Clinical and dosimetric comparison of acute bowel toxicities in carcinoma rectum patients receiving neoadjuvant chemoradiotherapy by using standard 3DCRT VS IMRT

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Abstract—Introduction: Colorectal cancer (CRC) is a 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. Around 40,000 people will be effected by rectal cancer for every year, with a 65% survival rate from past 5-year were estimated. 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 populations in women. However overall incidence and survival rates were increased due to the screening and early detection. Materials and Methods: The proposed study is a prospective, hospital based, comparative cohort study including the cases admitted to Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad, Telangana with clinical features and investigations suggestive of carcinoma rectum and fulfilling the inclusion criteria will be taken up for study. Patients considered as per inclusion criteria admitted in Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad, Telangana were selected and the dosimetric data was collected from the TPS planning.
system and clinically relevant data was collected from the patient’s record from hospital digital interface system. The data regarding the acute toxicities was collected during the patient’s visit to OPD during treatment and follow-up. The assessment was done by RTOG guidelines. Results: According to the sample size derived, each group of treatment technique was recruited with equal number of subjects i.e. 36 subjects into each group of treatment. The mean ± SD of mean dose distribution (D2%) of cases in 3DCRT group and IMRT group were 51.23 ± 2.86 and 52.2 ± 1.89 respectively. The mean dose distribution (D50%) of cases in 3DCRT group and IMRT group were 50.19 ± 3.67 and 50.3 ± 0.21 respectively. The mean dose distribution (D98%) of cases in 3DCRT group and IMRT group were 46.71 ± 2.31 and 48.15 ± 1.09 respectively. The mean ± SD of mean planning target volume (PTV) of cases in 3DCRT group and IMRT group were 47.73 ± 1.04 and 48.03 ± 0.88 respectively. The minimum – maximum dose range in 3DCRT and IMRT groups were 43.96 – 49.8 and 45.98 – 49.8 respectively. Conclusion: We can conclude that in the neoadjuvant treatment of rectal cancer with concurrent chemoradiation, advanced radiotherapy techniques like IMRT are better than 3DCRT both in dose homogeneity of target volume as well as dose sparing of the OARs. This clinically impacts on better tumor control, reduced treatment toxicity and a better quality of life.

**Keywords**---Colorectal cancer, TPS planning system, neoadjuvant, chemoradiation.

**Introduction**

Colorectal cancer (CRC) is a 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. Around 40,000 people will be effected by rectal cancer for every year, with a 65% survival rate from past 5-year were estimated. 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 populations in women. However overall incidence and survival rates were increased due to the screening and early detection.\(^1\)

Preoperative radiotherapy alone or in combination with chemotherapy (ChT), is the widely used standard therapy in patients with extra-peritoneal locally advanced rectal cancer (LARC) \(^2\). Neoadjuvant long-course chemoradiation is the gold standard for locally advanced rectal cancer, followed by surgical resection and adjuvant chemotherapy, which was shown to decrease the risk of loco-regional recurrence. Pre-operative chemoradiation compared to post-operative chemoradiation is associated with improved local control and reduced toxicity \(^3\).

Intensity-modulated radiation therapy (IMRT) has the capability to improve dose distributions to nearby dose-limiting structures having more benefits in the management of rectal cancer with a recent study showing a reduction in gastrointestinal toxicity. It may help to reduce the dose to bowel, bone marrow as
well as bladder and however reduces the side effects to associated organs like cervix, prostate, and anal cancers. In case of carcinoma of the cervix, pelvic IMRT is allowed sparing of pelvic bone marrow and which was associated with lower toxicity rates and favourable outcomes compared to standard radiation therapy (4). Additionally, for prostate cancer patients treated with androgen deprivation therapy, IMRT significantly reduced acute and late GI toxicities compared to 3DCRT. For anal canal carcinoma, IMRT appeared comparable to 3DCRT with regard to local control and survival while decreasing dermatologic, GI, and hematological toxicities and associated treatment breaks.

