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Original Article

Comprehensive analysis of impacts of lymph node yield on patient survival and recurrence in patients with stage II rectal cancer: A single institution study

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Abstract

Aim: Pathologic evaluation of rectal cancer is very important. Lymph node yields may be related to surgical technique or inadequate harvesting in the pathology department. The importance of lymph node yields >12 have been emphasized by many researchers to be adequate for staging. In stage II rectal cancer, the impacts of lymph node yield on locoregional recurrence and patient survival have not been studied. The aim of the present study is to evaluate the impact of lymph node yield on outcome and prognosis of the patients with stage II rectal cancer.

Material and Methods: Patients with stage II rectal cancer who were operated in our institution between 2008 and 2013 were retrospectively analyzed to determine the impact of lymph node yield on survival, locoregional and distant metastasis.

Results: Overall, local and distant recurrence rates were 13.9%, 4.65% and 9.30%; respectively. We did not find any significant difference in terms of locoregional and distant metastasis rates among Group I (lymph node<12) and II (lymph nodes>12) (p>0.05). The 5-year survival of the patients in Group 1 versus Group 2 were 86.7% versus 82%; respectively (p>0.05).

Conclusions: Results of the present study emphasize that lymph node yields may not have an impact on patient survival or recurrence. However, the patient groups were heterogeneous and the volume was low, therefore, more studies with higher volumes are needed.

Keywords: Rectal Cancer; Staging; Lymph Node Metastasis.

INTRODUCTION

Colorectal cancer is the third most common cancer for both male and female. On the other hand it is the second most common cause of cancer related death (1). In the United States it is estimated that 319.160 new cases of gastrointestinal cancers will be diagnosed in 2018 and 43.030 new rectal cancer cases are estimated (2). We did not encounter any data regarding the estimated rectal cancer incidence in our country; however, in Turkish Cancer Statistics it was reported to be the 8th and 10th most common cancer among men and women in 2006. Between 2006 and 2009 there were 5235 rectal cancer cases in total and this number had increased to 9497 cases in years 2009-2013. Therefore; the incidence of rectal cancer is increasing in our country as it is in the Western World (3,4).

There is no standard definition for high risk tumors in stage II rectal cancer. Nevertheless, pathologic characteristics such as perforation, poor differentiated tumor, serosal dissemination, venous, lymphatic or perineural invasion and low number of harvested lymph nodes were considered to have poor prognostic implications in patients with rectal cancer (5). For this reason, current guidelines suggest 12 or more lymph node evaluation in order to make a definitive staging in patients with rectal cancer (6–8). Therefore; worldwide colorectal cancer centers practice dissecting minimum number 12 lymph nodes for staging and evaluation of following colon and total mesorectal excisions (9,10). However, there are no definitive data regarding the prognostic implications in patients with dissected lymph nodes less than 12 (6). The aim of the present study is to evaluate the impact

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of dissected lymph node number on prognosis of the patients with stage II rectal cancer.

MATERIAL and METHODS

Evaluation of the patients for the study

The charts of 43 patients with stage II rectal cancer who underwent total mesorectal excision in our institution between 2008 and 2013 were retrospectively evaluated. Exclusion criteria were patients with stage 3-4 rectal cancer cases, patients who received any type of neoadjuvant therapy, patients with inflammatory bowel disease, hereditary colorectal cancer and patients with previous history of other organ cancers.

The preoperative staging included digital rectal examination, abdominal computerized tomography, thorax tomography and pelvic magnetic resonance imaging.

In all patients total mesorectal excision was performed starting with ligation of the inferior mesenteric vein and artery as a standard approach and rest of the operation was performed according to standard technical principles defined in literature (11).

The patients were grouped in to two groups according to the evaluated lymph node numbers indicated in the postoperative pathology report. The groups were <12 lymph nodes (Group 1) and ≥12 lymph nodes (Group 2). The patients that were included in these groups were evaluated according to the demographic characteristics, tumor histology, tumor characteristics such as perineural invasion, tumor differentiation, adjuvant chemotherapy, T stage, development of distant, regional or local recurrence.

Ethical Statement: There were no direct interactions with subjects and knowledge gained would not impact subject's clinical care, and therefore an institutional review board approval was not obtained.

