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Prognostic Value of Total Lymph Node Identified and Ratio of Lymph Nodes in Resected Colorectal Cancer

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Background: The extent of lymph node involvement is the most significant prognostic indicator in resected locoregional colorectal cancer.

Objectives: This study aimed to investigate the prognostic value of total lymph nodes identified and ratio of lymph nodes in resected colorectal cancer.

Patients and Methods: Two hundred seventy five patients with histologically proven resected locoregional invasive colorectal adenocarcinoma from 2003 to 2011 were included. All patients were treated with standard surgical resection for their colorectal cancer. Patients with incomplete data, or unresectable tumors or distant metastases were excluded from the study. All potential prognostic variables were evaluated for their impact on the local control, disease-free, and overall survival rates.

Results: Of the 275 patients, 162 were men and 113 were women with a median age of 54 (range 23-84) years. The mean total lymph nodes were significantly higher in colon cancer than rectal cancer (11 versus 7.5, P = 0.001). In node positive (stage III) patients, the mean lymph nodes ratio was 0.5 for rectal cancers and 0.37 for colon cancers respectively showing a nonsignificant (P = 0.05) trend toward higher lymph nodes ratio in rectal cancer patients. In univariate analysis, the mean total number of lymph node identified was a prognostic factor for 5-year disease free (P = 0.04) and overall survival (P = 0.02) rates. In node positive patients, lymph nodes ratio was a prognostic factor for 5-year local control (P = 0.04), disease free survival (P = 0.01), and overall survival (P = 0.01) rates. On multivariate analysis, advanced primary tumor stage, rectal primary site and the presence of perineural invasion were independent adverse prognostic factors for overall survival.

Conclusions: Total lymph nodes identified and ratio of lymph nodes are associated with oncological outcomes outcomes in patients with colorectal cancer.

Keywords: Colorectal Neoplasms; Colon; Rectum; Lymph Nodes; General Surgery; Prognosis; Survival

1. Background

Colorectal cancer is the fourth most frequently diagnosed cancer and the leading cause of cancer death in Iran (1). Most colorectal cancers tend to present as a locoregional disease (2). Currently, the American Joint Committee on Cancer (AJCC), the tumor node metastasis (TNM) staging system is commonly used for staging colorectal cancer. The presence and extent of regional lymph node involvement has been adopted as an element in the N stage of this staging system (3). The total number of lymph nodes examined can easily affect the N stage evaluation (4). Therefore, a minimum of 9 to 12 lymph nodes examination has been recommended for accurately staging colorectal cancer (5, 6). However, inadequate lymph nodes evaluation is a common problem in colorectal cancer and a high proportion of patients had a limited number of lymph nodes examined (7). According to two recent studies performed in our country, only a third of the patients with colorectal cancer underwent adequate lymph nodes examination (8, 9). These evidences point out that a potential risk of understaging is present in these patients. Some stage III patients with inadequate lymph nodes evaluation may be incorrectly classified as stage I or II (4, 10, 11). N stage is the most important prognostic factor in resected lo-

Implication for health policy/practice/research/medical education:
Inadequate lymph nodes examined, directly and indirectly, influences oncologic outcomes in patients with resected colorectal cancer. The lower total identified lymph nodes and the higher ratio of lymph nodes are associated with poorer oncologic outcomes in patients with colorectal cancer. Tumor stage may be more useful prognostic indicator than node stage in patients with inadequate lymph nodes staging.

coregional colorectal cancer (12). Several studies have investigated the association between the number of lymph node identified and overall survival in patients with colorectal cancer (13). Some reports indicate that larger number of harvested lymph nodes is associated with improved 5-year survival rates in patients with negative node (stages I and II) colorectal cancer (4, 14). In addition, some evidences from the literature found an important prognostic role for the lymph nodes ratio (i.e. the ratio of positive lymph nodes to the total number of lymph nodes examined) (11).

2. Objectives

This study aimed to investigate the prognostic value of total lymph nodes identified and ratio of lymph nodes in oncological outcomes (i.e. local control, disease free survival, and overall survival rates) of resected colorectal cancer in Shiraz, Southern Iran.