Various researchers have studied that the dose-volume relationship between the amount of small bowel receiving low and intermediate doses of radiation and the rates of severe diarrhoea. They found that a strong dose–volume relationship existed for the development of Grade 3 acute small bowel toxicity in patients receiving preoperative radiochemotherapy. Therefore, there has been great interest in the application of highly conformal treatment approaches, such as IMRT and VMAT, for producing highly conformal dose distributions in the target volumes and minimizing the dose to OARs. Several planning studies have done for the LARC by using different treatment approaches, such as proton therapy, VMAT, IMRT and 3DCRT (5).

Neoadjuvant chemoradiotherapy (NCRT), followed by surgery and adjuvant chemotherapy (ChT) is recommended as the standard for care of patients whomever affected by locally advanced rectal cancer (LARC). While this approach has improved local control, survival remains poor due to distant metastases, which is the major leading cause of death among these patients. The role of adjuvant ChT in the treatment of LARC remains unclear. However adjuvant ChT is may be often associated with least chance of getting tolerance and compliance, but must be modify the reduction in dose, and delays in beginning adjuvant treatment due to postoperative complication (6).

**Materials and Methods**

**Study Area:** The proposed study is a prospective, hospital based, comparative cohort study including the cases admitted to Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad, Telangana with clinical features and investigations suggestive of carcinoma rectum and fulfilling the inclusion criteria will be taken up for study.

**Study Population:** Patients belonging to both the sexes and belonging to age group of 18 years and older admitted to Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad, Telangana

**Study Design:** This study will be a prospective, hospital based comparative cohort study.

**Study Duration:** The study period is one year (i.e. from July 2020 to June 2021)

**Sample Size:** The mean PTV D50% in IMRT group was 52±0.4 while in 3DCRT group it was found that 52.3±0.5 from the previous published study (45).

Where,

\[ Z_{a/2} = 1.96 \] is the critical value of the Normal distribution at \( a/2 \) (with confidence level of 95%, \( a \) is 0.05).
$Z_\beta = 0.842$ is the critical value of the Normal distribution at $\beta$ (power of the test is 80%, $\beta=0.20$).

$\sigma^2 = 0.205$ is the estimated population variance based on the previous study.

d = 0.3 is the expected difference between the means.

Thus the sample size will be:

$$n = \frac{\left( Z_{\alpha/2} + Z_\beta \right)^2 \times 2 \times \sigma^2}{d^2}$$

$$n = \frac{(1.96 + 0.842)^2 \times 2 \times 0.205}{(0.3)^2} \approx 35.766 \approx 36$$

The minimum required sample per group is 36 per technique of treatment. Hence, 72 subjects were recruited for the study for both treatment techniques.

**Inclusion Criteria:**
1. Adult patient aged 18 or above.
2. Patient belonging to both sexes.
3. Willing to give informed consent.
4. Histologically proven Adenocarcinoma of Rectum
5. ECOG Performance status 0-1
6. Neoadjuvant Chemoradiation
7. Patients who are willing to give informed consent
8. Patients having non-metastatic disease

**Exclusion Criteria:**
1. Patients <18 yrs old.
2. ECOG Performance status 2 or more
3. Patient with known medical conditions placing them at risk of high gastrointestinal toxicity
4. Patients who has undergone multiple abdominal surgeries
5. Patients who have recurrence
6. Patients with previous history of pelvic radiation
7. Presence of any fistula
8. Metastatic Carcinoma Rectum

**Method of collection of data**

*Ethical clearance:* The ethical clearance will be obtained from Ethics and Research Committee.

*Informed Consent:* Patients will be screened for the eligibility and those fulfilling the selection criteria and their caretakers will be briefed about the nature of the study. The patients/caregivers expressing their willingness to participate in the study will be enrolled after obtaining a written informed consent.

*Data collection:* Patients considered as per inclusion criteria admitted in Basavataramak Indo American Cancer Hospital and Research Institute, Hyderabad, Telangana were selected and the dosimetric data was collected from the TPS planning system and clinically relevant data was collected from the patient’s record from hospital digital interface system. The data regarding the
acute toxicities was collected during the patient's visit to OPD during treatment and follow-up. The assessment was done by RTOG guidelines.

