Original Article

Indian Journal of Cancer Education and Research
Volume 7 Number 2, July - December 2019
DOI: http://dx.doi.org/10.21088/ijcer.2321.9815.7219.5

Comparision of Carcinoma Cervix Treated with Conventional vs Intensity Modulated Radiotherapy with Concurrent Chemotherapy

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Received on 17.04.2019, **Accepted on** 20.06.2019

Abstract

Introduction: Cervical cancer is the fourth most common cancer in women, and the seventh overall, Use of IMRT in pelvic malignancies has shown reduced radiation exposure to adjacent bowel and bladder. IMRT is superior to conventional techniques in normal tissue sparing for the treatment of cervical cancer. *Aims:* To assess and compare the acute toxicities of Conventional RT with concurrent chemotherapy & IMRT with concurrent chemotherapy. *Material and Methods*: This Prospective randomised study was conducted in the Department of Radiation Oncology for a period of 2 years in 120 patients, who satisfied the eligibility criteria with 60 patients in each group, A and B. 1 patient in Group A and 3 patients in Group B defaulted during External Beam Radiotherapy. 116 patients were evaluated at the end of study, 59 in IMRT arm (Group A) and 57 in Conventional RT arm (Group B). *Results:* All the patients in the study were of squamous histology with moderately differentiated being the most common grade in the groups, 61.7% in Group A and 48.3% in Group B. 98.3% patients in Group A and 95% patients in Group B completed the planned treatment. Out of those who completed treatment, 72.9% patients in Group A and 73.7% patients in Group B completed it in ≤ 56 days. The cause of treatment delay was acute toxicity in 31.3% of patients in Group A and 20% of patients in Group B. The most common acute toxicity seen was upper gastrointestinal toxicity seen in the form of nausea and vomiting. Complete response at first follow up was seen in 81% patients in Group A and 75.4% patients in Group B. After completion of study, locoregional control was seen in 89.8% patients in Group A and 87.6% patients in Group B. Locoregional failure was seen in 6.8% patients in Group A and 5.3%patients in Group B. Distant metastasis was seen in 3.4% patients in Group A and 5.3% patients in Group B. *Conclusions:* Toxicity between the two modalities was comparable with advantage of IMRT in reducing the acute lower gastrointestinal toxicity. The loco-regional control was comparative in both groups.

Keywords: Cervical cancer: Intensity Modulated Radiotherapy; External Beam Radiotherapy.

How to cite this article:
Sandhya Rani Nippani, Nanuvala Prathyusha. Comparision of Carcinoma Cervix Treated with Conventional vs Intensity Modulated Radiotherapy with Concurrent Chemotherapy. Indian J Canc Educ Res. 2019;7(2):81-89.

Introduction

Cervical cancer is the fourth most common cancer in women, and the seventh overall, with an estimated 5,28,000 new cases in 2012.[1] In developing countries like India, majority of the patients present in late or advanced stages. Concurrent radiotherapy with Cisplatin-based chemotherapy has been considered the standard of treatment in patients presenting in stage IB to IVA, which is based on the five randomized control trials.[2] However Grade 3 and 4 gastrointestinal and hematological toxicities are significantly higher in patients who are treated with chemoradiation as compared to patients who are treated with radiation alone. Conventional radiotherapy using bony landmarks

to define treatment volume has resulted in good tumour control with acceptable normal tissue toxicity. However these techniques has resulted in inadequate coverage of regional lymph nodes in the clinical target volume (CTV) and increased doses to normal tissues like small bowel, bladder, rectum and bone marrow.

IMRT represents a new technology in radiotherapy in computer treatment software and linear accelerator collimation capabilities, delivery that combines high-resolution imaging, advances inverse planning, and radiation beam flux modulation to produce highly conformal dose distributions unachievable using conventional approaches.Under similar target coverage, IMRT is superior to conventional techniques in normal tissue sparing for the treatment of cervical cancer and a number of groups have explored IMRT in the gynecologic setting as a method to minimize the gastrointestinal, genitourinary and bone marrow toxicity that occurs in conventional RT. Hypothesis made before our study is that subjects receiving 3DCRT and IMRT have a greater sparing of normal tissues as compared to conventional RT and hence reduced incidence of acute toxicities and thus improved quality of life. We undertook this study to study the acute toxicity profile of conformal radiotherapy i.e., 3 DCRT and IMRT and to compare the volume of normal tissue irradiated by these two techniques.

Materials and Methods

The prospective randomised study was conducted at MNJ institute of oncology/RCC, Hyderabad. The study period was from September 2015 to July 2017. A total of 120 patients were taken for the study from OPD after taking informed consent.

Complete history and physical examination including punch biopsy from the cervical lesion. Complete blood picture, renal function tests and liver function tests. Chest X-ray PA view. Ultrasound of the abdomen and pelvis. Cystoscopy on suspicion of a vesico vaginal fistula, colonoscopy on suspicion of a recto vaginal fistula and MRI pelvis if parametrium cannot assessed adequately on clinical examination. Any other investigation as and when needed.

