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Role of neoadjuvant therapy in lymph node and primary rectal tumor regression and prognosis

Abstract

Rectal tumors are important malignancies and prediction of prognosis after neoadjuvant therapy is important to improve the prognosis process. The purpose of this study was to determine therole ofneoadjuvant therapy in lymph node regression and primary rectal tumor as well as its association with prognosis**.** In this descriptive study, 40 consecutive patients with rectal tumorswho were referredtoTaleghani Hospital for surgery from 2011 to 2018 were enrolled. Moreover, theneoadjuvant therapy role in lymph node regression and the primary rectal tumor was determined as well as its association with prognosis.The results of this study demonstrate that there was no tumor regression in 20% of patients and it wasalso less than 25%, 25-50%, 50-75%, and complete in 22.5%, 35%, 20%, and 2.5% of the patients,respectively. The lymph node regression was complete in 5% of the patients and it wasalso less than 25% in 20% and more than 25% in 50% of them. In addition, it was no regression in 25% of the patients. The lymph node regression was related to N stage (P=0.018), primary tumor regression grade (P=0.001), yPT (P=0.008), and yPN (P=0.020); however, it was not related to prognosis (P > 0.05).Totally, according to the obtained results, it can be concluded thatneoadjuvant therapy plays a good role in lymph node regression and primary rectal tumor, but it has no association with prognosis.

Keywords: *Neoadjuvant therapy, Lymph node regression, Primary rectal tumor, Prognosis*

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Introduction

Colorectal cancers are common malignancies that have the third rank after lung and breast neoplasms (1). However, there are multiple screening methods known to reduce the morbidity and mortality of these cancers (2). Also, multiple risk factors including some environmental and genetic issues are involved in the pathogenesis of the disease. Moreover, the risk of postoperative recurrence rate is high that is ranged from 4 to 27 percent and preoperative chemotherapy is a useful method to improve the survival rate and reduce the recurrence rate (3). In this regard, the main benefit of preoperative chemotherapy is the complete clinical regression and pathological response (4). Complete pathological responses ranging from 10 to 30 percent would increase the survival rate as well asdecreasethe recurrence rate (5).

The pathological studies on the patients with preoperative chemotherapy have shown significant reductions in the number and size of the involved lymph nodes and the frequency of lymph node metastasis (6). Notably, there are different grading systems such as Mandard, Dowrak, and Dowrak/Rodel for tumor regression grading (TRG) (7). Also, some studies have demonstrated the association of TRG with lymph node status (8). Accordingly, Caricato et al. reported the association between LRG and TRG in primary tumors; however, theeffects of LRG on oncological outcomes arenot determined yet (9). Some studies have shown the association betweenlymph node micrometastasis and recurrence and survival rates (10). However, there are some opposite results in this regard (11,12). Hence, in this study,we reviewed the role of neoadjuvant therapy in lymph node and primary rectal tumorregression and prognosis.

Materials and methods

In this descriptive study, 40 consecutive patients with rectal tumorswho weretoTaleghani Hospital, Tehran, Iran for surgery from 2011 to 2018,were included. The inclusion criteria were rectal adenocarcinoma, pre-treatment biopsy, tumor stages II and III with a distal margin less than 12 cm from the anal ridge, lack of distant metastasis, and neoadjuvant therapy. In addition, the exclusion criteria were distant metastasis and lack of biopsy beforethe treatment initiation. This study was approved by the local ethical committee ID IR.SBMU.MSP.REC.1398.650.

Therole ofneoadjuvant therapy in lymph node regression and primary rectal tumor and its association with prognosis were determined in this study. Also, clinical outcomes were assessed according to TNM, staging groups, several lymph nodes, lymphatic and venous invasion (by Hematoxylin-Eosin (HE), tumor deposits, TRG, and LRG. Afterward, TDs were assessed by TNM5 and TNM-6. Primary tumor regression was assessed using theRodel Model as follows: no regression (0), less than 25% (1), between 25 and 50% (2), more than 50% (3), and complete (4). Moreover, the scores for LRG were as follows:complete fibrosis (0), more than 25% (1), less than 25% (2), and no regression (3). Also, MRI and CT scans were done in the preoperative phase. In positive LN cases with no remained tumoralcells and fibrosis in pathological assessment, it was assumed that neoadjuvant chemotherapy haskilled all tumoral cells.

Data analysis was performed by SPSS version 13.0 software. The utilized tests in this study were ANOVA and Chi-Square. The p values under 0.05 were considered statistically significant.

Results

This study demonstrated that there was no tumor regression in 20% of the patients, which was less than 25%, 25-50%, 50-75%, and complete in 22.5%, 35%, 20%, and 2.5%of them, respectively. The lymph node regression was complete in 5% of the patients, andit was less than 25% in 20%, more than 25% in 50%, and with no regression in 25% of them.

LRG had no significant difference in terms of age, sex, type of treatment, tumor differentiation, lymphovascular invasion, and 18-month and 24-month prognosis ($P > 0.05$). However,primary T and N stages,yPT(table 2), yPN (table 3), and TRG (table 1)were significantly related to LRG ($P < 0.05$)

Discussion

The prognostic significance of lymph noderegression and its correlation with TRG in patients with rectal cancer who have undergone neoadjuvant therapyare unidentified yet. In this study, 20 percent of the patients had no regression in LRG and 25 percent of them had no regression in TRG, and there was a significant association between LRG and TRG; however, the LRG was not related to prognosis. Li et al (13) reported that LRG was related to 5-year metastasis and mortality. Similarly, they reported a significant association between TRG and LRG, known as a long-term prognostic factor in rectal cancer patients. Notably, the lack of association with prognosis in our study may be due to the smaller sample size.

Hughes et al. (14) in their study assessed 211 patients under preoperative chemotherapy forT3-T4 rectal cancers. Accordingly, 18 percent of these patients had a complete pathological response, out of that,17% had positive lymph nodes. After performing the neoadjuvant chemotherapy, there was no recurrence. The overall survival was similar for those with a complete pathological response tothe remaining tumor. In line with our study, they found that LRG is not related to complete pathological response. In addition, Tomas et al. (15) assessed 649 patients who underwentneoadjuvant radiotherapy and chemotherapy. They found a significant association between yPT and LRG,which was seen in our study as well.Caricato et al. (10) assessed 35 patients with rectal cancer and there was no regression in 11% of the patients under neoadjuvant chemotherapy and similarly found a significant association between LRG and TRG.

Conclusion

Our study showed thatneoadjuvant therapy plays a good role in lymph node regression and primary rectal tumor; however, there is no association with prognosis. Therefore, further studies with a larger sample size and multi-center samplings are required to attain more definite results and clinical relevance.

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Conflict of interest

None.

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Ethics statement

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Table 1- Association between TRG and LRG in patients

	LRG				
TRG	0	1	2	3	TOTAL
0	0	0	0	8	8
1	0	0	7	2	9
2	0	13	1	0	14
3	1	7	0	0	4
4	1	0	0	0	1
TOTAL	2	20	8	10	40

Table 2- Association between yPT and LRG in patients

	LRG				
ypT	0	1	2	3	TOTAL
T0	1	0	0	0	1
T1	0	1	0	1	2
T2	1	11	1	3	16
T3	0	6	6	5	17
T4	0	2	1	1	4
TOTAL	2	20	8	10	40

Table 3- Association between yPN and LRG inpatients

	LRG				
yPN	0	1	2	3	total
N1	2	12	4	10	28
N2	0	8	2	0	10
N3	0	0	2	0	2
total	2	20	8	10	40