*Study Procedures:* All Patients with Rectal cancer were screened as per above inclusion and exclusion criteria. Then they were planned for Radiation. Patients eligible were counseled in detail about their treatment protocol and after taking the informed consent were included for dosimetric evaluation.

**Procedure for Radiation planning**

All the patients were simulated as per the departmental protocol i.e. CT simulation in supine position with hands on the chest, legs immobilized with knee rest, 500ml bladder protocol, IV contrast and 3mm CT slice thickness from L1 vertebral level up to mid-thigh. RTOG consensus guidelines were followed for contouring the target volumes and organs at risk (OAR). Two different radiotherapy plans for each patient i.e. 3DCRT and IMRT were generated.

*Treatment Prescription:* Dose of 50-50.4 Gy in 1.8-2 Gy/fraction was prescribed

**Radiation details:**

- **a.** Dose distribution of Target volume- comparison of mean PTV dose, CI and HI

<table>
<thead>
<tr>
<th>Plan</th>
<th>Mean Dose (CGy)</th>
<th>CI</th>
<th>HI</th>
</tr>
</thead>
<tbody>
<tr>
<td>3DCRT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IMRT</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conformity index and Homogeneity Index- CI defined as following

\[ CI \text{ (ref)} = \frac{\text{Volume } 95\%}{\text{Volume of PTV}} \]

V95 is the volume of PTV covered by at least 95% of the prescribed dose

HI is defined as following-

\[ HI = \frac{(D_{2\%} - D_{98\%})}{D_{50\%}} \]

D2%, D98% and D50% are the received dose by 2%, 98% and 50% of the target volumes

- **b.** OARs dose

<table>
<thead>
<tr>
<th>OAR</th>
<th>Plan</th>
<th>Mean Dose (CGy)</th>
<th>V50%</th>
<th>V40%</th>
<th>V15%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel</td>
<td>3DCRT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IMRT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Evaluation**

Documentation of patient clinical data was done. Tabulation of dose distribution of target volume, dose received by OARs i.e. mean dose, V15, V40 and V50 for small intestine were recorded. Dose conformity and uniformity indexes were measured and estimated according to International Commission on Radiation Unit and Measurement (ICRU).

*Statistical analysis:* The data obtained was entered into Microsoft Excel Worksheet. Data collected in the study was analyzed and interpreted using statistical analysis system (SAS), version 9.2 software for windows version 10. All results are shown in tabular as well as graphical format to visualize the statistically significant difference more clearly. In the entire study, the p-values less than 0.05 were considered to be statistically significant.
Results

A total of 72 patients participated in this study conducted at Basavatarakam Indo American Cancer Hospital and Research Institute, Hyderabad, Telangana between July 2020 to June 2021 with clinical features suggestive of carcinoma rectum were included in the study.

Table 1
The distribution sample size studied across two study groups

<table>
<thead>
<tr>
<th>Technique Treated</th>
<th>No. of subjects</th>
<th>% of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>3DCRT</td>
<td>36</td>
<td>50.0</td>
</tr>
<tr>
<td>IMRT</td>
<td>36</td>
<td>50.0</td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>100.0</td>
</tr>
</tbody>
</table>

According to the sample size derived, each group of treatment technique was recruited with equal number of subjects i.e. 36 subjects into each group of treatment.

Table 2
Inter-group sex distribution

<table>
<thead>
<tr>
<th>Gender</th>
<th>3DCRT</th>
<th>Percentage (%)</th>
<th>IMRT</th>
<th>Percentage (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>15</td>
<td>41.67</td>
<td>14</td>
<td>38.89</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>21</td>
<td>58.33</td>
<td>22</td>
<td>61.11</td>
<td>0.81</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>100</td>
<td>36</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Values are number and % of cases, P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant.
**Inter-group sex distribution**

Of 36 cases studied in 3DCRT Group, 21 (58.33%) were male and 15 (41.67%) were female. Of 36 cases studied in IMRT Group, 22 (61.11%) were male and 14 (38.89%) were female.

The sex distribution of cases studied did not differ significantly between two study groups (P-value>0.05).

