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Comparative Study of Hypofractionated Radiotherapy (39GY/13 fraction) Versus Conventional CCRT (50.4GY/28 fraction) in Inoperable Rectal Cancer

Research Article

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Abstract

Background: Rectal cancer is a major public health problem, being the commonly diagnosed cancer and the leading cause of cancer deaths worldwide. Locally advanced primary and recurrent rectal and rectosigmoid cancers have the potential to produce significant pelvic morbidity including pain, obstruction, tenesmus, etc. To add, many patients are not suitable candidates for surgical resection due to advanced age, comorbidities, etc. In such cases, only palliative measures of different radiotherapy regimens are applied from single doses to treatments lasting several weeks. The objective of this study was to describe the preliminary results of hypofractionated radiotherapy in patients with inoperable rectal cancer.

Methodology: This prospective study was conducted in Department of Radiation Oncology, National Institute of Cancer Research and Hospital, Mohakhali, Dhaka. Total 60 patients were enrolled according to selection criteria. Among them in Arm A there were 30 patients who received conventional CCRT of 50.4Gy in 28 fractions over 6 weeks, 1.8Gy per fraction. In Arm B, there were 30 patients who received hypofractionated radiotherapy schedule of 39Gy in 13 fractions over 17 days, 3Gy per fraction. Then treatment responses, locoregional control of disease and acute toxicities were compared between groups.

Results: In Arm A, mean age of the patients was 45.3±2.9 years and in Arm B, mean age of the patients was 46.0±2.9 years. Male to female ratio was 2.7:1. Response after completion of treatment revealed, those who presented with per rectal bleeding, had no bleeding after treatment. Total 26 (86.66%) patients of Arm A and 25 (83.33%) patients of Arm B had shown partial response, 4 (13.33%) patients from Arm A and 5 (16.66%) patients from Arm B had shown stable disease out of total 30 (100%) patients of each arm. In case of both the arms, rectal discomfort and nephrological toxicity were most prominent.

Conclusion: Hypofractionated radiotherapy schedule of 39Gy in 13 fractions is equally effective, offers satisfactory symptom and disease control in the treatment of inoperable rectal cancer.

Keywords: Rectal cancer; Inoperable carcinoma rectum; Hypofractionated radiotherapy; Conventional CCRT; Advanced age; Palliative care of cancer

Introduction

The term rectal cancer refers to a slowly developing cancer that begins as a tumor or tissue growth on the inner lining of the rectum. If this abnormal growth, known as a polyp, eventually becomes cancerous, it can form a tumor on the wall of the rectum or colon, and subsequently grow into blood vessels or lymph vessels, increasing the chance of metastasis to other anatomical sites. Between 5% and 10% of patients with rectal cancer present with Locally Advanced Rectal Cancer (LARC), and 10% of rectal cancers recur after surgery, of which half are limited to locoregional disease only (locally recurrent rectal cancer) [1]. Obesity, sedentary lifestyle, red meat consumption, alcohol, and tobacco are considered the driving factors behind the growth of rectal cancer [2]. Locally advanced primary and recurrent rectal and rectosigmoid cancers have the potential to produce significant

pelvic morbidity including pain, obstruction, tenesmus, hemorrhage and discharge. Pelvic radiotherapy is used to relieve these symptoms and delay local progression. During the last decade substantial progress has been made in treatment modalities: new and improved radiation techniques (conformal radiotherapy, altered fractionation, brachytherapy), chemotherapy (protracted infusion, use of radiosensitizers).

Many studies have attributed the increased risk of developing rectal cancer to living the "Westernized lifestyle" [2,3]. This term encompasses obesity, sedentary behavior, and a high-meat, high-calorie, fat-rich, fiber-deficient diet, and has been linked to increased colorectal cancer risk [4]. The landmark study that first connected dietary fat to risk of colon carcinogenesis took place in 1969, pioneered by Ernst Wynder and coworkers (1969). They discovered that Japanese individuals of higher Socioeconomic Status (SES) were more likely to develop colon cancer than those who were less affluent, possibly due to their more Westernized diet. It was then first hypothesized that dietary fat, through its influence on bacterial flora, has an effect on colon cancer pathogenesis [5]. Building on this hypothesis, later researchers theorized that high-fat diets promote carcinogenesis by the formation of deoxycholic acid and lithocholic acid. High fat intake stimulates the production of bile acids from the liver, which after contact with anaerobic bacteria in the colon, are dehydrogenated to form these compounds [6].

