ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 10 | October - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARATIVE ASSESSMENT OF TOXICITY REDUCTION ON HEMATOLOGICAL PARAMETERS BETWEEN TOTAL NEOADJUVANT THERAPY AND STANDARD THERAPY ON LOCALLY ADVANCED RECTAL CANCER

Radiotherapy

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ABSTRACT

Objective: The objective of the present study was to evaluate the toxicities on haematological parameters between the two arms (ARM-A: Neoadjuvant chemotherapy followed by NACTRT and Surgery along with Adjuvant Chemotherapy and ARM-B: NACTRT followed by Surgery along with Adjuvant chemotherapy) among locally advanced rectal cancer (LARC) patents of eastern India. **Materials and Methods:** A total of 90 patients of histologically proven LARC from the period of June 2023 to February 2025 were employed in the study. To compensate for attrition, if any, we recruited 45 patients in each group (ARM-A and ARM-B) as per randomization and after getting approval by Institutional Ethical committee. The Eastern Cooperative Oncology Group (ECOG) performance status was noted between 0–1. **Results:** The patients were diagnosed with LARC staged cT3 or cT4. The mean age (years) between the group was comparable. Gender distribution between the group was also comparable. The mean values of pre- and post-chemo CEA were significantly (P<0.001) altered in ARM-A when compared to ARM-B. Pre-chemo TNM and ypTNM distribution between the group were significantly (P<0.001) changed. The comparative analysis indicated significant change (P<0.001) between the group for haematological parameters such as anaemia, thrombocytopenia, lymphopenia and neutropenia. **Conclusion:** In conclusion, NACTRT in LARC patients was related to acceptable toxicities, minimal treatment disruptions and good tolerance. In this study, the toxicity of haematological parameters was significantly reduced NACTRT group.

KEYWORDS

Eastern India, Haematological Parameters, Locally Advanced Rectal Cancer, Neoadjuvant Chemoradiotherapy, Toxicity Reduction

INTRODUCTION

Locally advanced rectal cancer (LARC) is a common disease, and it has poor prognosis because it has high metastatic potential. This meta.analysis showed that Total Neoadjuvant Therapy (TNT) in LARC shows positive improvement in overall pathologic complete response rate compared with standard treatment. TNT is the best treatment strategy for LARC, especially for patients who have little desire for surgery.[1]

The treatment for patients with LARC differs significantly from patients presenting with rectal cancer confined within the mesorectum. Adequate preoperative imaging of the pelvis is therefore important to identify those patients who are candidates for multimodality treatment, including preoperative chemoradiation, intraoperative radiotherapy, and extended surgical resections. This has been shown to reduce morbidity and mortality and improve long-term survival rates.[2]

Moreover, the patients with primary rectal cancer (RC) are present with a tumour which remains confined within the mesorectal fascia. Such patients are treated with total mesorectal excision (TME). Prognosis after TME surgery is excellent. There is a significant reduction in local recurrences when preoperative short-term radiotherapy (5 × 5 Gy) is given one week prior to surgery.[2]

In several phase III trials, the combination of preoperative radiation and chemotherapy based on 5-fluoro-uracil has been shown to increase local control rates in LARC.[3,4] Furthermore, Neoadjuvant chemoradiotherapy (NACTRT) related toxicities were found to be much lower than those of adjuvant chemoradiation (CTRT) [5].

Interestingly, NACTRT followed by TME and postoperative adjuvant chemotherapy has been the standard treatment for patients with LARC worldwide. This method has reduced the local recurrence rate from 35% to 5.10% and has improved the significant rate of survival.[6-9] A recent study emphasized that the therapeutic efficacy by NACTRT in rectal cancer patients was associated with acceptable levels of toxicity and treatment tolerance in north-east part of India.[10]

The present study was evaluated the toxicities on haematological parameters between the two arms (ARM-A: Neoadjuvant chemotherapy followed by NACTRT and Surgery along with Adjuvant Chemotherapy and ARM-B: NACTRT followed by Surgery along with Adjuvant chemotherapy) among rectal cancer patents of eastern India.