**Table 3**

Inter-group age group distribution

<table>
<thead>
<tr>
<th>Age Group</th>
<th>3DCRT</th>
<th>Percentage (%)</th>
<th>IMRT</th>
<th>Percentage (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>21 to 30 Years</td>
<td>1</td>
<td>2.78</td>
<td>1</td>
<td>2.78</td>
<td></td>
</tr>
<tr>
<td>31 to 40 Years</td>
<td>3</td>
<td>8.33</td>
<td>3</td>
<td>8.33</td>
<td></td>
</tr>
<tr>
<td>41 to 50 Years</td>
<td>9</td>
<td>25.00</td>
<td>13</td>
<td>36.11</td>
<td>0.21</td>
</tr>
<tr>
<td>51 to 60 Years</td>
<td>17</td>
<td>47.22</td>
<td>7</td>
<td>19.44</td>
<td></td>
</tr>
<tr>
<td>61 to 70 Years</td>
<td>5</td>
<td>13.89</td>
<td>11</td>
<td>30.56</td>
<td></td>
</tr>
<tr>
<td>71 to 80 Years</td>
<td>1</td>
<td>2.78</td>
<td>1</td>
<td>2.78</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>100</td>
<td>36</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Min 24 Years
Max 75 Years
Mean±SD 53.69 ± 9.84 53.31 ± 10.93

Values are number and % of cases, P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant.
Among the study participants, more than 50% of the subjects were in the age group range of 40 to 70 years. The mean ± SD of age of cases in 3DCRT group and IMRT group were $53.69 \pm 9.84$ years and $53.31 \pm 10.93$ years respectively. The minimum – maximum age range in 3DCRT group was 24 – 75 years in IMRT group was 29 – 75 years. The distribution of age group did not differ significantly between two study groups (P-value>0.05).

**Inter-group age group and mean age distribution**

Among the study participant, more than 50% of the subjects were in age group range of 40 to 70 years. The mean ± SD of age of cases in 3DCRT group and IMRT group were $53.69 \pm 9.84$ years and $53.31 \pm 10.93$ years respectively. The minimum – maximum age range in 3DCRT group was 24 – 75 years in IMRT group was 29 – 75 years. The distribution of age group did not differ significantly between two study groups (P-value>0.05).
Table 4
Inter-group distribution of mean planning target volume (PTV)

<table>
<thead>
<tr>
<th>Dose Distribution of Target Volume</th>
<th>3DCRT</th>
<th>IMRT</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min</td>
<td>Max</td>
<td>Mean±SD</td>
<td>Min</td>
</tr>
<tr>
<td>PTV</td>
<td>43.96</td>
<td>49.8</td>
<td>47.73 ± 1.04</td>
</tr>
</tbody>
</table>

Values are min, max, mean and SD, P-value by independent sample t test. P-value<0.05 is considered to be statistically significant.

Figure 4: Inter-group distribution of mean planning target volume (PTV)

Inter-group comparison of mean planning target volume (PTV)

The mean ± SD of mean planning target volume (PTV) of cases in 3DCRT group and IMRT group were 47.73 ± 1.04 and 48.03 ± 0.88 respectively. The minimum – maximum dose range in 3DCRT and IMRT groups were 43.96 – 49.8 and 45.98 – 49.8 respectively. The distribution of mean planning target volume (PTV) differs significantly between two study groups (P-value<0.05).

Table 5
Inter-group (mean) dose distribution of planning target volume

<table>
<thead>
<tr>
<th>Dose Distribution of Target Volume</th>
<th>3DCRT</th>
<th>IMRT</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min</td>
<td>Max</td>
<td>Mean±SD</td>
<td>Min</td>
</tr>
<tr>
<td>D2%</td>
<td>41.4</td>
<td>57.08</td>
<td>51.23 ± 2.86</td>
</tr>
<tr>
<td>D50%</td>
<td>20.65</td>
<td>52.8</td>
<td>50.19 ± 3.67</td>
</tr>
<tr>
<td>D98%</td>
<td>40.7</td>
<td>52.43</td>
<td>46.71 ± 2.31</td>
</tr>
</tbody>
</table>
Values are min, max, mean and SD, P-value by independent sample t test. P-value<0.05 is considered to be statistically significant.