3. Patients and Methods

3.1. Population Study and Patient Evaluation

In this retrospective study, characteristics, prognostic factors and survival rates of 275 patients with histologically proven resected locoregional invasive colorectal adenocarcinoma were reviewed and analyzed. The patients were treated and followed-up at Namazi Hospital, Shiraz University of Medical Sciences during 2003 and 2011. Patients presenting in situ or metastatic disease, with pathologies other than adenocarcinoma, and with unresectable or inoperable disease were excluded. In addition, patients who achieved complete pathological response following neoadjuvant chemoradiation were excluded. We also excluded those with missing or incomplete medical records or who lacked complete pathological reports. All patients underwent standard curative surgical resection for their colorectal cancer. Colorectal cancers were pathologically restaged according to the 7th edition of the AJCC TNM staging system (3). Preliminary investigation included comprehensive history and physical examination, colonoscopy, abdominal and pelvic ultrasonography and computed tomography (CT) scans and/or pelvic magnetic resonance imaging (MRI) and/or transrectal ultrasonography.

3.2. Neoadjuvant and Adjuvant Therapies

Neoadjuvant or adjuvant chemoradiation included conventional external beam radiotherapy using megavoltage linear accelerator photons. A median dose of 50 (range 45-50.4) Gy external beam radiotherapy was delivered via a daily fraction of 1.8-2 Gy, with five fractions per week. Concurrent chemotherapy consisted of oral capecitabine, 825 mg/m^2 twice daily during the whole period of the radiotherapy with weekend breaks; or intravenous bolus 5-fluorouracil 425 mg/m^2/day and folinic acid 20 mg/m^2/day on days one to five of the first and last weeks of radiation. Adjuvant chemotherapy consisted of capecitabine 1000 mg/m^2 twice daily for 14 of every three-week cycles, plus oxaliplatin 130 mg/m^2 intravenously on day 1 (CAPEOX regimen); or 5-fluorouracil 200 mg/m^2 boluson day 1, followed by bolus 5-FU 400 mg/m^2 and then 5-FU 600 mg/m^2 over 22-hour infusion on days 1 and 2, (FOLFOX regimen). All patients receiving neoadjuvant chemoradiation underwent standard curative surgery with at least 4-6 weeks interval.

3.3. Statistical Analysis

Clinical and pathological variables were analyzed using the SPSS for windows version 17 statistical software (SPSS, Chicago, IL). The lymph nodes ratio was defined as the ratio of positive lymph nodes to the total number of lymph nodes identified. Local control rate was defined as the proportion of patients who were free of locoregional recurrent disease at 5 years. Disease-free survival rate was defined as the percentage of patients free of rectal cancer at 5 years; an overall survival rate was defined as the percentage of patients alive at 5 years. The survival durations were measured from the date of initial treatment till the events of locoregional failure (locoregional control), any type of treatment failure (disease free survival), death from any reason (overall survival) or the last follow-up. All potential tumor and patient characteristics were analyzed for their impact on the local control, disease-free and overall survival rates. Univariate analysis was performed for the local control, disease-free and overall survival rates using the Kaplan Meier method, and prognostic factors were compared using the Log-Rank test. Multiple-covariate analysis was performed using the stepwise hazards regression model for determining any association between total lymph node identified and ratio of lymph node and oncological outcomes. The hazard ratio (HR) for death, with 95% confidence interval (CI) was calculated for the variable groups. The stratified log-rank test was used to compare treatment results in each variable group (rectum versus colon). All P values were 2-tailed, and $P < 0.05$ was considered statistically significant.

4. Results

4.1. The patients and Tumor Characteristics

Of the 275 patients, 162 were men and 113 were women with a median age of 54 (range 23-84) years. At the time of diagnosis, 181 patients (66%) were node negative and 94 patients (34%) were node positive. The mean total lymph nodes were significantly higher in colon cancer than rectal cancer (11 versus 7.5, P = 0.001). However, there was no statistically significance difference in the mean positive lymph nodes between rectal cancers

and colon cancers. In addition, in node positive (stage III) patients, the mean lymph nodes ratio was 0.5 for rectal cancers and 0.37 for colon cancers respectively, showing a nonsignificant (P = 0.052) trend toward higher lymph nodes ratio in patients with rectal cancer (Table 1).

Table 1. The Patient and Tumor Characteristics by Primary Site

	Primary Sites			P value
	Rectum	Colon	Total	
Gender				0.903[a]
Male	86	76	162	
Female	61	52	113	
Age, y				0.017[b]
mean (SD)	56.7 (13.7)	52.8 (12.6)	54.6 (14.1)	
Tumor stage				0.770[a]
T0-1	4	4	8	
T2	38	27	65	
T3	100	92	192	
T4	4	5	9	
Total LN[c] examined				0.001[b]
mean (SD)	7.5 (7.1)	11.0 (10.4)	9.3 (9.1)	
Positive LNs				0.538[b]
mean (SD)	4.0 (3.9)	3.4 (5.4)	3.7 (4.7)	
LNs ratio in stage III				0.052[b]
mean (SD)	0.50 (03)	0.37 (0.2)	0.44 (0.3)	