MATERIALS AND METHODS

A total of 90 patients of histologically proven LARC from the period of June 2023 to February 2025 were employed in the study. This study was conducted in the Department of Radiotherapy (Radiation Oncology), R. G. Kar Medical College and Hospital, Kolkata, West Bengal – a tertiary care hospital in eastern India. Sample size was enrolled with a total of 90 patients of age group between 18-70 years. To compensate for attrition, if any, we recruited 45 patients in each group (ARM-A and ARM-B) as per randomization and after getting approval by Institutional Ethical committee, R. G. Kar Medical College and Hospital, Kolkata, West Bengal. The Eastern Cooperative Oncology Group (ECOG) performance status was noted between 0–1. The patients were diagnosed with LARC staged cT3 or cT4. The radiation planning for each ARM is as follows:

ARM-A	Radiation: 50 Gy for 5 weeks. Chemotherapy: NACT with mfolfirinox followed by concurrent oral Capecitabine twice daily for 5 days per week. Followed by Surgery followed by ACT with 6 cycles of FOLFOX for 3 months.
ARM-B	Radiation: 50 Gy for 5 weeks. Chemotherapy: Concurrent oral Capecitabine twice daily for 5 days per week followed by surgery followed by adjuvant chemotherapy with FOLFOX 6 Cycles for 3 months.

The study of toxicity on different haematological parameters was assessed in the patients of each ARM separately. Statistical analysis was performed by using SPSS (version, 21). Categorical data were summarized by frequency with their relative percentage. Chi-square test was used to test the association between categorical variables. Continuous data was represented by mean and standard deviation. The independent 'student-t' test was used between the ARM. A P<0.05 was considered statistically significant.

RESULTS

This was a prospective single hospital-based study with a sample size of 90 patients (each arm 45 nos.) employed from the period of June 2023 to February 2025 in tertiary hospital of eastern India. The demographic status and clinicopathological characteristics of patients between the group tabulated in Table 1. The mean age (years) between the group was comparable. Gender distribution between the group was also comparable. The mean values of pre- and post-chemo CEA were significantly (P<0.001) altered in ARM-A when compared to ARM-B. Pre-chemo TNM and ypTNM distribution between the group were significantly (P<0.001) changed.

The toxicity on haematological parameters of patients between the group tabulated in Table 2. The comparative analysis indicated significant change (P<0.001) between the group for haematological parameters such as anaemia, thrombocytopenia, lymphopenia and neutropenia.

Table 1: Demographic Status and Clinicopathological Characteristics Treated with Neoadjuvant Chemoradiotherapy for Rectal Cancer Patients

Characteristics	ARM – A (n = 45)	ARM – B (n = 45)	P value
Age (Years)			
Mean ± SD	46.27 ± 15.33	47.09 ± 16.39	0.80
Gender, n (%)			
Male	25 (55.56)	23 (51.11)	0.67
Female	20 (44.44)	22 (48.89)	
Pre-chemo CEA			
Mean ± SD	8.30 ± 0.29	7.65 ± 0.85	<0.001
Post-chemo CEA			
Mean ± SD	3.20 ± 2.57	6.26 ± 4.09	<0.001
Pre-chemo TNM, n (%)			
T3N0M0	5 (11.11)	22 (48.89)	<0.001
T4N1M0	40 (88.89)	23 (51.11)	
YpTNM, n (%)			
T2N0M0	40(88.89)	23(51.11)	<0.001
T4N1M1	0(0)	7(15.56)	
T4N2M1	5(11.11)	15(33.33)	

Table 2: Toxicity on Haematological Parameters Treated with Neoadjuvant Chemoradiotherapy for Rectal Cancer Patients

Characteristics	ARM – A (n = 45)	ARM – B (n = 45)	P value
Anemia, n (%)			
Absent	0 (0.0)	24 (53.33)	<0.001
Grade 1	30 (66.67)	14 (31.11)	
Grade 2	5 (11.11)	7 (15.56)	
Grade 3	10 (22.22)	0 (0.0)	
Thrombocytopenia, n (%)			
Absent	10 (22.22)	0 (0.0)	0.01
Grade 1	15 (33.33)	22 (48.89)	
Grade 2	15 (33.33)	15 (33.33)	
Grade 3	5 (11.11)	8 (17.78)	
Lymphopenia, n (%)			
Absent	5 (11.11)	0 (0.0)	<0.001
Grade 1	25 (55.56)	7 (15.56)	
Grade 2	10 (22.22)	30 (66.67)	
Grade 3	5 (11.11)	8 (17.78)	
Neutropenia, n (%)			
Absent	0 (0.0)	30 (66.67)	<0.001
Grade 1	35 (77.78)	15 (33.33)	
Grade 2	5 (11.11)	0 (0.0)	
Grade 3	5 (11.11)	0 (0.0)	

DISCUSSION

Mayer et al.[11] reported that patients with colon, rectal, and rectosigmoid cancer who were diagnosed at age <40 years and maximum frequencies (52%) were aged between 35-39 years. According to Waheed et al.,[12] the age group varied from 16-80 years in which most common age group in rectum cancer were between age was 45-64 years constituted of about 48%.

