



# Should there be a specific length of the colon-rectum segment to be resected for an adequate number of lymph nodes in cases of colorectal cancers? A retrospective multi-center study

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## ABSTRACT

**Objective:** This study aimed to evaluate the question as to whether there should be a certain length of the colon-rectum segment to be resected for correct lymph node staging in cases with colorectal cancer.

**Material and Methods:** The files and electronic datas of the patients had been undergone surgery for colorectal cancer between January 2011 and June 2016 were evaluated. The patients were divided into two groups; Group I=  $\geq 12$  lymph nodes, and Group II= lymph nodes less than 12 ( $< 12$ ) lymph nodes.

**Results:** Mean age of the 327 participants in this study was  $64.30 \pm 12.20$ . Mean length of resected colon-rectum segment was  $25.61 (\pm 14.07)$  cm; mean number of dissected lymph nodes was  $20.63 \pm 12.30$ . Median length of the resected colon was 24 cm (range: 14-5) in Group I and 20 cm (range: 5-9) in Group II; a significant difference was found between the groups ( $p= 0.002$ ). Factors associated with adequate lymph node dissection included type of the operation ( $p= 0.001$ ), tumor location ( $p= 0.005$ ), tumor T stage ( $p= 0.001$ ), condition of metastasis in the lymph node ( $p= 0.008$ ) and stage of the disease ( $p= 0.031$ ). Overall survival was  $62.4 \pm 1.31$  months, and Group I and Group II survival was  $61.4 \pm 1.39$  months and  $66.7 \pm 3.25$  months, respectively ( $p= 0.449$ ).

**Conclusion:** Results of the study showed that  $\geq 12$  lymph nodes would likely be dissected when the length of the resected colon-rectum segment is  $> 21$  cm. We conclude that the removed colonic size can be significant when performed with oncological surgical standardization.

**Keywords:** Colorectal cancer, colectomy, lymph nodes

## INTRODUCTION

Presence of lymph node metastasis represents the main basic prognostic factor in cases with non-metastatic colorectal cancers (1,2). Correct staging of lymph node status is important in the identification of patients cancer stage with colorectal cancer (CRC) who need adjuvant therapy to treat the microscopically prevalent disease (3).

In stage II cases, theoretically, more extensive removal of the isolated tumor cells or lymph nodes containing micro-metastases leads to increased survival by inhibiting locoregional or systemic metastasis at the site. Recently, the presence of tumor deposits in regional lymph nodes has also been reported as a poor prognostic factor in node-negative cases (4). All surgeons agree on the prevention of tumor cell spillage while removal of primary tumor bed with lymphatic drainage and resection of the surrounding organ invasion (5).

Prognosis of colorectal cancers are mainly determined by the tumor-node-metastasis (TNM) classification. The 7<sup>th</sup> American Joint Committee on Cancer (AJCC)-resistant system, which is currently widely accepted, is based on the lymph node (N) and tumor colon-rectum wall status (T) (6). Lymph node status plays a key role

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in determining the TNM classification and stage of disease and the creation of postoperative adjuvant chemotherapy protocol. Chemotherapy represents the standard treatment modality in CRC patients with lymph node involvement (7). In the event of an inadequate number of dissected lymph nodes, it is suggested that surgical surgery and pathological classification were inadequate (1). Although the number of dissected lymph nodes for proper staging might be controversial, the generally and clinically accepted fact is that  $\geq 12$  lymph nodes should be dissected. However, this number is not always attained (8,9).

The number of dissected lymph nodes depends on factors such as age, tumor location, type of surgical operation, experience of the surgeon and pathologist, histopathologic property, and the length of resected colon segment (10,11). However, no rules have been established and no standardization made to achieve optimal lymph node dissection and adequate number of lymph nodes (3). The relationship between resected colon segment and lymph nodes has been investigated in recently conducted studies, and the discussion has focused on the necessity of a specific colon-rectum length for adequate lymph node excision (1,3,7).

In our study, we aimed to evaluate the question as to whether there should be a certain length of the colon-rectum segment to be resected for correct lymph node staging in cases with CRC, and if so for how long. We also aimed at investigating whether there was any relationship between the number of lymph nodes dissected, lymph node positivity, and lymph node status.

## MATERIAL and METHODS

The files and electronic datas of patients with colorectal cancer who had undergone surgery either by emergency or through elective conventional methods between January 2011 and June 2016 at the General Surgery Clinics of three different Training and Research Hospitals were retrospectively evaluated. Patients were divided into two groups as those with adequately dissected number of lymph nodes (Group I= $\geq 12$  lymph nodes) and those with inadequately dissected number of lymph nodes (Group II=number of lymph nodes less than 12). The groups were evaluated in terms of factors such as age, sex, tumor location, length of resected colon-rectum segment, number of dissected lymph nodes, number of metastatic lymph nodes, and histologic grade. In addition, patients' overall survival from the time of diagnosis was calculated. Overall survival was compared according to the length of the resected colon found for at least 12 lymph nodes. Lymph node dissection was performed in the resection materials of pericolic fat tissue by experienced pathologists. The sections were dyed with Hematoxylin Eosin, immunohistochemical dyeing was performed in which required cases after light microscopic examination. Lymph node metastasis size larger than 0.2 mm or isolated tumor cells were considered positive for lymph node. The cases were evaluated for adjuvant chemotherapy ac-

