Original research article

Surgical Outcomes in Carcinoma Rectum after Radical Radiation

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Abstract

Background: The most frequent cancer in the world is colorectal cancer (CRC). It is the third most typical cancer in men to be diagnosed. Clinical staging is frequently used to determine when to start neoadjuvant chemotherapy and radiation therapy for rectal cancer (NACRT). Therefore, both for care and prognosis, the correctness of that first staging is crucial.

Methods: Fifteen rectal cancer patients who receive radical radiation (dose escalation in addition to standard neoadjuvant chemoradiation and undergo surgery). Rectal cancer patients who receive dose escalation in addition to standard neoadjuvant chemoradiation (prescribed whole pelvis radiotherapy dose of 50.4 Gy with additional 9 Gy BOOST to GTV Primary with a margin under standard fraction as 1.8 Gy per fraction for 5 days a week for 7 - 8 weeks with concurrent capecitabine during the days of radiation) will be included in the study. After receiving preop treatment, the clinical and radiological response shall be assessed and planned for surgery as indicated.

Results: N=6 patients underwent surgery at 6 weeks after chemoradiotherapy. N=7 patients after 7 weeks and n=2 patients after 8 weeks of chemoradiotherapy. Clinical (POSTNACTRT MRI) down staging of tumor: Stage 2A – 3 pts – all downgraded to stage 1 after NACTRT Stage 3B – 12 pts – 11 patients downgraded to lower stage after NACTRT. In our study, out of 15 patients, 5 patients (33.33%) had a complete pathological response. Rest 10 patients (66.67%) had an incomplete pathological response.

Conclusion: the Neoadjuvant CTRT with dose escalation (Radical RT) in carcinoma rectum patients is Pathological complete response is increased. Downsizing and down staging of tumor clinically (Post NACTRT MRI). Increased sphincter saving surgeries. The toxicity of radiation dose escalation is acceptable and tolerable The latest literature favors towards wait and watch and organ preserving approach after complete clinical response.

Keywords: Rectal cancers, Neoadjuvant CTRT, Radical Radiation Therapy,

Introduction

Colorectal cancer (CRC) is common cancer worldwide. It is the third most commonly diagnosed cancer in males and the second in females, with more than 1.4 million new cancer cases every year. [1] There is a geographical variation in the incidence rates with more than half of the cases of CRC occurring in developed countries. However, mortality is higher in less

developed countries that have limited resources and inadequate health infrastructure. Mortality rates have been decreasing in many Western countries due to a combination of various factors like early detection screening and improved treatment of CRC. [2] The age-standardized rate (ASR) for CRC in India is low at 7.2 per 100,000 population in males and 5.1 per 100,000 population in women. [3] Five-year survival of CRC in India is one of the lowest in the world at less than 40%. Locally advanced carcinoma rectum patients are treated by radical radiation (neoadjuvant chemoradiation including dose escalation) and undergo surgery (TME excision). Numerous studies have demonstrated the benefit of TME, and it is now considered the standard of care for the surgical management of middle and lower third rectal cancers. 20-22 Although some studies have suggested that an adequate TME might in and of itself be sufficient management for T2 and T3 rectal cancers, the majority of the literature still supports the use of adjuvant chemoradiation for stages II and III disease even when combined with TME the issue of pre- versus postoperative adjuvant therapy is a German trial of preoperative versus postoperative chemoradiation with radiation therapy given at 1.8 Gy per fraction and using continuous-infusion 5-FU chemotherapy as a 120-hour infusion, for which results have been reported by R Sauer et al., [4] This study demonstrates an advantage in sphincter preservation with the use of preoperative therapy. In a study by Jillian R et al., [5] Patients with locally advanced rectal cancer (LARC) who achieve complete pathologic response after neoadjuvant chemoradiation experience improved outcomes. Radiation dose escalation has been shown to improve the rates of tumor response.

We conducted a case-control study of patients with LARC who received a standard dose or concomitant boost chemoradiation before surgical resection. Thus, by escalating preoperative radiation dose, the number of patients with good clinical or radiological responses might be eligible for organ-preserving approaches.

Material and methods

This is a cross-sectional interventional study done at MNJ Institute of Oncology and Regional Cancer Centre, Hyderabad, Telangana, a tertiary referral center for the management of cancer patients in the state. The protocol for the study was approved by the Institutional Ethical committee. Written consent was obtained from all the participants of the study after explaining the nature of the study in the local language. Rectal cancer patients who are treated at MNJ Institute of Oncology and Regional Cancer Centre, Hyderabad from May 2020 to November 2021.