[a] Pearson Chi-Square
[b] Independent-samples t-test
[c] Abbreviation: LN, Lymph Node

Table 2. Distribution of Treatment Modalities and Primary Sites in 275 Patients With Colorectal Cancer

Treatment Modalities	Primary Site		Total
	Rectum	Colon	
Surgery, followed by concurrent ChTRT[a] and ChT	82	46	128
Surgery, followed by sequential RT and ChT	8	1	9
Surgery, followed by ChT alone	8	62	70
Surgery, followed by RT alone	3	1	4
Surgery alone	4	14	18
Neoadjuvant ChTRT, followed by surgery, followed by ChT	22	3	25
Neoadjuvant RT, followed by surgery, followed by ChT	7	0	7
Neoadjuvant ChT, followed by surgery, followed by ChT	13	1	14
Total	147	128	275

[a] Abbreviations: ChT, chemotherapy; ChTRT, chemoradiation; RT, radiotherapy

4.2. Treatment Schedules

Table 2 illustrates the distribution of different therapies used for the 275 patients with colorectal cancer. Accordingly, surgical resection followed by adjuvant concurrent chemoradiation followed by chemotherapy (55%) and neoadjuvant concurrent chemoradiation followed by surgical resection followed by chemotherapy (15%) were the most frequent treatment schedules used in patients with rectal cancer. Whereas, patients with colon cancer, surgery followed by adjuvant chemotherapy (48%) and surgery followed by adjuvant concurrent chemoradiation followed by chemotherapy (36%) were the most common treatment schedules used.

4.3. Univariate Analysis of Prognostic Factors

The 5-year local control, disease-free, and overall survival rates for all patients were 78.1%, 62.6%, and 70.5% respectively (Figures 1, 2, and 3). On univariate analysis, primary tumor stage (P = 0.01), lymph nodes ratio (P = 0.04) (Figure 4), and the presence of perineural invasion (P < 0.001) were found as prognostic factors for local control rate. The total lymph nodes identified was not a prognostic factor for local control rate (Figure 5).

We found primary tumor stage (P = 0.04), tumor grade (P = 0.02), the presence of lymphatic-vascular invasion (P = 0.001), the presence of perineural invasion (P < 0.001), the total lymph node identified (P = 0.04), positive lymph nodes (P = 0.004), and lymph nodes ratio (P = 0.01) as prognostic factors for disease free survival (Figures 6 and 7). In addition, primary tumor stage (P = 0.03), the presence of lymphatic-vascular invasion (P = 0.009), the presence of perineural invasion (P = 0.001), the total lymph node identified (P = 0.02), and lymph nodes ratio (P = 0.01) were prognostic factors for overall survival (Table 3).

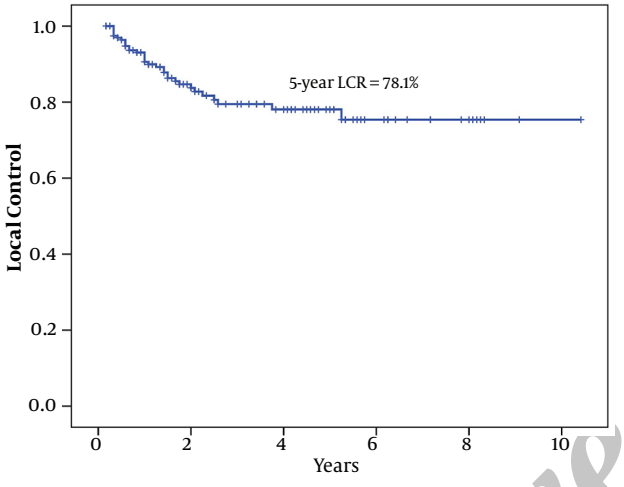

Figure 1. Kaplan-Meier Survival Curves of 5-Year Local Control in 275 Patients With Colorectal Cancer

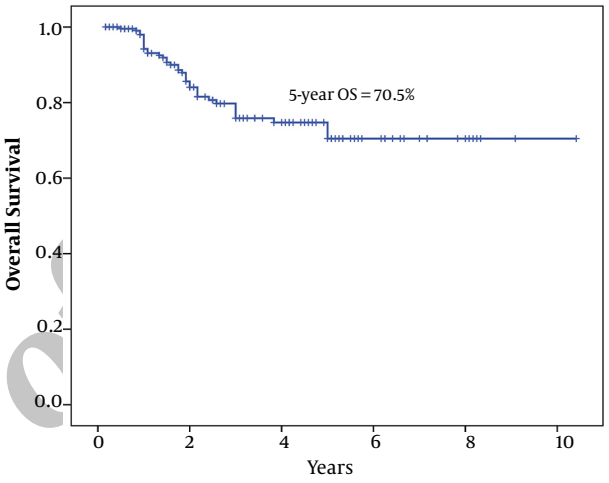

Figure 3. Kaplan-Meier Survival Curves of 5-Year Overall Survival in 275 Patients With Colorectal Cancer