ording to postoperative status and disease stages. Stage 3 and stage 2 cases were treated with adjuvant chemotherapy according to poor prognostic factors (obstruction, perforation, perineural invasion, lymphovascular invasion, etc.). Stage 1 cases were followed up without treatment. Patients who underwent palliative surgery (patients with colostomy), patients with peritonitis carcinomatosa, those who underwent metastatic, preoperative neoadjuvant therapy, total or subtotal colectomy, those whose data could not be accessed and patients with synchronous tumors in different segments were excluded from the study. Patient consent was not taken because of the retrospective design of the study. Approval was obtained from the Clinical Research Ethics Committee (Application date: 08/02/2017; Application No: 20, Dated: 15/02/2017 with Decision No: 1).

## Statistical Analysis

SPSS version 22.0 (IBM Corp., Armonk, NY, USA) and MedCalc 14 (Acaciaaan 22, B-8400 Ostend, Belgium) programs were used for the statistical analysis. Shapiro-Wilk test and variance homogeneity Levene test were used for evaluating the suitability of data for normal distribution. Independent-samples t-test was used in conjunction with Bootstrap results, while the Mann-Whitney U test was used with Monte Carlo results to compare quantitative data between two independent groups. Pearson chi-square and Fisher's Exact tests were tested with the Monte Carlo Simulation technique for comparison of categorical variables. Relative sensitivity and specificity between the classification and actual classification of the cutoff values calculated according to the group variables were examined and expressed by the Receiver Operating Curve (ROC) analysis. Variables were expressed in 95% confidence interval (CI), and a p value of  $< 0.05$  was considered statistically significant.

## RESULTS

Mean age of the 327 participants in the study was  $64.30 \pm 12.20$ . Mean length of the resected colon-rectum segment was  $25.61 (\pm 14.07)$  cm; mean number of dissected lymph nodes was  $20.63 \pm 12.30$ , mean number of metastatic lymph nodes was  $2.11 (0-31)$ , and mean tumor size was  $4.62 \pm 2.05$  cm.

Median length of the resected colon was 24 cm (range= 145-6) in Group I and 20 cm (range= 52-9) in Group II ( $p= 0.002$ ). Mean length of the resected colon-rectum in Group I and Group II, in patients who underwent anterior resection was  $22.45 \pm 7.62$  cm and  $18.00 \pm 7.41$  cm ( $p= 0.1480$ ), respectively; in cases with Low Anterior resection it was  $22.25 (42-6)$  and  $16 (52-9)$  cm in Group I and Group II, respectively ( $p= 0.010$ ); in those who underwent right hemicolectomy it was 25 cm (125-12) and 21 cm (39-10) in Group I and Group II, respectively ( $p= 0.452$ ); whereas in patients with sigmoid + left hemicolectomy it was reported to be  $25.25$  cm (145-10) and  $20 (46-9)$  cm in Group I and Group II, respectively ( $p= 0.029$ ). Detailed analyses of the cases are presented in Table 1. Data collected from each hospital is shown in Table 2.

**Table 1.** Comparison of the groups according to surgical type

Type of surgery	Groups		p
	Group I <sup>1</sup> Mean ± SD/ <sup>2</sup> Median (Max-Min)	Group II <sup>1</sup> Mean ± SD/ <sup>2</sup> Median (Max-Min)	
Anterior resection			
Total length of resected colon-rectum segment <sup>1</sup>	22.45 ± 7.62	18.00 ± 7.41	0.148
Number of metastatic lymph nodes <sup>2</sup>	0 (14-0)	0 (1-0)	0.365
Tumor size <sup>1</sup>	4.39 ± 1.66	4.35 ± 2.11	0.954
Tumor-proximal border distance <sup>2</sup>	10 (30-3)	9 (16-4)	0.275
Tumor-distal border distance <sup>2</sup>	5 (24.5-1)	4 (10-1.5)	0.450
Low anterior resection			
Total length of resected colon-rectum segment <sup>2</sup>	22.25 (42-6)	16 (52-9)	<b>0.010</b>
Number of metastatic lymph nodes <sup>2</sup>	1 (20-0)	0 (4-0)	0.134
Tumor size <sup>1</sup>	4.25 ± 1.56	3.31 ± 1.59	<b>0.047</b>
Tumor-proximal border distance <sup>2</sup>	12 (36-2)	10.75 (44-1)	0.626
Tumor-distal border distance <sup>2</sup>	4 (21-1)	2 (5-1)	<b>0.001</b>
Abdomino perineal resection			
Total length of resected colon-rectum segment <sup>2</sup>	27 (32-17.5)	33 (36.5-22.5)	0.125
Number of metastatic lymph nodes <sup>2</sup>	3 (31-0)	0 (4-0)	0.211
Tumor size <sup>1</sup>	5.11 ± 1.58	3.60 ± 2.16	0.158
Tumor-proximal border distance <sup>2</sup>	16 (24-3)	20 (28-11)	0.317
Tumor-distal border distance <sup>1</sup>	3.64 ± 1.88	7.3 ± 2.22	<b>0.007</b>
Right hemicolectomy			
Total length of resected colon-rectum segment <sup>2</sup>	25 (125-12)	21 (39-10)	0.452
Number of metastatic lymph nodes <sup>2</sup>	0.5 (31-0)	0 (6-0)	0.168
Tumor size <sup>1</sup>	5 (13-1.5)	4.75 (10-1.5)	0.866
Tumor-proximal border distance <sup>2</sup>	7.5 (36-0)	5 (14-1)	0.319
Tumor-distal border distance <sup>2</sup>	12 (74-2)	12 (24-2)	0.741
Sigmoid + left hemicolectomy			
Total length of resected colon-rectum segment <sup>2</sup>	25.25 (145-10)	20 (46-9)	<b>0.029</b>
Number of metastatic lymph nodes <sup>2</sup>	1 (12-0)	0 (4-0)	0.150
Tumor size <sup>1</sup>	4 (10-1.5)	3.75 (9-2)	<b>0.046</b>
Tumor-proximal border distance <sup>2</sup>	10 (109-1.5)	9 (24-1.8)	0.181
Tumor-distal border distance <sup>2</sup>	7 (26-1.7)	6.25 (30-1)	0.303
Total			
Total length of resected colon-rectum segment <sup>2</sup>	24 (145-6)	20 (52-9)	<b>0.002</b>
Number of metastatic lymph nodes <sup>2</sup>	1 (31-0)	0 (6-0)	<b>0.012</b>
Tumor size <sup>1</sup>	4.5 (13-0)	3.5 (10-1)	<b>0.001</b>
Tumor-proximal border distance <sup>2</sup>	10 (109-0)	9 (44-1)	0.669
Tumor-distal border distance <sup>2</sup>	7 (74-1)	4.75 (30-1)	<b>0.001</b>

