

A Prospective Study on Management of Rectosigmoid Carcinoma with Short Course Radiotherapy Followed By Surgery in a Tertiary Care Institute

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Abstract

Background: The primary management of colorectal malignancy is radical resection of the tumour bearing recto sigmoid area with or without anastomosis. Although radical resection is the main stay of therapy, surgery alone has a high local recurrence rates of 30-50%(1). A multi-disciplinary approach that includes colorectal surgery, medical oncology and radiation oncology is required for optimal treatment of patients with recto sigmoid carcinoma. Rectal adenocarcinomas are sensitive to ionising radiation. Radiation therapy can be delivered preoperatively, intraoperatively or postoperatively and with or without chemotherapy. Main aim of our study is to assess the role of preoperative short course radiotherapy in diagnosed cases of recto sigmoid carcinoma in respect of surgical resectability, histopathologically negative resection margins, increase anal salvage in lower rectal malignant lesions, intra operative blood loss and post operative complications..

Methods: - 50 patients with diagnosed recto sigmoid carcinoma after meeting the inclusion and exclusion criteria were included in our study. All the patients after assessment by Tumour Board were treated with preoperative short course radiotherapy. All the intraoperative and postoperative parameters were analysed and compared to other previous studies for the same.

Results: - Better resectability with negative proximal, distal and circumferential margin with reasonable perioperative blood loss has been achieved. Control of local recurrence has been well achieved only with a few postoperative complication like delayed perineal wound healing and pelvic adhesion.

Conclusions:- Preoperative short course radiotherapy is effective in downsizing the growth and allowing curative resection with negative margins which in turn control local recurrence.

Keywords: - Rectal carcinoma, Short course radiotherapy.

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I. Introduction

Colorectal carcinomas are malignant transformation of epithelial lining of colon and rectum, usually presents late in the course of the disease in our country.

It is the third most common malignant tumour throughout the western world. The American cancer society estimated that in 2017, colorectal cancer accounted for 9% of cancer death in men and 8% of cancer death in women, in the U.S. The 1- and 5- year survival rates for patients with colon and rectal cancer are 83% and 64%, respectively. When colorectal cancers are detected early and localised the 5- year survival rate is 90%. [2]

In India, the incidence rate of colon cancer is 4.3 and 3.4 per 100,000 population for male and female respectively (3). Patients with recto sigmoid carcinoma usually presents with passage of frank blood or blood mixed with mucous with increasing constipation or spurious diarrhoea. [4].

The primary management of colorectal malignancy is radical resection of the tumour bearing recto sigmoid area with or without anastomosis. Although radical resection of recto sigmoid is the main stay of therapy, surgery alone has a high recurrence rates. The local recurrence rate for rectal cancers treated with surgery alone is 30-50 % (1). A multi-disciplinary approach that includes colorectal surgery, medical oncology and radiation oncology is required for optimal treatment of patients with recto sigmoid carcinoma. Rectal adenocarcinomas are sensitive to ionising radiation. Radiation therapy can be delivered pre operatively, intra operatively, or post operatively and with or without chemotherapy.

There are two broad approaches to preoperative pelvic radiation therapy for resectable rectal cancer, one is short-course radiation and another is long course chemo radiotherapy. Although the radiation techniques are similar, the fractionation and timing of surgery differ. In general, short-course radiation delivers 25 Gy (5 Gy in five fractions) of radiation followed by surgery 7-10 days later. Long course chemo radiotherapy delivers 50.4 Gy (1.8 Gy in 28 fractions) of radiation concurrently with chemotherapy, followed by surgery 4 to 8 weeks later (5).

Main aim of our study is to assess the role of preoperative short course radiotherapy in diagnosed cases of recto sigmoid carcinoma in respect of surgical respectability, histopathologically negative resection margins, increase anal salvage in lower rectal malignant lesions, intra operative blood loss and post operative complications..

II. Methods

Study was done at tertiary medical college and hospitals, Kolkata, India, after taking approval from institutional Ethics committee (No/NMC/410, Dated 30.01.2018) and written consent of participants.

50 patients who presents with diagnosed recto sigmoid carcinoma in our tertiary care centre after meeting the inclusion and exclusion criteria were included in the study. All the patients after assessment by Tumour Board in our tertiary care centre were treated with preoperative short course radiotherapy.