Mayer et al.[11] reported that maximum patients were males of about 52.0%. Abotchie et al.[13] observed maximum males compared to females, who had the prevalence of rectal cancer. Purim et al.[14] also reported the higher incidence of rectal cancer in males compared to females. A contradictory study by Lumpkins et al.[15] revealed that a maximum females (63.0%) had prevalent with colorectal cancer compared to males (37.0%).

Li et al.[16] reported that 4 patients were pathologically diagnosed with stage T2, 22 patients with stage T3, and 10 patients with stage T4, respectively. 11 patients were pathologically diagnosed to have node-negative cancer (stage II), and 25 patients were diagnosed to have node-positive cancer (stage III). Chen et al.[17] observed that ypTNM stage could be an additional accurate factor, which reflected the prognosis and guiding adjuvant therapy of rectal cancer patients who underwent neoadjuvant chemoradiotherapy (nCRT). They also found that a significant association regarding ypTNM stage, which became the most important prognostic factor (HR = 2.704, 95% CI: 1.811-4.038, P<0.001).

Chardalias et al.[18] mentioned that an increasing trend of anaemia due to incidence of colorectal cancer. In another study, Wilson et al.[19] evaluated that anaemia was prevalent of about 66.1% of iron-deficient patients presented colorectal cancer. Kilpatrick et al.[20] studied among 1078 metastatic colorectal cancer (mCRC) patients in the FOLFOX4 study, cumulative incidence of CIT based on platelet count was 37% (grade 3 = 20%; grade 4 = 1.0%) during an average 8 months' follow-up. Teng et al.[21] reported that about 22.6% patients developed thrombocytopenia during concurrent chemoradiotherapy, whereas only 6.3% patients developed 2+ thrombocytopenia. Soyfer et al.[22] studied among 65 patients with sustained lymphopenia in which 52.0% were alive without disease (AWOD), 18.5% alive with disease (AWD) and 29.0% died.

Kim et al.[23] reported that about 55.3% experienced severe chemotherapy-induced neutropenia (CIN). Shitara et al.[24] observed mild neutropenia (grade 1-2) occurred (39.0%) and severe neutropenia (grade 3-4) occurred (30.0%) while the other patients (31%) did not encounter neutropenia. Kilpatrick et al.[20] reported that Neutropenia was absent in 44% of chemotherapy induced thrombocytopenia (CIT) episodes.

CONCLUSION

It is concluded that NACTRT in LARC patients was related to acceptable toxicities, minimal treatment disruptions and good tolerance. In this study, the toxicity of haematological parameters was significantly reduced NACTRT group.

Acknowledgement: Authors convey thanks to the patients and other staff members of the department to coordinate patients and necessary radiodiagnosis.

Conflict of Interest: Authors declare no conflict of interest in this study.