Independent T Test (Bootstrap)-Mann-Whitney U Test (Monte Carlo).  
SD: Standard deviation, Max: Maximum, Min: Minimum.

Less than 12 lymph nodes were found to have been removed in 60 (18.3%) cases. Factors associated with adequate/inadequate lymph node dissection are shown in Table 3.

It was demonstrated that mean length of the resected colon-rectum and the number of lymph nodes dissected did not

affect the presence of metastatic lymph nodes ( $p=0.853$  and  $p=0.088$ , respectively). Factors associated with the status of lymph node metastasis and lymph node grade are presented in Table 4. Evaluation of the factors associated with the number of dissected lymph nodes demonstrated that it was associated with the number of metastatic lymph nodes ( $p=0.003$ ), the mean length

**Table 2.** Mean colon lengths according to the surgical method of each hospital

Surgery type	A Hospital		B Hospital		C Hospital	
	Group I Mean ± SD/Median (Max-Min)	Group II Mean ± SD/Median (Max-Min)	Group I Mean ± SD/Median (Max-Min)	Group II Mean ± SD/Median (Max-Min)	Group I Mean ± SD/Median (Max-Min)	Group II Mean ± SD/Median (Max-Min)
Anterior resection	20.33 ± 6.32	18.00 ± 5.28	22.5 (± 13)	22.6 (± 9.82)	21 (± 6.8)	20.5 (± 5.6)
Low anterior resection	24.8 ± 10	19.6 (± 6.8)	23.5 (± 10.5)	18 (12-33)	15 (6-42)	23 (± 9.7)
Abdomino perineal resection	25.5 ± 7.1	-	25.3 (± 8.7)	30.4 (± 7.2)	-	-
Right hemicolectomy	24.8 (15-128)	29 (19-39)	29.8 (± 11.2)	27 (18-36)	26 (± 11.2)	23 (12-33)
Sigmoid + left hemicolectomy	28.4 ± 8.8	18.9 (± 6.7)	31.8 (± 11.3)	24 (± 13.2)	29.8 (± 7.4)	24 (13-46)
Total length of colon-rectum segment	25 (8-114)	24.5 (8-145)	25 (8-64.5)	22.5 (12-36)	23 (± 7.7)	21.9 (± 7.7)

of resected colon ( $p \leq 0.001$ ), tumor size ( $p \leq 0.001$ ), and distal surgical border ( $p \leq 0.001$ ). Factors associated with the number of dissected lymph nodes and the number of metastatic lymph nodes are shown in Table 5.

According to the surgical operation, the colon-rectum segment should be resected for a length of  $> 21$  cm during low anterior resection ( $p = 0.027$ ) and a length of  $> 20$  cm during sigmoid + left hemicolectomy ( $p = 0.027$ ) (Table 6). The possibility of dissecting  $\geq 12$  lymph nodes was found to be significant when  $> 21$  cm of the colon-rectum segment was resected in respect of the cut-off value ( $p = 0.005$ ) (Figure 1). The rate of patients receiving adjuvant therapy was 62% (Group I and Group II, respectively 63%, and 57%). Overall survival was  $62.4 \pm 1.31$  months, and Group I and Group II survival were  $61.4 \pm 1.39$  months and  $66.7 \pm 3.25$  months, respectively ( $p = 0.449$ ). In the absence of lymph node metastasis, survival was  $71.4 \pm 1.75$  months and survival was  $54.3 \pm 1.99$  months in the presence of metastatic lymph node ( $p = 0.001$ ). Survival analysis was  $63 \pm 1.65$  months in patients with a colon length greater than 21 cm and  $61.6 \pm 2.07$  months in those with a smaller colon length ( $p = 0.801$ ).