Treatment for patients with locally advanced and recurrent rectal cancer differs significantly from patients with rectal cancer restricted to the mesorectum. Adequate preoperative imaging of the pelvis is therefore important to identify those patients who are candidates for multimodality treatment, including preoperative chemoradiation protocols, intraoperative radiotherapy, and extended surgical resections [7]. The majority of patients with primary rectal cancer present with a tumor located within the mesorectal fascia, which is generally treated with Total Mesorectal Excision (TME). Results of TME surgery are excellent with a significant reduction in local recurrences when preoperative short-term radiotherapy (5×5Gy) is delivered one week prior to surgery [8]. In about 10% of all rectal cancer patients, the tumor extends into or beyond the enveloping fascia propria of the mesorectal compartment. Often these tumors infiltrate adjacent structures and therefore have a higher risk to develop a local recurrence [9].

Many patients with rectal cancer were not candidates for surgical resection because advanced age, comorbidities, or multiple synchronous metastases. In this scenario only comfort measures or different radiotherapy regimens are applied, from single doses to treatments lasting several weeks. Among that conventional CCRT 50.4Gy in 28 fractions with 5FU is most commonly used radiotherapy schedule. It is obvious that radiotherapy can reduce the distressing symptoms of patients as well as local control of tumour. However, shorter course of radiotherapy with a high biological effective dose would be more appropriate, assuming it offered satisfactory symptom and disease control. Recently, hypofractionated radiotherapy schedule of 39Gy in 13 fractions is used for treatment of inoperable rectal cancer. Hypofractionated radiation therapy involves the use of high doses per fraction to achieve improved tumour control. The study done in U.S. National Library of Medicine Clinical Trials.gov identifier: NCT03853733 hypofractionated therapy (39Gy in 13 Fractions) in patients with Advanced Inoperable rectal cancer is well tolerated and can provide excellent symptom and local control with acceptable toxicity as well as significantly less on treatment time. Therefore, aim of this study was to evaluate the preliminary results of hypofractionated radiotherapy in patients with inoperable rectal cancer.

Materials and Methods

This quasi-experimental study took place during January 2020 to December 2020. The study population comprised of patients suffering from rectal cancer who were not eligible for surgical resection, due to reasons like advanced age, comorbidities in locally advanced carcinoma of rectum (stage II-III) at the time of diagnosis, admitted in the department of Radiation Oncology of National Institute of Cancer Research and Hospital, Mohakhali, Dhaka. Purposive method of sampling was used. Samples were selected through inclusion and exclusion method from the patients of non-operable carcinoma rectum. Those who gave informed written consent were finally enrolled in the study. The following standard formula was used in determining sample size: For determination of sample size following formula will be applied:

$$n = \frac{p1(1-p1)+p2\,(1-p2)}{(P1-P2)2} x\ (Z\alpha + Z\beta)2$$

P1 = Proportion of patients developing outcome in one arm.

P2 = Proportion of patients developing outcome in another arm.

Zα = Z-value (two tail) at a definite level of significance e.g., 1.96 at 5% level of

significance.

Zβ = Z-value (one tail) at a definite power e.g 1.64 at 95% power.

(Haque Mozammel. ABC of research methodology and biostatistics 1st edn. 2009: 225.)

