that histological grade and submucosal invasion were risk factors, while in 2003, Sakuragi et al. [30] demonstrated that lymphovascular invasion and submucosal invasion were risk factors; and in 2005, Wang et al. [24] demonstrated that histological grade, lymphovascular invasion, inflammation around the tumor, and invasive budding in front of the tumor were risk factors.

In conclusion, the risk of LNM in colorectal cancers is significantly increased in patients with lymphovascular and perineural invasion. Together with more comprehensive studies that will be performed with developing technology and a greater breadth of knowledge, other risk factors affecting LNM will also be found. In this way, it would be helpful to plan adjuvant-neoadjuvant therapy and minimally invasive surgical procedures in colorectal cancers.

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