**Inter-group comparison of mean dose distribution**

The mean ± SD of mean dose distribution (D2%) of cases in 3DCRT group and IMRT group were 51.23 ± 2.86 and 52.2 ± 1.89 respectively. The mean dose distribution (D50%) of cases in 3DCRT group and IMRT group were 50.19 ± 3.67 and 50.3 ± 0.21 respectively. The mean dose distribution (D98%) of cases in 3DCRT group and IMRT group were 46.71 ± 2.31 and 48.15 ± 1.09 respectively.

**Table 6**

<table>
<thead>
<tr>
<th>Dose Distribution of Target Volume</th>
<th>3DCRT Min</th>
<th>Max</th>
<th>Mean±SD</th>
<th>IMRT Min</th>
<th>Max</th>
<th>Mean±SD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI</td>
<td>0.27</td>
<td>0.99</td>
<td>0.92 ± 0.09</td>
<td>0.27</td>
<td>0.99</td>
<td>0.91 ± 0.09</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Values are min, max, mean and SD, P-value by independent sample t test. P-value<0.05 is considered to be statistically significant.
Inter-group comparison of mean conformity index (CI)

The mean ± SD of mean conformity index (CI) of cases in 3DCRT group and IMRT group were 0.92 ± 0.09 and 0.91 ± 0.09 respectively. The minimum – maximum index range in both 3DCRT and IMRT groups were 0.27 – 0.99. The distribution of mean conformity index (CI) did not differ significantly between two study groups (P-value>0.05).

Table 7
Inter-group distribution of homogeneity index (HI)

<table>
<thead>
<tr>
<th>Dose Distribution of Target Volume</th>
<th>3DCRT</th>
<th>IMRT</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min</td>
<td>Max</td>
<td>Mean±SD</td>
<td>Min</td>
</tr>
<tr>
<td>HI</td>
<td>0.01</td>
<td>0.92</td>
<td>0.13 ± 0.15</td>
</tr>
</tbody>
</table>

Values are min, max, mean and SD, P-value by independent sample t test. P-value<0.05 is considered to be statistically significant.
Inter-group comparison of mean homogeneity index (CI)

The mean ± SD of mean homogeneity index (HI) of cases in 3DCRT group and IMRT group were 0.13 ± 0.15 and 0.17 ± 0.29 respectively. The minimum – maximum index range in 3DCRT and IMRT groups were 0.01 – 0.92 and 0.03 – 2.15 respectively. The distribution of mean homogeneity index (HI) did not differ significantly between two study groups (P-value>0.05).

Table 8
Inter-group distribution of bowel mean dose

<table>
<thead>
<tr>
<th>Dose Distribution in Bowel</th>
<th>3DCRT</th>
<th>IMRT</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Min</td>
<td>Max</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>Mean Bowel Dose</td>
<td>14.29</td>
<td>28.36</td>
<td>21.93 ± 2.78</td>
</tr>
</tbody>
</table>

Values are min, max, mean and SD, P-value by independent sample t test. P-value<0.05 is considered to be statistically significant.
Inter-group comparison of mean bowel dose

The mean ± SD of mean bowel dose of cases in 3DCRT group and IMRT group were 21.93 ± 2.78 and 20.89 ± 2.85 respectively. The minimum – maximum dose range in 3DCRT and IMRT groups were 14.29 – 28.36 and 13.01 – 27.15 respectively. The distribution of mean bowel dose differs significantly between two study groups (P-value<0.05).

Table 9
Inter-group (mean) dose distribution of bowel volume

<table>
<thead>
<tr>
<th>Dose Distribution in Bowel Volume</th>
<th>3DCRT</th>
<th>IMRT</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Min</td>
<td>Max</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>V15%</td>
<td>59.02</td>
<td>69.74</td>
<td>64.7 ± 2.72</td>
</tr>
<tr>
<td>V40%</td>
<td>13.46</td>
<td>28.4</td>
<td>21.24 ± 3.08</td>
</tr>
<tr>
<td>V50%</td>
<td>1.336</td>
<td>15.32</td>
<td>6.45 ± 3.31</td>
</tr>
</tbody>
</table>