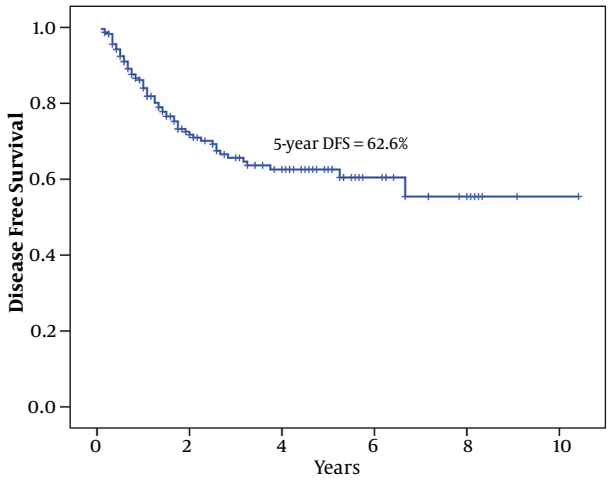

Figure 2. Kaplan-Meier Survival Curves of 5-Year Disease-Free Survival in 275 Patients With Colorectal Cancer

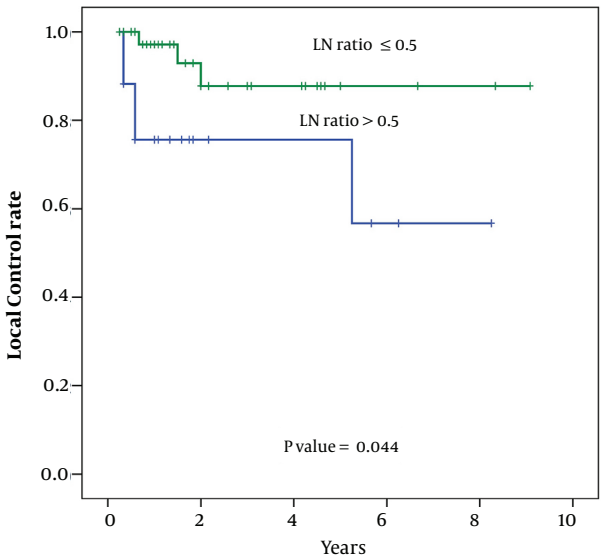

Figure 4. Kaplan-Meier Survival Analysis of Local Control Rate Categorized According to the Lymph Nodes Ratio in 275 Patients With Colorectal Cancer

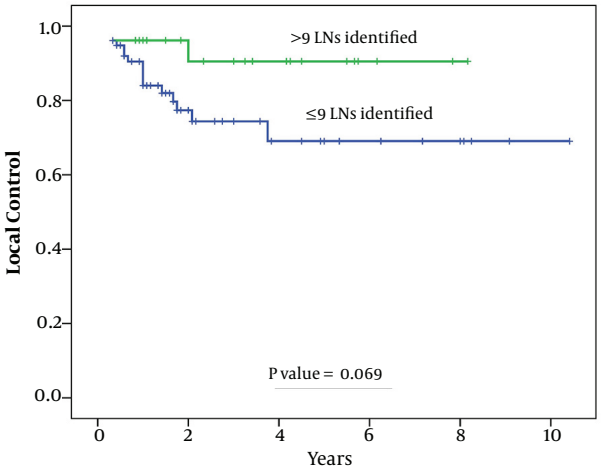

Figure 5. Kaplan-Meier Survival Analysis of Local Control Rate Categorized According to the Total Lymph Nodes Identified in 275 Patients With Colorectal Cancer