Inclusion criteria

1. Histopathology proven adenocarcinoma rectum within 12 cm from the anal verge
2. Locally advanced rectal cancer patients who receive dose escalation in addition
3. to standard neoadjuvant chemoradiation.
4. MRI staged tumor T3 orT4 and any lymph node-positive disease

Exclusion criteria

1. Patients are not fit for anesthesia for surgery
2. Metastatic disease
3. Recurrent rectal cancer

Fifteen rectal cancer patients who receive radical radiation (dose escalation in addition to standard neoadjuvant chemoradiation and undergo surgery). Rectal cancer patients who receive dose escalation in addition to standard neoadjuvant chemoradiation (prescribed whole pelvis

radiotherapy dose of 50.4 Gy with additional 9 Gy BOOST to GTV Primary with a margin under standard fraction as 1.8 Gy per fraction for 5 days a week for 7 - 8 weeks with concurrent capecitabine during the days of radiation) will be included in the study. After receiving preop treatment, the clinical and radiological response shall be assessed and planned for surgery as indicated. Patients were assessed five weeks after surgery regarding the response to treatment either regression or progression of the disease by clinical as well as by radiological methods. The decision for abdominoperineal excision of rectum or low anterior resection was made preoperatively and modified according to the per-operative findings. According to the standardized technique Total mesorectal excision was done. All patients who underwent low anterior resection had a protective ileostomy.

Postoperative Management

The patient leaves the operating room with a nasogastric tube and can have liquids on a postoperative day one. Isotonic intravenous fluids are run at a maintenance rate on POD #0 then decreased to three-quarters maintenance and changed to a dextrose-containing formula on POD #1. The foley catheter is removed on POD #5 to allow for any sympathetic and parasympathetic neuropraxia to resolve. An epidural approach is used for pain control with the addition of parenteral narcotics when needed.

The epidural is typically left in place for 3 days as long as it is functional. Subcutaneous heparin venothrombotic prophylaxis is continued postoperatively. The diet is advanced on POD #3 unless the patient is distended or nauseated. Histopathology will be reviewed and pathological complete response of tumor, organ preservation and complications of surgery shall be evaluated. Data will be collected and analyzed by Excel Stat using appropriate statistical tests.

Results

In this study out of the total n=15 cases of rectal cancers, the age range was from 27 years to 70 years. The mean age of the cases was 49.4 ± 9.5 years. Out of the total cases, the most common age group involved was 51 – 60 years with n=5(33.33%) cases, and n=3(20.0%) cases each in age groups 31 – 40, 41 – 50, and above 60 years. N=1(6.67%) cases were found in the age group below 30 years. In our study, out of n=15 cases, n=11(73.33%) cases were males and n=4(26.67%) were females.

The most common location of the tumor in our study is the mid and lower rectum. Out of fifteen patients, seven patients had tumors involving the mid and lower rectum, three patients had involvement of upper and mid rectum, two patients had involvement of upper, mid, and lower rectum. Only one patient had a tumor involving the lower rectum alone given in figure 1.

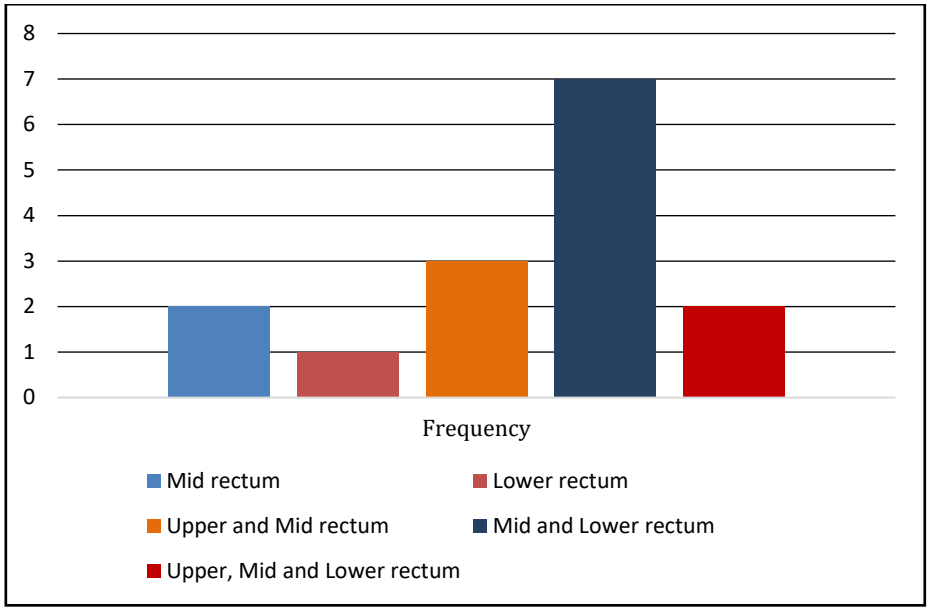

Figure 1: Location of tumors in the cases of the study

In our study, out of n=15 patients, n=6(40%) had a well-differentiated tumor, n=7(46.67%) had a moderately differentiated tumor and in only n=2(13.33%) of them, the tumor was poorly differentiated.