Values are min, max, mean and SD, P-value by independent sample t test. P-value<0.05 is considered to be statistically significant.
Inter-group comparison of mean dose distribution in bowel volume

The mean ± SD of mean dose distribution in bowel volume (V15%) of cases in 3DCRT group and IMRT group were 64.7 ± 2.72 and 63.6 ± 3.11 respectively. The mean dose distribution in bowel volume (V40%) of cases in 3DCRT group and IMRT group were 21.24 ± 3.08 and 15.18 ± 2.13 respectively. The mean dose distribution in bowel volume (V50%) of cases in 3DCRT group and IMRT group were 6.45 ± 3.31 and 2.1 ± 2.14 respectively. The distribution of mean dose in bowel volume (V15%, V40% and V50%) differs significantly between two study groups (P-value<0.05).

Table 10
Inter-group distribution of RTOG Toxicity Grading

<table>
<thead>
<tr>
<th>RTOG Toxicity Grading</th>
<th>3DCRT Percentage (%)</th>
<th>IMRT Percentage (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>6 16.67</td>
<td>24 66.67</td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>22 61.11</td>
<td>12 33.33</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Grade 3</td>
<td>8 22.22</td>
<td>0 0.00</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>36 100</td>
<td>36 100</td>
<td></td>
</tr>
</tbody>
</table>

Values are number and % of cases, P-value by Chi-Square test. P-value<0.05 is considered to be statistically significant.
Inter-group distribution of RTOG Toxicity Grading

Of 36 cases treated with 3DCRT technique, 6 (16.67%) were into grade 1, 22 (61.11%) subjects were into grade 2 and 8 (22.22%) subjects were into grade 3 toxicity categories. Of 36 cases treated with IMRT technique, 24 (66.67%) were into grade 1, 12 (33.33%) subjects were into grade 2 and no subjects were into grade 3 toxicity categories. The distribution of RTOG toxicity grading in cases studied differs significantly between two study groups (P-value<0.05).

Discussion

According to the study criteria and objectives, 72 carcinoma rectum subjects (36 subjects treated with 3DCRT and 36 subjects treated with IMRT technique) willing to give written informed consent were recruited in the study. The demographic, investigational dosimetric and volumetric data was collected and analyzed. Here in this study our aim was to compare the acute bowel toxicities and dosimetry of OARs in carcinoma rectum using Neoadjuvant chemoradiotherapy by IMRT and 3DCRT. The objectives included were to assess the incidence of acute bowel toxicities and dosimetric analysis of organs at risk in carcinoma rectum patients treated using IMRT and 3DCRT.

The data collected from the subjects including demographic information such as age, age group, sex and dosimetric parameters like planning target volume (PTV), D2%, D50% and D98% and dose distribution of target volume, dose received by OARs i.e. mean dose, V15, V40 and V50 for small intestine were recorded. The categorical variables were measured in percentages and the continuous variables were measured in mean ± standard deviations. As there are limited studies comparing these 2 different techniques i.e., 3DCRT, IMRT in rectal cancer, our study was undertaken to establish a radiotherapy technique which will reduce the dose received by the OARs in rectal cancer without compromising the dose to the tumor.
**Demographic data analysis**

According to the observed sex distribution among the carcinoma rectum patients, the subjects treated with 3DCRT were 58.33% of male and 41.67% of female population whereas the subjects treated with IMRT were 61.11% of male and 38.89% of female population. The distribution of sex did not differ significantly between two study groups (P-value>0.05).

As per the observations in the current study, more than 50% of the subjects were in age group range of 40 to 70 years. The mean ± SD of age of cases in 3DCRT group was 53.69 ± 9.84 years and IMRT group was 53.31 ± 10.93 years. The distribution of age group did not differ significantly between two study groups (P-value>0.05).

**Dosimetric data analysis**

The mean planning target volume (PTV) of dose in subjects treated with 3DCRT technique was 47.73 Gy and in subjects treated with IMRT technique was 48.03 Gy. The distribution of mean planning target volume (PTV) differs significantly between two study groups (P-value<0.05). The mean of maximum dose received by atleast 2% planning target volume i.e. D2% distribution in subjects treated with 3DCRT technique was 51.23 Gy and IMRT technique was 52.2 Gy. The D2% distribution differs significantly between two study groups (P-value<0.05).