## DISCUSSION

The rate of inadequately dissected lymph nodes has been on a decrease these past years; it is around 25% and continues to pose a health problem (3). The relationship of resected colon-rectum segment with lymph nodes has been investigated in various studies. Stracci et al. have reported inadequate lymph node dissection below 20 cm (7). In this study,  $\geq 12$  lymph nodes were observed to have been dissected in 50% of the cases when the 10-19 cm colon segment was resected, and

in 38% of cases when less than 16 cm were resected. On the other hand, resection of less than 10 cm saw showed us the dissection of an adequate number of lymph nodes in only 19.5% of the cases. In that study, the rate of dissecting  $\geq 12$  lymph nodes has been observed to increase as the years progressed; in 2002 the rate was 43%, whereas in 2008 it was found to have increased to 68% (7). In our study, this rate was reported to be good at 81.7%. In some rare literature studies, this rate has been found to have approached 96%. No difference was found in the number of dissected lymph nodes between the currently widely used laparoscopic surgery and conventional surgery in patients with CRC (5,7).

In another study, Gravante et al. have shown that tumors might vary depending on their location, and as a result, a general view might be overlooked; however, it is their suggestion that it would be appropriate to resect 36 cm of the segment during surgical procedure in the rectum and 42 cm of the segment during the Hartmann procedure (3). The length of the colon segment here mentioned seems to be longer when compared to results from literature studies and results of our study. Moreover, in this study,  $< 12$  lymph nodes are dissected in 30.3% of the cases.

Neufeld et al. have demonstrated that  $< 12$  lymph nodes were dissected from sigmoid colon resections less than 15.1 cm, whereas  $> 12$  lymph nodes were dissected from segments more than 20.3 cm (12). The authors have argued that surgeons have an important role in determining lymph node spread. In the study conducted by Valsecchi et al., it has been demonstrated that  $< 12$  lymph nodes were dissected when the resected

**Table 3.** Comparison of the groups according to demographic data

	Groups		p
	Group I	Group II	
	n (%)	n (%)	
Gender			
Female	106 (39.7)	19 (31.7)	0.247
Male	161 (60.3)	41 (68.3)	
Type of surgery			<b>0.001</b>
Anterior resection	58 (21.7)	7 (11.7)	
Low anterior resection	42 (15.7)	16 (26.7)	
Abdominoperineal resection	9 (3.4)	5 (8.3)	
Right hemicolectomy	96 (36)	10 (16.7)	
Sigmoid colon + Left hemicolectomy	62 (23.2)	22 (36.7)	
Tumor location			<b>0.005</b>
Left colon	33 (12.4)	13 (21.7)	
Rectum	52 (19.5)	21 (35)	
Right colon	86 (32.2)	9 (15)	
Sigmoid colon	84 (31.5)	16 (26.7)	
Transverse colon	12 (4.5)	1 (1.7)	
T Stage			<b>0.001</b>
T0	1 (0.4)	0 (0)	
T1	9 (3.4)	5 (8.3)	
T2	18 (6.7)	12 (20)	
T3	140 (52.4)	28 (46.7)	
T4	98 (36.7)	13 (21.7)	
Tis	1 (0.4)	2 (3.3)	
N Stage			<b>0.024</b>
N0	119 (44.6)	35 (58.3)	
N1	85 (31.8)	20 (33.3)	
N2	63 (23.6)	5 (8.3)	
Lymph node metastasis			0.107
No	125 (46.8)	35 (58.3)	
Yes	142 (53.2)	25 (41.7)	
Histological grade			0.138
Well	57 (22)	10 (16.9)	
Moderately	149 (57.5)	42 (71.2)	
Poor	53 (20.5)	7 (11.9)	
TNM stage			<b>0.031</b>
Stage 0	2 (0.7)	2 (3.3)	
Stage 1	21 (7.9)	10 (16.7)	
Stage 2	98 (36.7)	24 (40)	
Stage 3	146 (54.7)	24 (40)	
Elective/Emergency surgery			<b>0.007</b>
Emergency surgery	28 (10.5)	14 (23.3)	
Elective surgery	239 (89.5)	46 (76.7)	
Lymphovascular Invasion			0.133
No	159 (59.6)	42 (70)	
Yes	108 (40.4)	18 (30)	
Perineural invasion			0.239
No	189 (70.8)	47 (78.3)	
Yes	78 (29.2)	13 (21.2)	

Pearson Chi-Square Test (Monte Carlo), Fisher Exact Test (Exact).