Here

P1 = 50% (0.5)

P2 = 80% (0.8)

Zα = 1.96

Zβ = 1.64

n = Sample size

$$n = \frac{(0.5\ x\ 0.5) + (0.8x0.2)}{(0.5 - 0.8\ )2} x\ (1.96 + 1.64)2 = 60$$

(Satar et al.2017)

By using this formula, the sample size was calculated as 60. So, total of 60 patients were included in this study, distributed in two arms (A and B), 30 patients in each arm. Total sample size was 60, distributed in 2 arms, Arm A and Arm B, each consisted of 30 patients. Arm A had those who received conventional CCRT of 50.4Gy in 28 fractions over 6 weeks, 1.8Gy per fraction with tablet Capecitabine 825mg/m2 per day in BID on the day of radiotherapy. Radiotherapy was given in 2D technique. In Arm B, there were 30 patients who received hypofractionated radiotherapy schedule of 39Gy in 13 fractions over 17 days, 3Gy per fraction.

Specific management

Arm A (30 Patients)	Arm B (30 Patients)
Tumor dose: 5040 cGy	Tumor dose: 3900 cGy
Number of fractions: 28	Number of fractions: 13
Dose per fraction: 180 cGy	Dose per fraction: 300 cGy
Number of fractions per week: 5	Number of fractions per week: 5
Duration: 6 weeks	Duration: 17 days
Number of fields: 2	Number of fields: 2

Inclusion criteria

a. Patients with rectal cancer who were not candidates for surgical resection due to advanced age, comorbidities at the time of diagnosis.

b. Histologically proved carcinoma of rectum.

c. Patients planned for treated with radiotherapy.

d. Stage IIA, IIB, IIIA, IIIB temporary inoperable.

Exclusion Criteria

a. Patients with also other than carcinoma of rectum.

b. Patients with <18 years old >75 years.

c. Patients with distant metastases.

d. Patients with history of prior chemotherapy or radiotherapy.

e. Prisoners.

f. Pregnant and lactating women.

A pre tested semi-structured questionnaire was used for data collection. The questionnaire contained questions related to:

i. socio-demographic and

ii. clinical characteristics and other relevant information. The questionnaire was then pretested on 6 respondents with similar types of background who were not included in the study sample. Then the questionnaire was finalized after necessary corrections. Data was collected by face-to-face interview with the patients. Data were entered, compiled and analyzed using SPSS version 22.

Treatment Planning

Treatment by radiotherapy

The purpose of radiotherapy treatment was to kill the tumor cells with ionizing radiation sparing the surrounding healthy tissues as much as possible. External beam irradiation was used to treat the whole pelvis.

Definition of target volume

The target volume encompassed the primary tumor, adjacent lymph nodes and the presacral region.

Simulation

During EBRT, all patients were simulated accordingly using conventional simulator. Patients were supine, arms above chest, knee and lower leg immobilization to prevent pelvic rotation, and aligned using orthogonal laser beams with anterior and lateral markings using markers. Palpation of primary tumor was carried out in treatment position and a radio-opaque marker was placed on the anal verge and Digital Rectal Examination (DRE) was performed to determine the distance from the anal verge marker to the inferior edge of the tumor. A comfortably full bladder protocol was used for planning and treatment as this displaces small bowel superiorly.

Treatment field

All patients received pelvic radiotherapy through 2 fields (anterior to posterior and posterior to anterior pelvis). The fields were marked by marker pen. After marking by lead wire, the fields were then verified by images before radiotherapy, if needed.

Boundary of 2D radiotherapy planning field

a. Superior border: Sacral promontory, L5/S1 border as defined on lateral sagittal view.

b. Inferior border: 3cm below the inferior edge of the tumor. For lower third tumors, the border should lie below the anal marker to cover the perineum.

c. Lateral border: 1-2cm lateral to widest true bony pelvic diameter.

Beam energy

A Cobalt 60 teletherapy with SSD of 80/100cm.

Medical and supportive care

Patients were managed symptomatically with antibiotics, steroid, analgesics, antiemetic, vitamins, blood transfusion if hemoglobin percentage below 10gm/dl, intravenous fluid infusion, skin cares and others according to their need throughout the treatment period.