Inclusion criteria

All the patients of diagnosed recto sigmoid carcinoma managed in our tertiary care centre were included.

Exclusion criteria

1. Patients with age < 12 years.
2. Pregnant patients
3. Age > 70 years
4. HIV patient.
5. Patients with previous history of pelvic radiation.

Parameters to be studied:

1. Incidence
2. Age at diagnosis
3. Sex ratio
4. Diagnostic procedure
5. Histological type and grade
6. Nodal status
7. Stage [TNM]
8. Prognostic index
9. Neo-Adjuvant therapy
10. Intra operative period and post operative period

Study technique:

All the patients after assessment by Tumour Board in our tertiary care centre were treated with preoperative short course radiotherapy. All the intra operative and post operative various parameters are analysed and compared to other previous studies for the same and previous studies of preoperative long course chemo radiotherapy.

All the selected patients had undergone both clinical and radiological (CECT Scan/CEMRI Scan) assessment for resectability before and 7 days after preoperative Short course Radiotherapy.

Follow up of post operative patients were done for assessment of complications on 3rd, 6th, 12th week and then 6 months.

The data and outcome was analysed and compared using statistical software - MEDCALC SOFTWARE VERSION 16.4.2.0.

III. Results

Table 1: Distribution of our study population according to age & sex at presentation

Age groups in years	Male	Female	Total (%)
20-29	05	01	06 (12%)
30-39	06	02	08 (16%)
40-49	07	04	11 (22%)
50-59	10	04	14 (28%)
60-69	07	03	10 (20%)
>70	01	00	01 (02%)
Total population	36	14	50

The average age of the population in our study was 46.9 years with the youngest patient being of 22 years and the oldest being 70years. The maximum incidence of carcinoma rectum was in the age group of 50-59 years (28%) with male to female ratio of 2.57:1.

Table 2: Duration of presenting symptoms in our study population

Duration	Number of population	Percentage (%)
Less than 3 months	10	20%
3 – 6 months	21	42%
6-12 months	16	32%
More than 12 months	3	6%

Table 3: Distribution of common presenting symptoms in our study population

Presenting symptoms	Number of population	Percentage (%)
Bleeding per anum	45	90%
Altered bowel habits	44	88%
Tenesmus	38	76%
Mucous in Stools	45	90%
Weight loss	32	64%
Perianal or lower abdominal pain	33	66%
Anaemia	36	72%
Melaena	02	04%
Lump in lower abdomen	00	00%
Lower limb edema	00	00%

Table 4: Digital rectal findings of our study population

Location of growth	Number of population (%)	Fixity to surrounding structure	Upper extent of growth palpable	Upper extent of growth not palpable
Lower 1/3	36 (72%)	24	22	14
Middle 1/3	7 (14%)	07	00	07
Upper 1/3	7 (14%)	--	--	--

Most patients presented between 4-8 months after the onset of symptoms and the average duration of symptoms was 7 months with most common presentation being bleeding per anum in the form of fresh blood mixed with stool. On digital rectal examination, two third of the patients presented with fixed rectal growth at lower rectum.

Table 5: Distribution of study population is according to offered primary surgical treatment.

Surgical treatment offered	Number of population (%)	Pathological stage of the specimen			
		I	II	III	IV
Abdominoperineal excision	36 (74%)	00	16	20	00
Anterior excision/low anterior excision	10 (20%)	00	04	06	00
Unresectable	4 (08%)	--	--	--	--

Surgical intervention in the form of abdomino perineal excision and anterior resection was done in 74% and 20% of cases respectively. Four cases were inoperable, and referred for palliative chemotherapy.

Table 6: Distribution of study population is according to microscopic features.

Histopathological Findings	Number of population (%)
Well differentiated adenocarcinoma	13 (28.26%)
Moderately differentiated adenocarcinoma	30 (65%)
Poorly differentiated adenocarcinoma	05 (10.86%)
Signet ring cell adenocarcinoma	02 (4.34%)
Lymphovascular invasion	12 (26.08%)
Perineural invasion	07 (15.21%)
Circumferential margin positivity	02 (4.34%)

Post surgical specimen examination revealed that most of the operable growths were macroscopically ulceroproliferative in nature and microscopically moderately differentiated adenocarcinoma (60%). In one patient signet ring cell was present and another had mucinous component of adenocarcinoma. Lymphovascular invasion was present in 12 cases and perineural invasion was present in 07 cases, whereas both were present in 04 cases. Circumferential margin was positive in 2 cases.