**Table 4.** Factors associated with the lymph node stage and status of lymph node metastasis

	N Stage			p	Lymph node metastasis		p
	N0	N1	N2		No	Yes	
	Median (Max-Min)	Median (Max-Min)	Median (Max-Min)		Median (Max-Min)	Median (Max-Min)	
Age	66 (96-38)	64 (93-21)	65 (86-35)	0.661	66 (96-38)	64 (93-21)	0.267
Total length of resected colon-rectum segment	23 (114-6)	23 (75-9)	23 (145-8)	0.948	23 (114-6)	23 (145-8)	0.853
Dissected number of lymph nodes	16 (75-0)	17 (73-3)	20 (81-9)	<b>0.004</b>	16 (75-0)	18 (81-3)	0.088
Tumor size	4 (13-0)	4.5 (10-1.5)	4 (13-1.5)	0.534	4 (13-0)	4.5 (13-1.5)	0.192
Gender, n (%)							
Female	58 (37.7)	35 (33.3)	32 (41.1)	0.189	61 (38.1)	64 (38.3)	0.971
Male	96 (62.3)	70 (66.7)	36 (52.9)		99 (61.9)	103 (61.7)	
Type of surgery, n (%)							
Anterior resection	33 (21.4)	22 (21)	10 (14.7)	0.711	34 (21.3)	31 (18.6)	0.831
Low anterior resection	26 (16.9)	17 (16.2)	15 (22.1)		26 (16.3)	32 (19.2)	
Abdominoperineal resection	6 (3.9)	3 (2.9)	5 (7.4)		6 (3.8)	8 (4.8)	
Right hemicolectomy	53 (34.4)	32 (30.5)	21 (30.9)		55 (34.4)	51 (30.5)	
Sigmoid colon + Left hemicolectomy	36 (23.4)	31 (29.5)	17 (25)		39 (24.4)	45 (26.9)	
Tumor location, n (%)							
Left colon	20 (13)	17 (16.2)	9 (13.2)	0.718	22 (13.8)	24 (14.4)	0.859
Rectum	33 (21.4)	20 (19)	20 (29.4)		33 (20.6)	40 (24)	
Right colon	45 (29.2)	29 (27.6)	21 (30.9)		47 (29.4)	48 (28.7)	
Sigmoid colon	48 (31.2)	35 (33.3)	17 (25)		50 (31.3)	50 (29.9)	
Transverse colon	8 (5.2)	4 (3.8)	1 (1.5)		8 (5)	5 (3)	
Histological Grade, n (%)							
Well	33 (21.7)	22 (22)	12 (18.2)	0.390	35 (22.2)	32 (20)	0.249
Moderately	97 (63.8)	56 (56)	38 (57.6)		99 (62.7)	92 (57.5)	
Poor	22 (14.5)	22 (22)	16 (24.2)		24 (15.2)	36 (22.5)	
Elective/Emergency surgery, n (%)							
Emergency surgery	29 (18.8)	9 (8.6)	4 (5.9)	<b>0.008</b>	29 (18.1)	13 (7.8)	<b>0.005</b>
Elective surgery	125 (81.2)	96 (91.4)	64 (94.1)		131 (81.9)	154 (92.2)	
Lymphovascular Invasion, n (%)							
No	108 (70.1)	56 (53.3)	37 (54.4)	<b>0.010</b>	37 (54.4)	88 (52.7)	<b>0.001</b>
Yes	46 (29.9)	49 (46.7)	31 (45.6)		31 (45.6)	79 (47.3)	
Perineural invasion, n (%)							
No	115 (74.7)	75 (71.4)	46 (67.6)	0.548	120 (75)	116 (69.5)	0.264
Yes	39 (25.3)	30 (28.6)	22 (32.4)		40 (25)	51 (30.5)	

Pearson Chi-Square Test (Monte Carlo), Fisher Exact Test (Exact), Kruskal Wallis Test (Monte Carlo), Post Hoc Test: Dunn's Test. Max: Maximum, Min: Minimum.

colon segment was less than 19.6 cm, whereas  $\geq 12$  lymph nodes were dissected with over 29.9 cm of resected colon segment (9). It has been indicated that the mean number of lymph nodes was significantly higher in the ascending colon and cecum when evaluation was made according to tumor location; and during right hemicolectomy and subtotal colectomy when evaluation was made according to mode of surgery.

Unlike in these studies, the case series by Lav et al. involving 205 cases have demonstrated that lymph nodes were dissected more with right colon tumors than with left colon tumors (1).

Especially for right colon resection, the authors did not suggest any length. However, there were certain handicaps in this study such as the small sample size, and a wide range of resection types all divided into three categories including cases with right hemicolectomy, left colon + sigmoid resection and subtotal resection. In another study, it was suggested that the pedicle or mesocolon and not the resected colonic segment was more important (13).

Comparison of our study with the studies mentioned above demonstrates that an adequate number of lymph nodes was