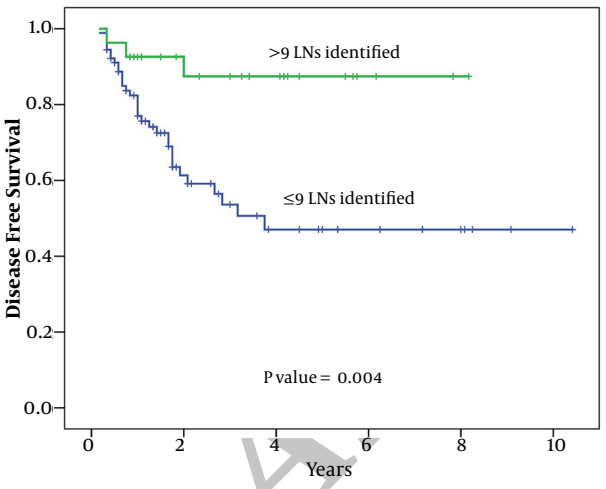

Figure 6. Kaplan-Meier Survival Analysis of Disease Free Survival Rates Categorized According to the Total Lymph Nodes Identified in 275 Patients With Colorectal Cancer

Figures 8 and 9 illustrate the prognostic impact of total lymph nodes identified and lymph nodes ratio on the 5-year overall survival rates in our patients. On stratified Log-Rank test analysis according to the primary site (rectum versus colon), higher tumor stage (P = 0.01), the presence of lymphatic-vascular invasion (P = 0.006), the presence of perineural invasion (P = 0.009) and lymph nodes ratio more than 0.5 (P = 0.02) were found to have a negative prognostic influence on the overall survival (Table 4).

In subgroup analysis of node negative patients, the to

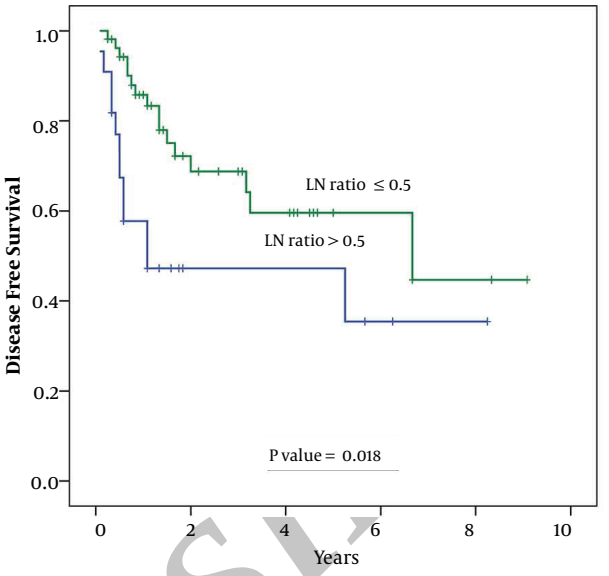

Figure 7. Kaplan-Meier Survival Analysis of Disease Free Survival Rates Categorized According to the Lymph Nodes Ratio in 275 Patients With Colorectal Cancer

tal lymph nodes examined was a prognostic factor only for overall survival (P = 0.006); but not for local control (P = 0.10), or disease free survival (P = 0.06). In addition, in subgroup analysis of node positive patients, we found lymph nodes ratio as a prognostic factor for 5-year local control (P = 0.04), disease free survival (P = 0.01), and overall survival (P = 0.01) rates. However, the total examined lymph nodes was not found as a prognostic factor for local control (P = 0.80), disease free survival (P = 0.44), or overall survival (P = 0.95) in this group.

4.4. Multiple Regression Analysis of Prognostic Factors

Prognostic factors that were significant in univariate analysis were assessed using multiple regression analysis. On this analysis, poorly differentiated tumors (HR = 3.868, 95% CI = 1.297-11.532, P = 0.015), and the presence of perineural invasion were independent adverse prognostic factors for local control (HR = 6.355, 95% CI = 2.344-17.230, P < 0.001). Poorly differentiated tumors (HR = 4.613, 95% CI = 1.929-11.031, P = 0.001), the presence of lymphatic-vascular invasion (HR = 3.514, 95% CI = 1.127-10.958, P = 0.03), and perineural invasion (HR = 4.079, 95% CI = 1.991-8.355, P < 0.001), and lymph nodes ratio more than 0.5 (HR = 2.173, 95% CI = 1.100-4.293, P = 0.02) had a negative influence on disease free survival. In addition, Advanced primary tumor stage (HR = 2.625, 95% CI = 1.195-5.766, P = 0.01), rectal primary site (HR = 2.503, 95% CI = 1.142-5.485, P = 0.02), and the presence of perineural invasion (HR = 3.099, 95% CI = 1.198-8.014, P = 0.02) were independent adverse prognostic factors for overall survival.