Table 1: Histological type of tumor in the cases of study

Histology type	*Frequency (%)*
Well-differentiated	6 (40%)
Moderately differentiated	7 (47%)
Poorly differentiated	2 (13%)

In the majority of them (n=12 patients) in our study, the clinical stage of the tumor at the time of presentation to our hospital was Stage 3B followed by Stage 2A (n=3 patients) depicted in table 2.

Table 2: Pre-Treatment Clinical Stage of tumors

Clinical stage of tumor	*Frequency (%)*
Stage 1 (T1, T2, N0, M0)	0
Stage 2 A (T3, N0, M0)	3(20%)
Stage 2 B (T4a, N0, M0)	0
Stage 2 C (T4b, N0, M0)	0
Stage 3 A (T1, T2, N1, M0)	0
Stage 3 B (T3, T4, N1, M0)	12(80%)
Stage 3 C (Any T, N2, M0)	0
Stage 4 (Any T, Any N, M1)	0

N=6 patients underwent surgery at 6 weeks after chemoradiotherapy. N=7 patients after 7 weeks and n=2 patients after 8 weeks of chemoradiotherapy. Clinical (POSTNACTRT MRI) downstaging of tumor: Stage 2A – 3 pts – all downgraded to stage 1 after NACTRT Stage 3B – 12 pts – 11 patients downgraded to lower stage after NACTRT. In our study, out of 15 patients, 5 patients (33.33%) had a complete pathological response. Rest 10 patients (66.67%) had an incomplete pathological response.

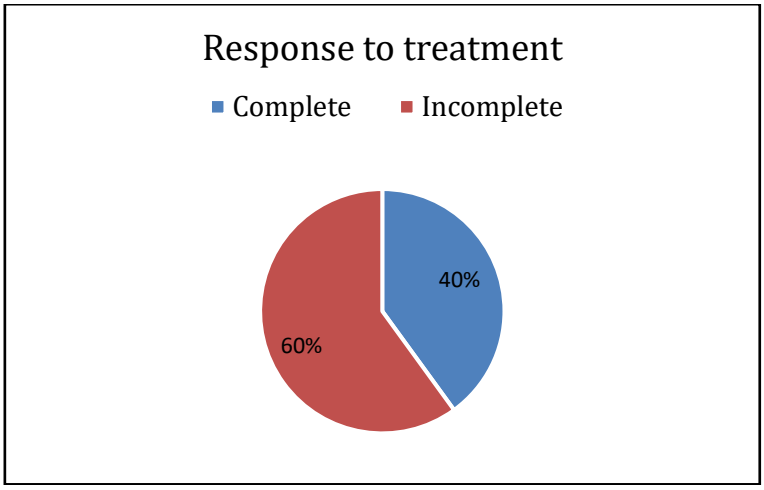

Figure 2: Response based on pathology after treatment

Of the n=15 cases, n= 10 patients were tentatively planned for APR before NACTRT with dose escalation. A sphincter conservation surgery was possible in two of them after neoadjuvant chemoradiotherapy and those patients underwent low anterior resection. Before neoadjuvant chemoradiotherapy, only five low anterior resections were planned. After it, seven anterior resections were done with covering ileostomy to protect the anastomosis as well as to reduce leak-related complications. Finally, abdominoperineal resection APR was performed in n=8(53.33%) patients and Low anterior resection (LAR) in 7(46.67%) patients after Radical RT. The following complications were reported in the case of the study. Anastomosis leakage occurred in n=1 of cases of LAR in which the patient developed fever and elevated WBC counts postoperatively. As patient already had diversion ileostomy and was managed conservatively. Anastomosis stenosis occurred in 1case of LAR, because of which ileostomy couldn't be reversed early and patient was considered for dilatations. Stoma retraction occurred in n=1 of the cases of APR which was refashioned and sutured. In our study, n=2 cases developed pelvic abscess postoperatively and were managed by guided aspiration of abscess and IV antibiotics. In our study, perineal wound complications occurred in n=4 cases out of n=8 patients of APR which was managed conservatively but resulted in prolonged hospital stay and delay in adjuvant chemotherapy. In our study, n=1 patient developed vesicocuteneous fistula which was managed by prolonged foley catheterization. N=1 patient developed urinary retention after removal of foleys on postoperative day 5 which was managed by reinsertion of foleys for 2 weeks. N=10 patients developed sexual dysfunction.