**Table 5.** Factors associated with the number of metastatic lymph nodes and the number of dissected lymph nodes

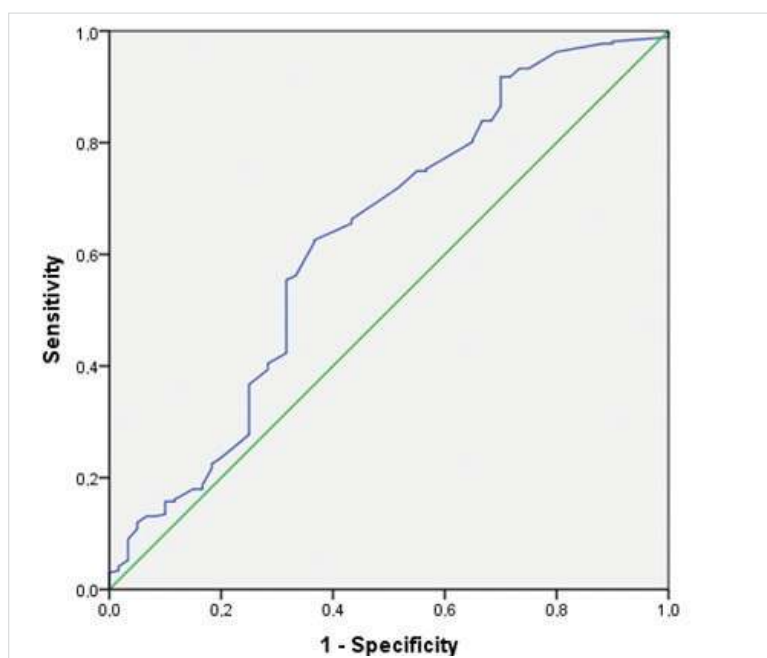
<b>Metastatic lymph nodes</b>	<b>r</b>	<b>p</b>
Total length of resected colon-rectum segment	0.033	0.558
Dissected number of lymph nodes	0.166	<b>0.003</b>
Tumor size	0.063	0.258
Tumor-proximal border distance	-0.055	0.322
Tumor-distal border distance	0.036	0.520
<b>Dissected lymph nodes</b>	<b>r</b>	<b>p</b>
Total length of resected colon-rectum segment	0.305	<b>&lt; 0.001</b>
Number of metastatic lymph nodes	0.166	<b>0.003</b>
Tumor size	0.258	<b>&lt; 0.001</b>
Tumor-proximal border distance	0.017	0.758
Tumor-distal border distance	0.265	<b>&lt; 0.001</b>

Partial Correlation Test/Control Variables: Age & Gender. r: Correlation coefficient.

**Table 6.** Relationship between surgical types and removal of at least 12 lymph nodes

		<b>Dissected number of lymph nodes (<math>\geq 12</math>/<math>&lt; 12</math>)</b>				<b>p</b>
		<b>Cut-off</b>	<b>Sensitivity</b>	<b>Specificity</b>	<b>AUC <math>\pm</math> SH</b>	
<b>Total</b>	<b>Total length of resected colon-rectum</b>	> 21	0.60	0.63	0.610 $\pm$ 0.039	<b>0.005</b>
Type of surgery						
	Anterior resection	> 21	0.53	0.86	0.68 $\pm$ 0.11	0.126
	Low anterior resection	> 21	0.52	0.75	0.65 $\pm$ 0.07	<b>0.027</b>
	Abdominoperineal resection	> 37	0.29	1.00	0.51 $\pm$ 0.11	0.957
	Right hemicolectomy	> 21	0.71	0.60	0.58 $\pm$ 0.11	0.429
	Sigmoid + Left hemicolectomy	> 20	0.67	0.59	0.66 $\pm$ 0.07	<b>0.027</b>

ROC: Receiver Operating Curve, Analysis: Honley&Mc Nell-Youden index J, AUC: Area under the ROC curve, SE: Standard error.

**Figure 1.** The predictive values' total length of the resected colon-rectum were evaluated by ROC curve analysis.

considered to have been dissected when a colon-rectum length of more than 21 cm was resected regardless of the mode of the surgical operation or tumor location. On the other hand, classification according to surgical operation showed that the length of resected colon-rectum was significant with low anterior resection and sigmoid+ left hemicolectomy. The use of limited segmental colonic resections is traditionally not recommended because of the potential for local recurrence or metastatic disease and may increase the risk of skipping lymph nodes containing metastatic deposits (14). In addition, in stage-II patients, the dissection of more lymph nodes in theory, including isolated tumor cells or micro-metastases, leads to increased survival by preventing both locoregional and systemic recurrence (15). Norwood et al., in their case series involving 2449 cases, have found that an adequate number of lymph nodes varied according to preoperative chemotherapy, age, length of resected colon segment, and the type of surgical operation; and observed that there was less survival in the group with inadequately dissected lymph nodes (16). On the other hand, Tsai et al. have demonstrated that survival was higher in N0 patients with  $\geq 18$  dissected lymph nodes (8). In high-volume hospitals, colorectal surgery specialists tend to perform more extensive lymphadenectomy operations through the resection of more colonic segments (1).

It has also been suggested that metastatic lymph nodes may be found approximately 8 to 10 cm of the colonic segment around the tumor, and hence the removal of the distal and proximal surgical margin with a 5 cm safety margin is recommended (17). In our study, median length of the proximal margin was found to be 10 cm, while mean distal margin length was 6.5 cm. However, comparison of the groups with adequate and inadequate lymph node dissection demonstrated that the proximal surgical margin was 10 cm in the group with adequate lymph node dissection and 9 cm in the group with inadequate lymph node dissection both groups, whereas the median length of distal surgical margin was 7 cm in the group with adequate lymph node dissection and 4.75 cm in the group with inadequate lymph node dissection; the difference between the groups was found to be significant. This result shows that there was a relationship between the increased safety of the surgical margin and the number of dissected lymph nodes.