The mean of maximum dose received by atleast 50% planning target volume i.e. D50% distribution in subjects treated with 3DCRT technique was 50.19 Gy and IMRT technique 50.3 Gy. The D50% distribution did not differ significantly between two study groups (P-value>0.05). The mean of maximum dose received by atleast 98% planning target volume i.e. D98% distribution in subjects treated with 3DCRT technique was 46.71 Gy and IMRT technique 48.15 Gy. The D98% distribution differs significantly between two study groups (P-value<0.05).

According to the dosimetric comparison study carried out by Jun Zhao et. al, in 2016, on VMAT, IMRT and 3DCRT for locally advanced rectal cancer to compare the dosimetric differences among volumetric modulated arctherapy (VMAT), fixed-field intensity modulated radiotherapy (IMRT) and three-dimensional conformal radiotherapy (3DCRT) for the LARC. Based on the comparable dosimetric parameters for target volume, it was concluded that IMRT shows better sparing for OARs and normal tissue.

These results were in concordance with other studies. Hence it can be established that IMRT plans are more homogenous in dose coverage to the target as compared to 3DCRT plan. The mean dose received by the target and the CI and HI remains the same with the 2 different techniques.

**Dose volume data analysis**

The mean percentage of bowel of dose in subjects treated with 3DCRT technique was 21.93 Gy and IMRT was 20.89 Gy. The distribution of mean percentage bowel differs significantly between two study groups (P-value<0.05).
The mean percentage of bowel receiving at least 15 Gy (V15%) of dose in subjects treated with 3DCRT technique was 64.7 Gy and IMRT was 63.6 Gy. The distribution of mean percentage bowel differs significantly between two study groups (P-value<0.05).

The mean percentage of bowel receiving at least 40 Gy (V40%) of dose in subjects treated with 3DCRT technique was 21.24 Gy and IMRT was 15.18 Gy. The distribution of mean percentage bowel differs significantly between two study groups (P-value<0.05).

The mean percentage of bowel receiving at least 50 Gy (V50%) of dose in subjects treated with 3DCRT technique was 6.45 Gy and IMRT was 2.1 Gy. The distribution of mean percentage bowel differs significantly between two study groups (P-value<0.05).

**RTOG toxicity grade analysis**

Among the 36 subjects treated with 3DCRT technique, 16.67% were into grade 1, 61.11% subjects were into grade 2 and 22.22% subjects were into grade 3 toxicity categories whereas out of 36 subjects treated with IMRT technique 66.67% were into grade 1 and 33.33% were into grade 2 and no subjects was into grade 3 toxicity categories. The distribution of RTOG toxicity grading in cases studied differs significantly between two study groups (P-value<0.05).

According to the study carried out by Bong Kyung Bae et. al (26) in 2017 to evaluate the feasibility of simultaneous integrated boost intensity-modulated radiotherapy (SIB-IMRT) for by comparing with 3-dimensional conformal radiotherapy (3D-CRT). Acute gastrointestinal, genitourinary, hematologic, and skin toxicities were compared between the two groups based on the RTOG toxicity criteria and concluded that IMRT reduced the dose to small bowel substantially and hence decreased GI toxicity. Thus IMRT is better radiotherapy techniques than 3DCRT in reducing the dose to the small bowel in rectal cancer patients.

**Conclusion**

Our data suggest that IMRT is superior to 3DCRT in the homogenous dose distribution of the target volume without compromising on the mean dose of the PTV in the treatment of pre-operative rectal cancer. We also conclude that the mean dose received by the OARs is significantly low with IMRT as compared to 3DCRT in the treatment of rectal cancer patients.

We can conclude that in the neoadjuvant treatment of rectal cancer with concurrent chemoradiation, advanced radiotherapy techniques like IMRT are better than 3DCRT both in dose homogeneity of target volume as well as dose sparing of the OARs. This clinically impacts on better tumor control, reduced treatment toxicity and a better quality of life.
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