Table 3: Intraoperative and postoperative complications in the cases of study

Complication	*Frequency*	*Percentage*
Intraoperative		
Bleeding	1	20
Postoperative complications		
Anastomosis leakage	1	20
Anastomotic stenosis	1	20
Stoma complications	1	20
Pelvic abscess	2	40
Perineal wound complications	4	26.67
Urological complications	2	13.33
Sexual dysfunctions	10	66.67

Discussion

The role of radiation therapy in the treatment of rectal cancer has evolved over the past several decades. The efficacy and safety of neoadjuvant chemoradiotherapy (NACRT) have been demonstrated by several studies, most of which utilize low doses of radiation from 45–50.4 Gy. Of interest, the impact of radiation dose escalation beyond 50.4 Gy on PCR rates has been examined in a recent meta-analysis of patients treated with doses over 60 Gy which showed increased PCR rates (20%) and acceptable short-term toxicity. Surgical outcomes have been assessed in cases of radiation dose escalation. While the effect of a boost beyond historic doses of 45–50.4 Gy is under current investigation, there remains a gap in the literature delineating effective methods of planning and applying a radiotherapy boost. The mean age of cases with rectal tumors in this study was 49.4 years. Jillian R et al., [5] in a similar study found the mean age 56 years similarly J Zhao et al., [6] found the mean age of detection of rectal tumors was 59 years. Based on the distribution of rectal tumors between males and females in the current we found 73% of cases in males and 27% cases in females. Similarly, Couwenberg et al., [7] found that rectal tumors are most common in males with 75% of all cases. J Zhao et al., [6] found the distribution of 70% in males and 30% in females in their study. Based on the histopathological distribution of cases in the study we found approximately 40% of cases with well-differentiated rectal tumors, 47% with moderately differentiated tumors, and 13% with poorly differentiated tumors. J Zhao et al., [6] in their study reported 22% of cases with well-differentiated tumors, 60% with moderately differentiated tumors, and 18% with poorly differentiated rectal tumors. The pre-NACTRT MRI staging in this study showed 20% of cases in the IIA category and 80% of cases in the IIIB category. Jillian R et al., [5] in their study showed 50% in the IIA category and 44% in the IIIB category. As most studies conducted dose escalation on locally advanced rectal cancer, stages included were II and III in the studies. The interval between NACTRT and surgery in the current study was 7 weeks. Alongi et al., [9] reported the interval between NACTRT and surgery as 8 weeks, and Couwenberg et al., [7] reported the interval as 12 weeks. The post-NACTRT MRI shows downstaging following treatment in 93% of cases of the present study whereas J Zhao et al., [6] in their study showed 86% of cases downstaging following treatment and Jermey T et al., [8] showed 65% of cases downstaging following treatment.

The pathological complete response to treatment in this study was approximately 40%. Vestermark L et al., [10] in their study found pathological complete response in 34% of cases V Picardi et al., found lower pathological complete response in 27.7% of the cases. Different studies have shown variation in pathological complete response because these studies' analyses have several limitations. First, most included data are from retrospective or small single-arm trials. Variation in histopathological response assessment and PCR definition may have affected the overall pooled estimate. Although the reporting quality of treatment details and near-term outcomes within these trials was generally adequate, the short follow-up and significant heterogeneity between cohorts limit the conclusions that can be drawn. But most studies have shown an increase in PCR due to dose escalation. PCR rates are also increased in some studies by prolonging the gap between CTRT and surgery. When compared to other studies we have a lower rate of organ preserving surgeries because we performed only low anterior resection in our study, whereas other studies performed ultra-low anterior resection by doing coloanal anastomosis. Thus, sphincter-saving surgeries are higher in number in other studies. In our study, n=2 patients developed anastomosis-related complications like leakage and stenosis respectively. N=4 out of n=15 patients developed wound-related complications which resulted in prolonged hospital stay and delay in adjuvant chemotherapy. Sexual dysfunction in n=10 patients out of 15, of which n=2 recovered within 3 months of follow-up.

Jermey Tey et al., [8] the surgical complications were about 5% in the dose escalated sample studied. In the study by N. Hearn et al., [11] wound complication rates were 7% and overall surgical morbidity was 15%. The rate of the anastomotic leak also did not seem to be increased with the radiotherapy boost. The limitations of our study are findings could not be generalized as it is a single-institution study with a small sample size and patients have to be evaluated for long-term sequelae.

Conclusion

In our study, the Neoadjuvant CTRT with dose escalation (Radical RT) in carcinoma rectum patients is Pathological complete response is increased. Downsizing and Down staging of tumor clinically (Post NACTRT MRI). Increased sphincter saving surgeries. The toxicity of radiation dose escalation is acceptable and tolerable. The latest literature favors towards wait and watch and organ preserving approach after complete clinical response. If the proportion of good responders can be increased by dose escalation, this strategy could provide an option to increase the number of patients that may benefit from organ preserving strategies in the future.

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