Statistical Analysis

Continuous variables were expressed as median and range. Discrete variables are expressed as the percentage of the study population. The relationship between the dependent and independent variables were analyzed using Student t test and Mann Whitney U Test. A multivariate analysis model was established by using Cox regression method, considering the parameters, which had a p value less than 0.25 in univariate analysis. Any p value less than 0.05 were considered as statistically significant. All statistical analysis was performed using Statistical Program for Social Sciences software version 17 (SPSS v17, IBM, USA).

RESULTS

Forty-three patients with stage II rectal cancer who were operated in our institution were included in the study. In 15 (34.88%) patients total numbers of harvested lymph nodes were <12 and it was ≥12 in 28 patients (65.11%). There were 7 (46.7%) and 11(39.3%) male patients in Group 1 and Group 2; respectively. The mean age of the patients in Group1 and Group 2 were 56.9±12.5 and 60.1±9.7 years; respectively. The two study groups were statistically similar in terms of age and gender (Table 1).

Table 1. The demographic characteristics of the patients in the study

Study Parameters	Group 1 (n=15)	Group 2 (n=28)	P
Gender			
Male	7 (46.7)	11 (39.3)	
Female	8 (53.3)	17 (60.7)	0.640
Age (years)	56.9±12.5	60.1±9.7	0.362

There was statistically significant difference among the study groups in terms of tumor histology, lympho-vascular and perineural invasion, adjuvant chemotherapy, locoregional or distant metastasis, adjuvant treatment. There was a significant difference among the study groups in terms of differentiation of the tumors, number of metastatic lymph nodes and T stage (pT3/pT4) (p<0.05) (Table 2).

Table 2. Tumor related characteristics and prognosis of the patients in the study groups

Study Parameters	Group 1 (n=15)	Group 2 (n=28)	P value
Histologic type of the tumors			
Adenocarcinoma. NOS	14 (93.3)	27 (96.4)	0.999
Mucinous Tumors	1 (6.7)	1 (3.6)	
Lymphovascular invasion	1 (%6.7)	6 (%21.4)	0.391
Perineural invasion	5 (%33.3)	4 (%14.3)	0.238
Tumor differentiation			
Well/moderate	5 (33.3)/ 10 (66.7)	1 (3.6) / 27 (96.4)	0.015*
Adjuvant Chemotherapy	7 (46.7)	9 (32.1)	0.348
Number of harvested lymph nodes	9 (1-11)	15.5 (12-36)	0.000*
T stage pT3 /pT4	11 (73.3)/ 4 (26.7)	27 (96.4) / 1 (3.6)	0.043*
Rate of recurrence	2 (13.3)	4 (14.3)	0.999
Locoregional recurrence	0	2 (7.1)	0.535
Distant metastasis	2 (13.3)	2 (7.1)	0.602
Recurrence rate according to the adjuvant thera-py			
Received			
Did not received	0	2 (7.1)	0.999
Distant Metastasis according to adjuvant therapy			
Received	0 (n=7)	1 (11.1) (n=9)	0.201
Did not receive	2 (25.0) (n=8)	1 (5.3) (n=19)	0.999

*p< 0.05

There was no difference in terms of the 5 year survival of the patients Group 1 versus Group 2 being 86.7% versus 82%; respectively (p>0.0.5) (Figure 1). Multivariate analysis denied any variable as a significant factor for survival.

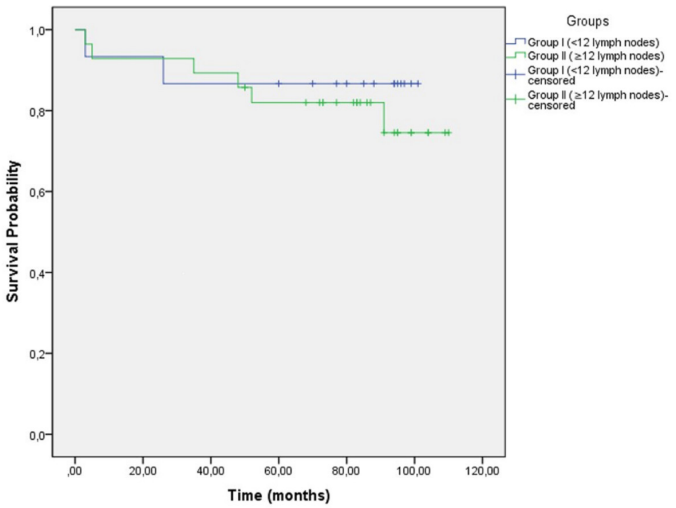

Figure 1. The 5-year survival of the patients in Group 1 versus Group 2 were 86.7% versus 82%; respectively (p=0.545)