Assessment during treatment

During radiotherapy patient was assessed to see the treatment response and toxicities. Duration of treatment was measured from the first day of treatment to the last day of follow-up. Response was observed by RESIST criteria & toxicities observed by RTOG acute radiation morbidity criteria. Collected data was checked regularly important table & graph was prepared. Appropriate statistical test was applied in the study where necessary. Follow up examinations were clinical examination and laboratory tests if needed.

Response criteria includes

a. Relief of signs & symptoms and reduction of tumor size: Pain in the pelvis, urinary and rectal symptoms, anaemia and loss of appetite - these major complaints were taken as parameters of symptoms. Symptomatic response was assessed 2-week interval after radiotherapy according to RECIST criteria.

b. Toxicity Reporting: To assess toxicity, Toxicity criteria of the Radiation

Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC) 1995 was used to score all acute toxicities. (Table 1) below illustrates categorically staging of rectal cancer with Tumor Lymph Nodes and Metastasis (TNM) staging and their description. (Table 2) shows WHO guideline of responses as per Response Evaluation Criteria in Solid Tumors (RECIST) criteria. These are included for better vision.

Table 1: Rectal Cancer Staging.

AJCC Stage	TNM Stage	Description
0	Tis N0 M0	Tumor is confined to mucosa
I	T1 N0 M0	Tumor invades submucosa
I	T2 N0 M0	Tumor invades muscularis propria
IIA	T3 N0 M0	Tumor invades subserosa or beyond, no other organs involved
IIB	T4 N0 M0	Tumor invades adjacent organs or perforates visceral peritoneum
IIIA	T1-2 N1 M0	Metastasis to 1-3 regional lymph nodes with tumor invasion of submucosa and/or
IIIB	T3-4 N1 M0	Metastasis to 1-3 regional lymph nodes with tumor invasion of subserosa or adjacent organs
IIIC	Any T, N2 M0	Metastasis to 4 or more lymph nodes

IV	Any T, any N, M1	Metastasis to distant organs

Abbreviations: AJCC: American Joint Committee on Cancer; Tis: Tumor (carcinoma) in situ.

Table 2: WHO Guideline of Responses (RECIST Criteria).

Responses	Description
Complete Response (CR)	Disappearance of all known diseases, confirmed at ≥ 4 weeks.
Partial Response (PR)	≥ 50% decrease (length) from baseline, confirmed at ≥ 4 weeks.
Progressive disease (PD)	≥ 25% increase (length) in one or more lesions or appearance of new lesions
Stable disease (SD)	Neither PR nor PD criteria met

*RECIST = Response Evaluation Criteria in Solid Tumors.

Operational Definition

Rectal cancer

Rectal cancers are defined as the cancers that arise from the lining epithelium of rectum. Approximately ninety five percent of rectal cancers are adenocarcinoma. Other histological types include squamous cell carcinoma, melanoma, small-cell carcinoma, carcinoid, sarcoma, and lymphoma.

Locally advanced cancer

Cancer that has spread from where it started to nearby tissue or lymph nodes but has not spread from the original (primary) tumor to distant organs or distant lymph nodes (NCI Dictionary of cancer terms).

Locally advanced rectal cancer

a. Tumor invasion through the mucosa, sub mucosa, muscularis propria, serosa and other colorectal segments by way of the serosa (T1-4).

b. Any deep tumor invasion with or without metastasis to regional lymph node(s).

c. No distant metastasis.

Inoperable Rectal Cancer

The patient is physiologically incapable of resection due to age and mental illness, cardiac status, pulmonary status.

Determinants of Operability

a. Age and mental illness per se are not factors in deciding operability. Elderly patients, arbitrarily defined as individuals more than 70 years of age, experience the same degree of benefit from therapy as younger patients provided that they have adequate nutritional and PS.

b. Cardiac status. The presence of uncontrolled cardiac failure, uncontrolled arrhythmia, or a recent myocardial infraction (within 6 months) makes the patient inoperable.

c. The presence of pulmonary hypertension or inadequate pulmonary reserve makes the patients inoperable.