Table 3. Univariate Analysis of Prognostic Factors for 5-Year Local Control, Disease Free Survival and Overall Survival Rates in 275 Patients With Colorectal Cancer

	Patients, No.	5-year LC[a] Rate, %	P value[b]	5-year DFS Rate, %	P value[b]	5-year OS Rate, %	P value[b]
Age, y			0.71		0.76		0.32
< 55	143	78.9		63.8		72.8	
≥ 55	132	76.3		60.5		66.3	
Sex			0.75		0.50		0.49
Male	162	78.0		60.5		68.3	
Female	113	78.3		65.8		74.2	
Tumor stage			0.01		0.04		0.03
T0-1	8	100.0		100.0		100.0	
T2	65	82.4		75.8		75.6	
T3	192	78.0		59.1		68.7	
T4	9	38.1		31.3		44.4	
Tumor size, cm			0.66		0.45		0.32
≤ 5	182	77.3		59.4		65.7	
> 5	93	79.4		66.8		76.6	
Tumor grade			0.08		0.02		0.22
Well differentiated	189	79.5		65.3		73.3	
Moderately differentiated	66	80.1		63.7		69.0	
Poorly differentiated	15	42.9		33.0		50.0	
Lymphatic-vascular invasion			0.08		0.001		0.009
Negative	136	83.4		73.9		81.8	
Positive	109	67.4		46.2		51.4	
Not mentioned	30	88.0		70.1		79.9	
Perineural invasion			< 0.001		< 0.001		0.001
Negative	134	77.2		61.4		73.0	
Positive	49	49.0		29.0		41.3	
Not mentioned	92	89.6		81.2		84.8	
Ob and/or Per			0.12		0.19		0.19
Negative	74	68.4		56.9		64.6	
Positive	50	86.2		76.0		85.5	
Not mentioned	151	80.2		59.2		62.5	
Total LN examined			0.18		0.04		0.02
≤ 9 LNs	186	75.3		55.8		63.4	
> 9 LN	89	83.2		74.5		85.1	
Positive lymph nodes			0.61		0.004		0.39
≤ 1 positive LNs	214	77.6		65.9		70.4	
> 1 positive LNs	61	80.9		49.2		71.7	
Lymph node ratio in stage III			0.04		0.01		0.01
≤ 0.5	64	87.8		59.6		83.9	
> 0.5	30	75.6		47.3		55.1	

[a] Abbreviations: DFS, disease free survival; LCR, local control rate; Ob, obstruction; OS, overall survival; Per, perforation
[b] Log-Rank test

Table 4. Univariate Analysis of Prognostic Factors For 5-Year Overall Survival Rates by Stratification of Primary Site in the 275 Patients With Colorectal Cancer

	Rectum			Colon			P value[c]
	Patients, No.	5-year OS[a]	P value[b]	Patients, No.	5-year OS	P value[b]	
Age, y			0.11			0.29	0.39
< 55	72	67.6		71	80.3		
≥ 55	75	45.9		57	93.9		
Sex			0.45			0.89	0.56
Male	86	55.9		76	88.9		
Female	61	68.5		52	82.0		
Tumor stage			0.09			0.29	0.01
T0-1	4	100.0		4	100.0		
T2	38	59.7		27	100.0		
T3	100	56.4		92	83.6		
T4	4	33.3		5	50.0		
Tumor size, cm			0.43			0.74	0.62
≤ 5	104	55.5		78	85.9		
> 5	43	68.4		50	85.0		
Tumor grade			0.21			0.18	0.09
Well differentiated	105	63.0		84	89.6		
Moderately differentiated	36	55.1		31	85.9		
Poorly differentiated	2	66.7		12	40.0		
Lymphatic-vascular invasion			0.008			0.58	0.006
Negative	75	76.7		61	89.1		
Positive	56	35.6		53	79.1		
Not mentioned	16	66.7		14	90.0		
Perineural invasion			0.06			0.07	0.009
Negative	73	64.2		61	89.1		
Positive	29	37.1		20	63.0		
Not mentioned	45	79.4		47	89.4		
Ob and/or Per			0.66			0.42	0.59
Negative	52	63.3		22	68.6		
Positive	18	78.6		32	89.2		
Not mentioned	77	21.9		74	90.5		
Total LN examined			0.02			0.98	0.53
≤ 9 LNs	108	49.0		78	88.6		
> 9 LN	39	88.0		50	82.6		
Positive lymph nodes			0.94			0.372	0.45
≤ 1 positive LNs	110	59.4		104	86.3		
> 1 positive LNs	73	67.3		24	80.8		
Lymph node ratio in stage III			0.08			0.16	0.02
≤ 0.5	29	79.9		35	88.1		
> 0.5	19	57.7		11	53.3		

[c] stratified Log-Rank test
[a] Abbreviations: Ob, obstruction; OS, overall survival; Per, perforation
[b] Log-Rank test