DISCUSSION

The most important factor that determines the prognosis of the patients with rectal cancer following surgical therapy is the stage of the tumor. Total dissected number of lymph nodes following curative resection of rectal cancer is a factor for validation of the accuracy of staging of the tumor and guides the appropriate therapy of the patient in the postoperative period (12). This is especially important in patients with tumors without local lymph node metastasis (13). Furthermore, inadequate number of lymph node evaluation leads to inadequate staging of the patient which results in inadequate treatment and leads to poor prognosis (14). For this reason, AJCC and UICC guidelines suggest evaluation of at least 12 negative lymph nodes for appropriate staging (12). Stocchi et al (9) have found that in stage II colon cancer patients with a lymph node yield less than 12 were associated with poorer prognosis when compared to patients with a lymph node yield more than twelve.

Patient prognosis in rectal cancer depend upon few histopathologic characteristics obtained as a result of pathologic evaluation (15). These factors are the depth of invasion of the bowel wall (16), number of metastatic lymph nodes (17), presence of extramural invasion (18), presence of tumor in the circumferential tumor margin (19), tumor related ulcerations in the peritoneal surface of the rectum (20).

Vascular and lymphatic invasion is an important factor determining local and distant recurrence (21). Nikberg et al (1) have reported lymphovascular invasion to be 15% in their study. In the present study we have also found that lymphovascular invasion was 16.28% in our patients. The lymphovascular invasion in Group I and Group II was 6.7% and 21.4%; respectively. However, this difference did not reach statistical significance. Peng et al (21) have reported that lymphovascular invasion rate increased from 8% to 24% with H&S staining. In the present study, after H&S staining lymphovascular invasion in Group I and Group II increased to 33.3% and 14.3% (overall 20.9%); respectively. This difference also did not reach statistical significance. However; with increasing patient numbers this tendency may become more prominent and statistical difference may become significant.

Currently with multimodality treatment, stage II rectal cancer has low local recurrence rate (<5%); but the distant metastasis rates are still high reaching 20% (22). In stage II rectal cancer (T3-T4 N0 M0) patients with high rates of lymphovascular and perineural invasion the risk of local recurrence increases (1). Nikberg et al (1) have reported overall recurrence rates as 17%. In the present study, overall, local and distant recurrence rates were 13.9%, 4.65% and 9.30%, respectively. We did not find any significant difference in terms of locoregional and distant metastasis rates among Groups I and II.

In stage III rectal cancer adjuvant therapy following total mesorectal excision is a standard treatment approach; however this is not the case for stage II rectal cancer and the criteria for chemotherapy is controversial (23,24). Multimodality therapy including chemotherapy following total mesorectal excision has been reported to decrease local recurrences (25). Furthermore chemotherapy and radiotherapy has been implicated to control and decrease local recurrences (26). In the present study, recurrence rates tended to be higher in patients that did not receive chemotherapy when compared to patients that did receive chemotherapy; but this did not reach statistical significance. This may be related to the fact that number of patients in Group II were higher that Group I and furthermore; the rate of moderately differentiated tumors was higher in our study. We did not find statistically significant difference in locoregional and distant recurrences among Group I and Group II. For this reason, in stage II rectal cancer patients recognition of high risk patients is very important to avoid giving unnecessary therapy to patients and also to avid toxic side effects of chemotherapy (27). Limitations of the present study were the retrospective study design and low patient volume.

CONCLUSION

In conclusion, we did not find any significant difference in terms of locoregional and distant metastasis in patients with 12 or more dissected lymph nodes when compared to patients with less than 12 dissected lymph node numbers. The 5-year survival rates did not also differ significantly among the groups.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports

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