Results

(Table 3-6)

Table 3: Socio-Demographic Characteristics of the Respondents (n=60).

Characteristics	Arm A		Arm B	
Age (years)	**Frequency**	**Percentage**	**Frequency**	**Percentage**
20-29	0	0	0	0
30-39	2	6.6	1	3.3
40-49	10	33.3	13	43.3
50-59	8	26.6	9	30
60-69	9	30	7	23.3
>70	1	3.3	0	0
Range	32-72		30-64	
Mean ± SD	45.3±9.2		46.0±9.4	
Gender				
Male	19	63.3	22	73.3
Female	11	36.7	8	26.7
Area of residence				
Rural	11	36.6	13	43.3
Urban	19	63.3	17	56.6

*SD = Standard Deviation.

(Table 3) demonstrates the socio-demographic characteristics of the patients. In terms of age, for Arm A, highest number, 10 (33.3%), of participants belonged to age group 40-49 years, followed by 9 (30.0%) in group 60-69 years. Mean age was 45.3±9.2 years. For Arm B, maximum respondents, 13 (43.3%) belonged to same group, i.e., 40-49 years, second being 50-59 years group, which had 9 (30.0%) cases. Mean age was 46.0±9.4. Regarding gender, both Arm A and B contained majority males, i.e., 19 (63.3%) and 22 (73.3%) respectively. In concern to area of residence, there was similarity as well in both arms, i.e., for A and B, maximum patients, meaning 19 (63.3%) and 17 (56.6%) hailed from urban areas respectively.

Table 4: Response of Patients According to Signs and Symptoms (at final week of Radiotherapy) (n=60).

Signs/Symptoms n=30 (each arm)	Pre-Treatment n (%)	Post-Treatment n (%)	Response n (%)	Chi-Square	P-Value
Per-rectal bleeding					
Arm A	19 (63.3)	0 (0.0)	19 (100)	0.0053	0.942*
Arm B	22 (73.3)	0 (0.0)	22 (100)		
Altered bowel habit					
Arm A	25 (83.3)	7 (23.3)	18 (72)	0.775	0.678*
Arm B	28 (93.3)	5 (16.7)	23 (82.1)		
Pelvic pain					
Arm A	14 (46.7)	2 (6.6)	12 (85.7)	0.649	0.772*
Arm B	11 (36.7)	3 (10.0)	8 (72.7)		
Dysuria					
Arm A	6 (20)	2 (6.6)	4 (66.6)	0.41	0.155*
Arm B	7 (23.3)	0 (0.0)	7 (100.0)		
Loss of appetite					
Arm A	19 (63.3)	12 (40.0)	7 (36.8)	0.0057	0.106*
Arm B	18 (60.0)	10 (33.3)	8 (44.4)		
Anaemia					
Arm A	21 (70.0)	9 (30.0)	12 (57.1)	2.603	0.106*
Arm B	23 (76.6)	3 (10.0)	20 (86.9)		

*Fishers Exact Test.

(Table 4) illustrates the response of patients as per their signs and symptoms at the final week of radiotherapy. It is seen that, those who presented with per rectal bleeding, had no bleeding after treatment. Few patients had persistent symptoms of altered bowel habit. Some of the patients had pelvic pain, dysuria, anaemia and loss of appetite even after completion of treatment. Chi square test did not reveal any significant association in any of the domains between the two groups of patients.

Table 5: Response Evaluation through Clinical Examination and Investigations After Completion of Treatment (n=60).

Findings n=30 (each arm)	Partial Response (PR) n (%)	Stable Disease (SD) n (%)	Chi-Square	P-Value
DRE findings				
Arm A	26 (86.66)	4 (13.33)	0.48	0.488*
Arm B	24 (80.0)	6 (20.0)		
Proctoscopy findings				
Arm A	26 (86.66)	4 (13.33)	0.13	0.717*
Arm B	25 (83.33)	5 (16.66)		
Per-Abdominal findings				
Arm A	26 (86.66)	4 (13.33)	0.13	0.717*
Arm B	25 (83.33)	5 (16.66)		
Imaging findings				
Arm A	26 (86.66)	4 (13.33)	0.13	0.717*
Arm B	25 (83.33)	5 (16.66)		

*Fisher's Exact Test.