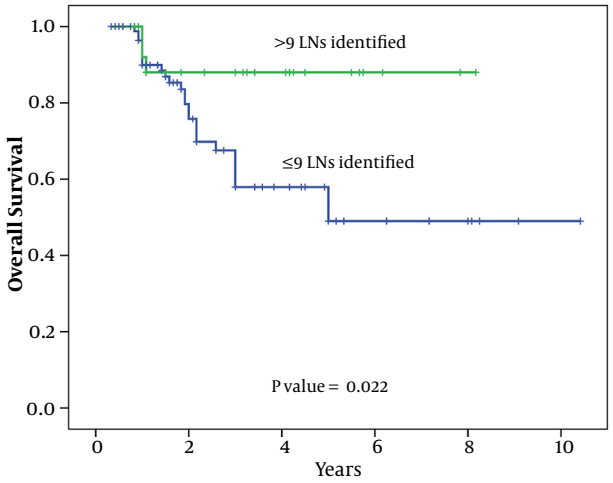

Figure 8. Kaplan-Meier Survival Analysis of Overall Survival Rates Categorized According to the Total Lymph Nodes Identified in 275 Patients With Colorectal Cancer

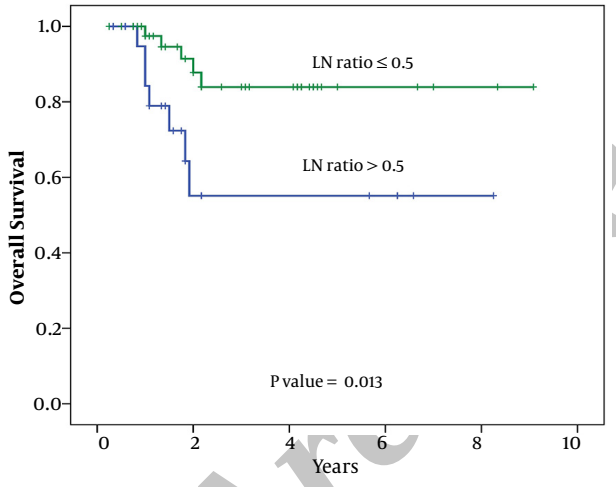

Figure 9. Kaplan-Meier Survival Analysis of Overall Survival Rates Categorized According to the Lymph Nodes Ratio in 275 Patients With Colorectal Cancer

5. Discussion

Inadequate lymph nodes examined directly and indirectly influence oncological outcomes in patients with resected colorectal cancer (13). Inadequate lymph nodes examination due to inadequate surgical excision can directly compromise locoregional control and survival in these patients. In addition, inadequate lymph nodes examination can indirectly underestimate node staging, which leads to classification of patients with real stage III colorectal cancer as stage I or II disease incorrectly. Subsequently, some patients with stage III are deprived from optimal treatments (8, 13).

In this retrospective study, we investigated the prognostic value of total lymph nodes identified and ratio of lymph nodes in patients who underwent curative resection for colorectal cancer. Univariate and multivariate analysis of the present study showed that lower total lymph nodes identified and higher ratio of lymph nodes were associated with poorer oncologic outcomes in these patients. In addition, tumor stage was found as a more significant prognostic factor than node stage in our patients with inadequate lymph nodes evaluation and staging.

The correlation between total number of lymph nodes identified and oncological outcome of the colorectal cancer has been extensively evaluated (Table 5) (15 - 32). Some studies found that more lymph nodes examined improves survival for patients with node negative colorectal cancer (15, 18, 20, 23, 24). In a retrospective study, Desolneux et al. investigated prognostic variables in 362 patients with resected node-negative (stages I and II) colorectal cancer. They found inadequate total lymph nodes examined as an independent poor prognostic factor (15). In another study, Iachetta et al. evaluated the association between number of lymph nodes examined and survival in patients with stage IIA disease (T3N0M0). They concluded that patients with stage IIA colorectal cancer with more than or equal to 20 lymph nodes examined show better survival compared to those with fewer lymph nodes examined (18). These evidences were in agreement with the results of our report in which the total lymph nodes identified was a prognostic factor for overall survival. Prognostic value of total lymph nodes identified and ratio of lymph nodes in resected node positive colorectal cancer have been evaluated by several investigators (19 , 26 - 35).