Consistent with the literature datas, our study demonstrated that the mean number of dissected lymph nodes did not affect the node positive or node negative rate (15). However, when compared with the dissection of  $\geq 12$  lymph nodes, dissection of an adequate number of lymph nodes was found to be significant in the presence of metastatic lymph nodes. In addition, evaluation of lymph node status demonstrates that the mean number of total dissected lymph nodes was 16 in N0, 17

in N1 and 20 in N2. A significant inter-relationship was found, which shows that the correct classification/staging could be performed as the number of dissected lymph nodes increased. Correct staging would also allow us to comment on the prognosis of the disease and guide us in the creation of a chemotherapy scheme.

Lymph node dissection has been in practice for the past 100 years; however, the current commonly accepted technique involves removal of the pedicle from the main vascular pedicle preceding the main lymphatic duct of each colonic segment (14). In our study, no relation was found between lymph node dissection and sex, histologic grade, lymphovascular, or perineural invasion; however, similar to literature studies a relation was found in respect of tumor location, presence of elective-emergency surgical intervention, disease stage and type of surgery (1,3,18). The total length of resected colon-rectum in our study was also not shown to change with emergency or elective surgery. However, the number of lymph nodes dissected during elective surgery was found to be significantly high, similar to other literature studies, which suggests that meso-excision may be extensive during elective surgery (5,16).

Overall survival is known to be affected by many factors such as tumor type, tumor differentiation, tumor localization, tumor size, disease stage, lymph node involvement (19). In our study, if the length of the removed column is over 21 cm or the number of removed lymph nodes is 12 or greater did not provide survival advantage. In addition, we found that the presence of metastatic lymph nodes worsened overall survival like the literature.

### Limitations

Our study is a retrospective study. Furthermore, due to the very centered nature of the study, no uniformity was created during the examination of the specimens. In addition, although surgery was performed according to surgical principles, no standardization was established for the width of the mesocolon and attachment level of the main vascular structure. In addition, it should be kept in mind that patients with advanced rectal cancer were not included in the study due to neoadjuvant treatment. While these results are interpreted; it should be kept in mind that the measurements are made after 10% formol fixation, which may lead to a reduction of about 30-40% of the final length according to the measurements during surgery (20).

In conclusion, the results of this study show that in colorectal cancer operations, at least 12 lymph nodes could be removed when the colon resection was over 21 cm long. However, we found that the length of the removed colon did not show survival advantage independent from the disease stage. We conclude that the removed colonic size can be significant when performed with mesodissection with as oncologic standard surgery.



**Ethics Committee Approval:** Approval was obtained from the Clinical Research Ethics Committee (Application date: 08/02/2017; Application No: 20, Dated: 15/02/2017 with Decision No: 1).