REFERENCES

1. Liu S, Jiang T, Xiao L, Yang S, Liu Q, Gao Y, et al. Total neoadjuvant therapy (TNT) versus standard neoadjuvant chemoradiotherapy for locally advanced rectal cancer: A systematic review and meta-analysis. Oncologist. 2021;26(9):e1555-e1566.
2. de Wilt JH, Vermaas M, Ferenschild FT, Verhoef C. Management of locally advanced primary and recurrent rectal cancer. Clin Colon Rectal Surg. 2007;20(3):255-63.
3. Bosset J, Calais G, Mineur L, Maingon P, Stojanovic-Rundic S, Bensadoun R, et al. Fluorouracil-based adjuvant chemotherapy after preoperative chemoradiotherapy in rectal cancer: long-term results of the EORTC 22921 randomised study. The Lancet. Oncology. 2014;15(2):184-190.
4. Sauer R, Becker H, Hohenberger W, Rödel C, Wittekind C, Fietkau R, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. The New England Journal of Medicine. 2004;351(17):1731-1740.
5. Braendengen M, Tveit KM, Berglund A, Birkemeyer E, Frykholm G, Påhlman L, et al. Randomized phase III study comparing preoperative radiotherapy with chemoradiotherapy in nonresectable rectal cancer. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology. 2008;26(22):3687-3694.
6. Havenga K, Enker WE, Norstein J, Moriya Y, Heald RJ, van Houwelingen HC, et al. Improved survival and local control after total mesorectal excision or D3 lymphadenectomy in the treatment of primary rectal cancer: an international analysis of 1411 patients. Eur J Surg Oncol. 1999;25(4):368-74.
7. Bosset JF, Collette L, Calais G, Mineur L, Maingon P, Radosevic-Jelic L, et al. Chemotherapy with preoperative radiotherapy in rectal cancer. N Engl J Med. 2006;355(11):1114-23.
8. Gérard JP, Conroy T, Bonnetain F, Bouché O, Chapet O, Closon-Dejardin MT, et al. Preoperative radiotherapy with or without concurrent fluorouracil and leucovorin in T3-4 rectal cancers: results of FFCD 9203. J Clin Oncol. 2006 Oct 1;24(28):4620-5.
9. Sebag-Montefiore D, Stephens RJ, Steele R, Monson J, Grieve R, Khanna S, et al. Preoperative radiotherapy versus selective postoperative chemoradiotherapy in patients with rectal cancer (MRC CR07 and NCIC-CTG C016): a multicentre, randomised trial. Lancet. 2009;373(9666):811-20.
10. Penumur M, Chanayil GR, Goswami S, Goswami BC, Paul M, Bora G. Acute toxicities and treatment tolerance of neoadjuvant chemoradiation in rectal cancer: A tertiary cancer centre analysis. Asian Pacific Journal of Cancer Biology. 2024,9(2):163-7.
11. Meyer JE, Narang T, Schnoll-Sussman FH, Pochapin MB, Christos PJ, Sherr DL. Increasing incidence of rectal cancer in patients aged younger than 40 years: an analysis of the surveillance, epidemiology, and end results database. Cancer. 2010;116(18):4354-9.
12. Waheed DA, Wani M, Gadda IR, Mustafa SA. Blood group characteristics in rectal cancer. A study conducted in a tertiary care center, Srinagar, Kashmir, India. Asian Pac J Cancer Care. 2023;8(2):307-10.
13. Abotchie PN, Vernon SW, Du XL. Gender differences in colorectal cancer incidence in the United States, 1975-2006. J Womens Health (Larchmt). 2012;21(4):393-400.
14. Purim O, Gordon N, Brenner B. Cancer of the colon and rectum: potential effects of sex-age interactions on incidence and outcome. Med Sci Monit. 2013;19:203-9.
15. Lumpkins CY, Greiner KA, Daley C, Berkley-Patton J, Hu J, Palla S. An exploratory analysis of the role of religion in colorectal cancer screening among safety-net clinic patients. J Geriatr Med Gerontol. 2019;5(1):058.
16. Li S, Yao W, Liu R, Lu Y, Zhang H, Liang X. Severe lymphopenia as a prognostic factor in rectal cancer patients receiving adjuvant chemoradiotherapy: a retrospective study. Sci Rep. 2023;13(1):7566.
17. Chen Y, Sun J, Dong X, Sun D, Qu Y. Significance of ypTNM stage in determining the prognosis and therapy after surgery for locally advanced rectal cancer. World J Surg Oncol. 2023;21(1):174.

18. Chardalias L, Papaconstantinou I, Gklavas A, Politou M, Theodosopoulos T. Iron deficiency anemia in colorectal cancer patients: Is preoperative intravenous iron infusion indicated? A narrative review of the literature. Cancer Diagn Progn. 2023;3(2):163-8.
19. Wilson MJ, Dekker JWT, Harlaar JJ, Jeekel J, Schipperus M, Zwaginga JJ. The role of preoperative iron deficiency in colorectal cancer patients: prevalence and treatment. Int J Colorectal Dis. 2017;32(11):1617-24.
20. Kilpatrick K, Shaw, JL Jaramillo R, Toler A, Eisen M, Sangaré L, et al. Occurrence and management of thrombocytopenia in metastatic colorectal cancer patients receiving chemotherapy: Secondary analysis of data from prospective clinical trials. Clinical Colorectal Cancer. 2021;20(2):170-6.
21. Teng Y, Ma D, Yan Y, Geng J, Liu Z, Zhu X, et al. Retrospective cohort study for thrombocytopenia during concurrent chemoradiotherapy for rectal cancer. Front Oncol. 2024;13:1289824.
22. Soyfer V, Lugovoy E, Nikolaevski-Berlin A, Korzets Y, Schlocker A, Gutfeld O, et al. The effect of long-standing lymphopenia after radiation therapy on survival in rectal cancer. Surgical Oncology. 2024;56:102119.
23. Kim S, Kang SIL, Kim S, Kim JH. Prognostic implications of chemotherapy-induced neutropenia in stage III colorectal cancer. Journal of Surgical Research. 2021;267:391-6.
24. Shitara K, Matsuo K, Takahari D, Yokota T, Ura T, Muro K. Neutropenia as a prognostic factor in metastatic colorectal cancer patients undergoing chemotherapy with first-line FOLFOX. Journal of Clinical Onchology. 2009;27:4115-4115.