Johnson et al. performed a large study on patients who underwent surgery for stage III colon cancer between 1988 and 1997 using the data from the surveillance, epidemiology and end results (SEER) cancer registry (33). They found that the number of negative nodes was a significant independent prognostic factor for patients with stages IIIB and IIIC colon cancer. In a retrospective study, Thomas et al. performed a multivariate analysis to find out independent prognostic factors in 1098 patients, which had undergone colorectal cancer resections. They concluded that the presence of positive lymph nodes may not be an accurate indicator for stage III colorectal cancer; and the evaluation of ratio of lymph nodes is a more important prognostic factor in these patients (35). Various cut-off points were considered for the total examined lymph nodes (range 6-40) and lymph nodes ratio (range 0.07-0.69) by researchers in the literature (13 , 36). In the present study and based on the mean total lymph nodes and ratio of the lymph nodes, we chose 9 lymph nodes and 0.5 as a cut-off points for the total examined lymph nodes and ratio of the lymph nodes, respectively.

Table 5. The Prognostic Value of Total Lymph Nodes Examined and Ratio of Lymph Nodes in Oncologic Outcomes of the Colorectal Cancer in the Literature and the Present Study

	Country	Patients, No.	Primary Site	Stage	Oncologic Outcome	Prognostic Value	
						TLNE[a]	LN Ratio
Nadoshan (9)	Iran	128	Rectum	III	DFS, OS	+	+
Desolneux (15)	Germany	362	Colorectal	I-II	OS	+	-
Ogino (17)	The USA	716	Colorectal	I-IV	OS	+	+
Iachetta (18)	Italy	657	Colorectal	IIA	OS	+	-
Shao (19)	China	507	Colorectal	II-III	OS	+	+
Peeples (20)	The USA	913	Colorectal	II	OS	+	-
Choi (21)	Hong Kong	664	Colorectal	II	DFS, OS	+	-
Vather (22)	The New Zealand	4309	Colorectal	II-III	OS	+	+
Tsai (23)	Taiwan	259	Colorectal	II	OS	+	-
Law (25)	Canada	115	Colon	II	DFS, OS	+	-
Wong (26)	China	533	Colorectal	III	DFS, OS	-	+
Elias (27)	Lebanon	164	Colorectal	III	DFS, OS	-	+
Shimomura (28)	Japan	266	Colorectal	III	DFS	-	+
Park (29)	Korea	186	Colorectal	III	OS	-	+
Tsikitis (30)	The USA	329	Colon	III	DFS, OS	-	+
Lee (31)	Korea	154	Rectum	III	DFS, OS	-	+
Klos (32)	Netherlands	281	Rectum	II-III	OS	-	+
Johnson (33)	The USA	20702	Colon	III	DSS	+	-
Lu (34)	Taiwan	612	Colorectal	III	DFS, OS	-	+
Ren (37)	China	145	Colorectal	III	DFS	-	+
Present study	Iran	275	Colorectal	I-III	DFS, OS	+	+

[a] Abbreviations: DFS, disease free survival; DSS, disease-specific survival; LN, lymph node; OS, overall survival; TLNE, total lymph node examined

In Iran, Nadoshan et al. investigated the prognostic value of lymph node ratios in selected patients with node positive rectal cancer treated with neoadjuvant chemoradiation. They chose 12 lymph nodes and 0.2 as cut-off points for the total examined lymph nodes and ratio of the lymph nodes, respectively. The results of their study indicated that the total lymph nodes identified and ratio of lymph nodes were important prognostic factors for disease free and overall survival in patients with stage III rectal cancer (9). In accordance with the literature, in our study and by analysis of subgroup patients with stage III, we found lymph node ratio as a prognostic factor for local control, disease free survival, and overall survival in 94 patients with node positive colorectal cancer; however, the total identified lymph nodes was not a prognostic factor for local control, disease free survival, or overall survival. Moreover, compared to the report of Nadoshan et al, our study included a larger population and covered both patients with colon and rectal cancer. The total lymph nodes identified and ratio of lymph nodes are associated with oncological outcomes in patients with colorectal cancer. Tumor stage may be a more useful prognostic indicator than node stage in patients with inadequate lymph nodes staging.

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Authors' Contribution

Leila Ghahramani: Involved in design, writing and revising the manuscript, and approval of the final version. Leila Moadshoar: Involved in conception, design, data collection, literature review, writing the manuscript, and approval of the final version. Sayed Hasan Hamedi: Involved in conception, design, data collection, literature review and writing the manuscript, and approval of the final version. Samira Razzaghi: Involved in conception, design, data collection, literature review and writing the manuscript, and approval of the final version. Saeedeh Pourahmad: Involved in analysis, and interpretation, writing, and revising the manuscript,

and approval of the final manuscript. Mohammad Mohammadianpanah: Involved in design and data collection, and in literature review, writing, and revising the manuscript, and approval of the final version.

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