**Informed Consent:** Patient consent was obtained.

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## REFERENCES

- Lavy R, Madjar-Markovitz H, Hershkovitz Y, Sandbank J, Halevy A. Influence of colectomy type and resected specimen length on number of harvested lymph nodes. *Int J Surg* 2015;24:91-4. [\[CrossRef\]](#)
- Üstüner MA, İlhan E, Yeldan E, Argon A, Vardar E. Clinical and pathological factors affecting lymph node metastasis in patients operated on with the diagnosis of colorectal cancer. *The Journal of Tepecik Education and Research Hospital* 2016;26:15-22. [\[CrossRef\]](#)
- Gravante G, Parker R, Elshaer M, Mogeckwu AC, Humayun N, Thomas K, et al. Lymph node retrieval for colorectal cancer: estimation of the minimum resection length to achieve at least 12 lymph nodes for the pathological analysis. *Int J Surg* 2016;25:153-7. [\[CrossRef\]](#)
- Rahbari NN, Bork U, Motschall E, Thorlund K, Büchler MW, Koch M, et al. Molecular detection of tumor cells in regional lymph nodes is associated with disease recurrence and poor survival in node-negative colorectal cancer: a systematic review and meta-analysis. *J Clin Oncol* 2012;30:60-70. [\[CrossRef\]](#)
- Han J, Noh KT, Min BS. Lymphadenectomy in colorectal cancer: therapeutic role and how many nodes are needed for appropriate staging? *Curr Colorectal Cancer Rep* 2017;13:45-3. [\[CrossRef\]](#)
- Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol* 2010;17:1471-4. [\[CrossRef\]](#)
- Stracci F, Bianconi F, Leite S, Liso A, La Rosa F, Lancellotta V, et al. Linking surgical specimen length and examined lymph nodes in colorectal cancer patients. *Eur J Surg Oncol (EJSO)* 2016;42:260-5. [\[CrossRef\]](#)
- Tsai HL, Lu CY, Hsieh JS, Wu DC, Jan CM, Chai CY, et al. The prognostic significance of total lymph node harvest in patients with T2-4N0M0 colorectal cancer. *J Gastrointest Surg* 2007;11:660-5. [\[CrossRef\]](#)
- Matias EV, Leighton J, Tester W. Modifiable factors that influence colon cancer lymph node sampling and examination. *Clin Col Cancer* 2010;9:162-7. [\[CrossRef\]](#)
- Willaert W, Mareel M, Van De Putte D, Van Nieuwenhove Y, Pattyn P, Ceelen W. Lymphatic spread, nodal count and the extent of lymphadenectomy in cancer of the colon. *Cancer Treat Rev* 2014;40:405-13. [\[CrossRef\]](#)
- Stocchi LV, Fazio W, Lavery I, Hammel J. Individual surgeon, pathologist, and other factors affecting lymph node harvest in stage II colon carcinoma: is a minimum of 12 examined lymph nodes sufficient? *Ann Surg Oncol* 2011;17:405-12. [\[CrossRef\]](#)
- Neufeld D, Bugyev N, Grankin M, Gutman M, Klein E, Bernheim J, et al. Specimen length as a perioperative surrogate marker for adequate lymph adenectomy in colon cancer: the surgeon's role. *Int Surg* 2007;92:155-60. [\[CrossRef\]](#)
- Nash GM, Row D, Weiss A, Shia J, Guillem JG, Paty PB, et al. A predictive model for lymph node yield in colon cancer resection specimens. *Ann Surg* 2011;253:318-22. [\[CrossRef\]](#)
- Jamie M, Young-Fadok T. Extended lymphadenectomy in colon cancer is debatable. *World J Surg* 2016;37:1799-807. [\[CrossRef\]](#)
- Wouter W, Ceelen W. Extent of surgery in cancer of the colon: is more better? *World J Gastroenterol* 2015;21:132-8. [\[CrossRef\]](#)
- Norwood MGA, Sutton AJ, West K, Sharpe DP, Hemingway D, Kelly MJ. Lymph node retrieval in colorectal cancer resection specimens: national standards are achievable, and low numbers are associated with reduced survival. *Colorectal Dis* 2010;12:304-9. [\[CrossRef\]](#)
- Rocha R, Marinho R, Aparicio D, Fragoso M, Sousa M, Gomes A, et al. Impact of bowel resection margins in node negative colon cancer. *Springer Plus* 2016;5:1959. [\[CrossRef\]](#)
- Nawa T, Kato J, Kawamoto H, Okada H, Yamamoto H, Kohno H, et al. Differences between right- and left-sided colon cancer in patient characteristics, cancer morphology and histology. *J Gastroenterol Hepatol* 2008;23:418-23. [\[CrossRef\]](#)
- Liu Q, Luo D, An H, Zhang S, Cai S, Li Q, et al. Survival benefit of adjuvant chemotherapy for patients with poorly differentiated stage IIA colon cancer. *J Cancer* 2019;29:1209-15. [\[CrossRef\]](#)
- Wang L, Shen J, Song X, Chen W, Pan T, Zhang W, et al. A study of the lengthening and contractility of the surgical margins in digestive tract cancer. *Am J Surg* 2004;187:452-5. [\[CrossRef\]](#)



## ORJİNAL ÇALIŞMA-ÖZET

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## Kolorektal kanserlerde yeterli lenf nodu sayısı için çıkarılacak kolon-rektum segmentinin belirli bir uzunluğu olmalı mı? Retrospektif çok merkezli bir çalışma

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### ÖZET

**Giriş ve Amaç:** Bu çalışma, kolorektal kanserli olgularda doğru lenf nodu evrelemesi için rezeke edilecek kolon-rektum segmentinin belirli bir uzunluğunun olup olmadığı sorusunu değerlendirmeyi amaçlamaktadır.

**Gereç ve Yöntem:** Kolorektal kanserli hastaların Ocak 2011-Haziran 2016 tarihleri arasında ameliyat geçiren dosyaları ve elektronik verileri değerlendirildi. Hastalar iki gruba ayrıldı; Grup I=  $\geq 12$  lenf nodu ve Grup II= 12'den az lenf nodu sayısı.

**Bulgular:** Çalışmaya yaş ortalaması  $64,30 \pm 12,20$  olan 327 olgu dahil edilmiştir. Rezeke edilen kolon-rektum segmentinin ortalama toplam uzunluğu  $25,61 (\pm 14,07)$  cm; diseke edilen ortalama lenf nodu sayısı  $20,63 \pm 12,30$  idi. Çıkarılan ortalama kolon-rektum uzunluğu Grup I'de 24 cm (145-6) ve Grup II'de 20 cm (52-9) olup gruplar arasında anlamlı fark bulunmuştur ( $p= 0,002$ ). Yeterli lenf nodu diseksiyonu ile ilişkili faktörler; operasyonun türü ( $p= 0,001$ ), tümör yeri ( $p= 0,005$ ), tümör T evresi ( $p= 0,001$ ), lenf nodunda metastaz durumu ( $p= 0,008$ ) ve hastalığın evresi ( $p= 0,031$ ) olarak bulunmuştur. Ortalama sağkalım  $62,4 \pm 1,31$  ay idi. Grup I ve Grup II'de sırasıyla,  $61,4 \pm 1,39$  ay ve  $66,7 \pm 3,25$  idi ( $p= 0,449$ ).

**Sonuç:** Bu çalışma, çıkarılan kolon-rektum uzunluğu  $> 21$  cm olduğunda  $\geq 12$  lenf nodu çıkarılabileceğini gösterdi. Çıkarılan bu kolon-rektum uzunluğunun onkolojik cerrahi standardizasyonu ile beraber yapıldığında anlamlı olacağını düşünüyoruz.

**Anahtar Kelimeler:** Kolorektal kanser, kolektomi, lenf nodu

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