(Table 5) shows the response of patients according to clinical examination findings and investigations completion of total treatment including radiotherapy and surgery. Total 26 (86.66%) patients of Arm A and 25 (83.33%) patients of Arm B had shown partial response, 4 (13.33%) patients from Arm A and 5 (16.66%) patients from Arm B had shown stable disease out of total 30 (100%) patients of each arm. Chi square tests were done and no significant association was found among the both arms.

Table 6: Distribution of Patients According to Toxicity (n=60).

Toxicities	Treatment Arms (Total 30)		Chi-Square	P-Value
	Arm A	Arm B		
	n (%)	n (%)		
Skin reaction				
Grade 0	6 (20.0)	7 (23.33)	0.392	0.821*
Grade I	16 (53.33)	17 (56.66)		
Grade II	8 (26.66)	6 (20.0)		
Vaginal mucositis				
Grade 0	4 (13.33)	10 (33.33)	0.618	0.1734*
Grade I	21 (70.0)	17 (56.66)		
Grade II	5 (16.66)	3 (10.0)		
Bladder toxicity				
Grade 0	5 (16.66)	9 (30.0)	0.278	0.507*
Grade I	17 (56.66)	15 (50.0)		
Grade II	8 (26.33)	6 (20.0)		
Small gut toxicity				
Grade 0	12 (40.0)	13 (43.33)	0.342	0.842*
Grade I	9 (30.0)	7 (23.33)		
Grade II	9 (30.0)	10 (33.33)		
Rectal discomfort				
Grade 0	5 (16.66)	8 (26.66)	0.801	0.439*
Grade 1	14 (46.66)	12 (40.0)		
Grade II	11 (36.66)	10 (33.33)		
Nephrological toxicity				
Grade 0	24 (80.0)	26 (86.66)	0.274	0.667*
Grade I	4 (13.33)	3 (10.0)		
Grade II	2 (6.66)	1 (3.33)		

*Fisher's Exact Test.

(Table 6) illustrates distribution of the patients according to toxicity. In case of both the arms, rectal discomfort and nephrological toxicity were most prominent. After that, in arm A and B bladder toxicity (Grade I) and skin reaction (Grade I) were also seen respectively. Chi square tests were conducted to see the associations of the toxicities between both then arms. None of them were statistically significant.

Discussion

In this study, regarding arm A, maximum number of patients (33.3%) were in the age group 40-49 years, mean age of the patient was 45.3±9.2 years. In arm B, maximum numbers (43.3%) were found in the age group of 40-49 years. Mean age of the patients was 46.0±9.4 years. Most of the patients were of male gender and resided in urban areas. Previous study reported that, a population of those over 65 years old were about three times more likely to be diagnosed with rectal cancer than those 50-64 years old, and about 30 times more likely to be diagnosed than those 25-49 years old [2]. Researchers believe, this may be a reflection of a more sedentary lifestyle, hence they recommended lowering the screening age to 45 years in order to detect cases in younger adults early [10]. Cancers of the colon and rectum are among the most common and deadly neoplasms, and their global incidence and mortality are likely to increase in the coming decades. In 2018, nearly 2 million diagnoses and 1 million deaths are expected due to this neoplasm [2]. The incidence of rectal cancer has been exacerbated by the proliferation of poor diet and sedentary lifestyle in developed nations. However, successes in treatment and early diagnosis have enabled a reduction in mortality from the disease.