Table 7: Distribution of study population according to Dukes and TNM classification examined specimen.

Dukes stage	Number of population (%)	TNM Stage	Number of population (%)
A	00 (00%)	I	00 (00%)
B	20 (43.47%)	II	20 (43.47%)
C1	07 (15.21%)	IIIA	07 (15.21%)
C2	19 (41.3%)	IIIB	10 (21.73%)
D	00 (00%)	IIIC	09 (19.56%)
Total specimen -46		IV A	00
		IV B	00

Most of the selected population in our study were operated in stage C of Dukes classification (56.51%) and stage III of TNM classification (56.50%).

Table 8: Resectability of the Tumour after preoperative Short course Radiotherapy

Resectability	Number of population (%)
Well demarcated resection plane is possible	28 (56%)
Average resection plane with difficulty	18 (36%)
Unresectable	4 (08%)

Table 9: Distribution of population according to perioperative blood transfusion

perioperative blood transfusion	Number of population (%)
2 units blood transfusion	31 (62%)
More than 2 units of blood transfusion	08 (16%)
Less than 2 units of blood transfusion	07 (14%)

Table 10: Distribution of study population according to post operative complications.

Post operative complications	Number of population (%)
Superficial abdominal wound infection	08 (17.39%)
perineal wound infection	07 (15.21%)
Delayed perineal Wound Healing	08 (17.39%)
Anastomotic leak	00 (00%)
Intestinal Obstruction	04(08.69%)
Genitourinary complication	05 (10.86%)
Pulmonary complication	00 (00%)
Incisional hernia	00 (00%)

In most of the patients resectability enhanced after preoperative Short course Radiotherapy with reasonable perioperative blood loss. Approximately 33.33% of cases developed postoperative complications, which were managed conservatively. Four (8.69%) patients developed postoperative intestinal obstruction, which was managed by reexploration and adhesiolysis. Four patients died within 6 months of primary surgical treatment resulting in mortality rate of about 8.7%.

IV. Discussion

Most of the previous series revealed that carcinoma rectum is commonest in the 6th -7th decade of life. (4, 6).

The average age of the population in our study was 46.9 years with maximum incidence in the age group of 50-59 years (28%).

According to study by Paymaster, male: female ratio for rectal carcinoma in India is 2.9:1(7), while Glen & McSherry recorded a ratio of 1.5:1 (8) which corroborates with our findings of 2.57:1. In one recent study, Liang et al mentioned that gender was not a prognostic factor (9).

In Western country the duration of symptoms prior to presentations is less than 6 months in majority of cases (10), whereas majority of our study population presented between 4 to 8 months after the onset of symptoms and some of the patients presented much later, more than a year. Average duration of symptoms for carcinoma rectum was 7 months.

The study under consideration could not find any relation between duration of symptoms and the age, sex, tumour site, tumour differentiation or the extent of tumour.

The symptoms encountered in this study conform to those found in other studies all over the world. Bleeding per annum was the most common symptom and often associated with alteration of bowel habits. While short duration of bleeding per rectum associated with a better prognosis (11), longer duration of symptoms was associated with anaemia, weight loss and poor nutritional status (12)

Copeland and Ranson , in their study mentioned that increased dietary meat augments the risk of large bowel cancer(13). All the participants of our study were non vegetarian but intake of red meat was not a regular phenomenon.

In our series about 86% of rectal growths were palpable on digital rectal examination which is comparable to series by Zeighler in 1972 (84.2%), Norman.S. Williams (90%) and most of the Indian authors

Macroscopically, 53% had ulcerative growths and 43% had polypoidal growths although combinations of ulceroproliferative lesion were more prevalent. High incidence of ulcerative growths and the relative lower incidence of polypoidal ones were probably a reflection of the late presentation of our study and that also is corroborated by the series of Bhajekar & Jussawalla in Indian population (14, 15)

Microscopically 65% of population had moderately differentiated, 28.26% well differentiated and 10.86% poorly differentiated adenocarcinoma. Lymphovascular invasion was present in 12 cases and perineural invasion was present in 07 cases, whereas both were present in 04 cases. Circumferential margin was positive in 2 cases. According to various literatures, the usual histological variety of colorectal malignancy is moderately differentiated adenocarcinoma. Literature by dukes' et al reported that 56.7% are moderately differentiated, 36.65 are poorly differentiated & 6.7% are well differentiated adenocarcinoma (16). Incidence of poorly differentiated (10.86%) and mucinous tumors (~25%) are similar to various series (17, 18). Lin et al in 2005 mentioned that poorly differentiated and mucinous tumors represent 51% of all tumors in younger population.