The findings revealed, those who presented with per rectal bleeding, had no bleeding after treatment. Few patients had persistent symptoms of altered bowel habit. Response after completion of treatment revealed, total 26 (86.66%) patients of Arm A and 25 (83.33%) patients of Arm B had shown partial response, 4 (13.33%) patients from Arm A and 5 (16.66%) patients from Arm B had shown stable disease out of total 30 (100%) patients of each arm. Multimodality therapy is often used for tumor downstaging or downsizing, anal sphincter, or other organ preservation, as well as improvements in Local Control (LC) or even Overall Survival (OS). Preoperative Chemoradiotherapy (CRT) has been shown comparable or superior to postoperative treatment in terms of various end points, and preoperative radiation dose and time interval are significant predictors of the pathological complete response (pCR) rate and downstaging [11]. However, different viewpoints exist regarding the optimal dose–time fractionation schedule of Preoperative Radiotherapy (RT) and time to surgery. In 2017, the Stockholm III trial used three regimens: either short-course RT (5×5Gy) with surgery within 1 week or after 4-8weeks or 25×2Gy with surgery after 4-8weeks [12]. No significant differences in local and distant recurrences or in RFS and OS were reported among the three different RT regimens. A hypofractionated RT schedule (30Gy in 10 once-daily fractions) was tested in China to minimize side effects without compromising therapeutic efficacy [13].

After a median follow up of 63.8 months, 5-year DFS and OS rates were 64.5% and 75.6% respectively. Moreover, grade ≥ 3 acute toxicity

rates was only 1.2%, and the total grade ≥ 3 late RT toxicity rate was down to 2.7% [14]. In order to verify the hypothesis that hyperfractionated radiotherapy may provide a favorable long-term outcome compared to conventional RT, the pelvis was irradiated twice daily, with a minimal interfraction interval of 6h, and a total dose of 39-42Gy was administered in doses of 1.5Gy per fraction [15]. The results showed that the physical, emotional, and social functioning of long-term survivors were significantly better with hyperfractionated radiotherapy; however, there was no significant difference regarding toxicities. Result of another study shows sphincter-saving rate (89.5% vs. 94.3%, short-course RT vs. long-course RT), pathologic complete remission (21.1% vs. 13.2%), downstaging (47.4% vs. 26.4%), and treatment complications including anastomotic site leakage, bowel adhesion, and hematologic toxicity associated with short-course RT were not significantly different from those associated with long-course RT (Mi et al., 2017). Furthermore, many trials demonstrated that there were no significant differences in severe late toxicity and quality of life between short-course RT, and conventionally fractionated CRT [12].

In this study, frequency of common toxicities were seen. In case of both the arms, rectal discomfort and nephrological toxicity were most prominent. After that, in arm A and B bladder toxicity (Grade I) and skin reaction (Grade I) were also seen respectively. Chi square tests were conducted to see the associations of the toxicities between both then arms. None of them were statistically significant. Previous study noted that preoperative RT can induce serious side effects such as diarrhea, urinary tract infection, sexual dysfunction, and secondary malignancies [15-17]. Meanwhile, toxicities and complications related to RT have also increased with the greater dose of RT [18,19].

Conclusion

This study showed that hypofractionated radiotherapy schedule was equally effective, more appropriate, offered satisfactory symptom and disease control to conventional fractions of radiotherapy in the treatment of inoperable rectal cancer. It was found that overall outcome, locoregional control and imaging findings were almost similar in both technique of treatment. Although conventionally fractionated chemoradiotherapy has been adopted as a standard treatment for patients with inoperable rectal cancer, hypofractionated radiotherapy improved local control and reduced treatment-associated toxicity.

Limitations

This single-center study had several limitations. The time period was narrow. Sample size was also very short. All relevant investigations could not be performed due to financial constraints. Lastly, sampling technique was purposive so there could be selection bias.

Recommendations

Use of hypo fractionated radiotherapy schedule of 39Gy in 13 fractions over 17 days, 3Gy per fraction may be recommended. Longer duration of study to see the late toxicities of treatment and analyze five -year survival could be done. Awareness of the community & physicians towards treatment at different steps may bring changes in treatment outcome of rectal cancer. Further in-depth and large-scale prospective study is required in our country in this field.

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