In our series Preoperative CEA level was raised in 46% of cases and in most of poorly differentiated tumour, CEA level was more or less normal.

In our series 92%cases of carcinoma rectum radical resection were attempted and even in advanced cases palliative resection done to reduce the tumour burden. Abdomino perineal excision was done in 74% of cases and anterior resection was done in 20% of cases. Four (8%) cases were inoperable and referred for palliative chemotherapy. All curative post surgical patients were treated with adjuvant chemotherapy.

Preoperative short course radiotherapy has been shown to improve local control and survival rate. Neoadjuvant short course radiotherapy is well tolerated and bears no high risk of postoperative morbidity. The growth became well resectable with demarcated plane in 56% cases and in 36% cases resection was done with some difficulty.

62% of patients received only 2 units of blood transfusion which falls within normal limits for our centre. Only in 16% of cases excessive perioperative blood loss occurred and an average of 4 units of blood transfusion needed to stabilize the vitals.

However four (8.69%) patients developed intestinal obstruction in post operative period of abdominoperineal excision which might be due to radiation therapy induced post operative adhesion. Two (4.34%) patients reported local recurrence at 12 months follow up and were sent for palliative chemotherapy.

J Tonac et al reported in their series that incidence of local recurrence after primary radical surgery for carcinoma rectum is about 21 % (19) and Waad Farhat, Houssein Ammar et al mentioned in their recent series in 2019 that recurrence rate is 44.6% at 5 years. The multivariate analysis identified four parameters independently associated with the risk of recurrence after curative surgery: 1. distal margin ≤ 2 cm, 2. extracapsular invasion of lymph node metastasis, 3. tumor stenosis, 4. parietal invasion (20).

Table 11: Previous Landmark studies for short course radiation therapy trials and their results in the form of disease free survival

Study	Treatments	Local recurrence (%)	Disease free survival	Overall survival
Swedish Trial(21) (13 years)	Short course RT	9%	72%	38%
	Observation	26%	62%	30%
	P value	<.001	.04	.008
Dutch Trial(22) 6 Yrs	Short course RT	5.6%	75.4%	64.2
	Observation	10.9%	72.4%	63.5
	P value	<.001	.013	Not significant
Medical Research council CR 07(23) 3yrs	Short course RT	4.4	77.5	80.3
	Selective post operative chemoradiation	10.6	71.5	78.6
	P value	Not significant	.013	Not significant
Polish Trial (24) 4 yrs	Short course RT	15.6	58.4	67.2
	Chemoradiation	10.6	55.6	66.2
	P value	Not significant	Not significant	Not significant
TROG(25)	Short course RT	7.5 % (3 yrs)	Not reported	74% (5 yrs)
	Chemoradiation	4.4	Not reported	70
	P value	Not significant	Not reported	Not significant

There are multiple landmark studies, where results of preoperative short course radiotherapy were compared with observation or chemoradiation and they mentioned that it was significantly better than observation and equivalent to long course chemoradiation.

In respect of local control of disease our study showed that two (4.34%) patients reported local recurrence on 12 months follow up which is comparable to other studies.

In respect to the post operative complications, we found that eight (17.39%) patients had superficial abdominal wound infection, seven (15.21%) patients had perineal wound infection and eight (17.39%) patients had delayed perineal wound healing which was significantly more than normal. We also found that four (8.69%) patients presented with the features of intestinal obstruction which needed relaparotomy and pelvic adhesionolysis. These higher incidences of gross pelvic adhesions might be due to radiation induced tissue inflammation.

V. Conclusion

Preoperative short course radiotherapy is really effective in downsizing and downgrading the disease and allowing curative resection with negative margin.

It is also effective in the control of local recurrence without affecting long term survival. The only drawback of this therapy is that it can cause excessive pelvic and perineal tissue damage leading delayed wound healing and pelvic adhesion.

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