Inclusion Criteria

1. Positive biopsy for squamous cell carcinoma.
2. Stage IIA-IIIB Carcinoma cervix patient according to FIGO Guidelines.
3. Age 30–80 yrs.
4. Informed consent.
5. Karnofsky performance score 80–90%.
6. No evidence of Metastatic disease.

Exclusion Criteria

1. Post Hysterectomy patients (carcinoma vault) will be excluded.
2. Patients with Metastatic disease outside pelvis.
3. Immuno-compromised patients and HIV positive patients will be excluded.
4. Patients who refuse informed consent will be excluded.
5. Pregnancy.
6. Presence of synchronous double primary.

Randomization to Groups

After patients signed the consent form, they were randomized into either Group A or Group B by Simple Randomization.

Group A: Concurrent chemo-radiation using IMRT followed by Brachytherapy.

Group B: Concurrent chemo-radiation using Conventional RT followed by Brachytherapy.

Patients in both the groups were treated with a total dose of 50 Gy in 25 fractions, 2 Gy per fraction for 5 days a week along with concurrent chemotherapy, injection cisplatin i.v. 40 mg per m^2 followed by brachytherapy, 3 fraction 7 Gy per week.

Chemotherapy with cisplatin of a uniform dose of 50 mg was given to patients intravenously immediatelythe next day after the 1^{st} fraction of cisplatin and was ensured that the patient had taken radiotherapy on the day of infusion after 4 hours after cisplatin therapy and even the next day after that. Patient was given tablet zofer 8 mg thrice a day for 3 days as routine anti emetic therapy after cisplatin. Thereafter it was repeated weekly for the entire duration of EBRT.

Treatment Monitoring was done. Technique of High Dose Rate Intracavitary brachytherapy Response is assessed as per the RECIST 1.1 Criteria after the last fraction of HDR-ICBT and after 6 weeks and 3 months. *p*-value was caluculated by chi square test at 95% confidance interval *p*-value were considered significant when *p* is less than or equal to 0.05.

Results

A total of 120 patients, who satisfied the eligibility criteria, were included in the study with 60 patients in each group. The age range in Group A was 30–65 years with the median age of 50 years. Moderately Differentiated Squamous Cell Carcinoma was the most common type with 37 patients (73.3%) in Group A & 29 patients (48.3%) in Group B. Exophytic growth was the most common type with 51 patients (85%) in Group A and 43 patients (71.7%) in Group B (Table 1).

Table 1: Distribution of age and histology of cells in cancer

Age group (in years)	Group A (*n*=60)	Group B (*n*=60)
30–39	6 (10%)	5 (8%)
40–49	21 (35%)	24 (40%)
50–59	19 (31.7%)	27 (45%)
60–69	14 (23.3%)	4 (6%)
Histology		
Well Differentiated	15 (25%)	25 (41.7%)
Moderately Differentiated	37 (61.7%)	29 (48.3%)
Poorly Differentiated	8 (13.3%)	6 (10%)
Exophytic	51 (85%)	43 (71.7%)
Ulcero infiltrative	3 (5%)	3 (5%)
Endophytic	6 (10%)	14 (23.3%

Table 2: Treatment Profile in both groups in study

EBRT duration	Group A	Group B
<35	29 (48.3%)	27 (45%)
36–38	24 (40%)	17 (28.3)%
>39	6 (10%)	13 (21.7%)
Did not complete	1 (1.7%)	3 (5%)
Number of cycles		
3	1 (1.7%)	2 (3.3%)
4	22 (36.7%)	27 (45%)
5	37 (61.6%)	31 (51.7%)

Out of 120 patients, 4 did not complete EBRT. 1 patient defaulted in Group A and 3 in Group B. The duration of EBRT in Group A was ≤35 days in 29 patients (48.3%). (Table 2)

Majority patients in both arms received 4-5 cycles as shown in the table below. 1 patient in Group A and 2 in Group B received 3 cycles.

All patients in both groups started ICRT within 1 week of completion of EBRT.

Overall treatment Time was ≤8 weeks (56 days) in 43 patients (72.9%) in Group A & 42 patients (73.7%) in Group B (Table 3)

Table 3: Gap between EBRT & ICRT and Overall Treatment Time

Gap (in days)	Group A (*n*=59)	Group B (*n*=57)
3-5	54 (91.5%)	56 (98.2%)
6-7	5 (8.5%)	1 (1.8%)
Over treatment time		
<56	43 (72.9%)	42 (73.7%)
57–63	15 (25.4%)	15 (26.3%)
>63	1 (1.7%)	0

Table 4: Acute Toxicities observed in both groups in study

Grade	Group A (*n*=59)	Group B (*n*=57)
Anemia (Acute Hemoglobin Toxicity)		
No Toxicity	9 (15.3%)	12 (21%)
1	13 (22%)	13 (22.8%)
2	36 (61%)	30 (52.7%)
3	1 (1.7%)	2 (3.5%)
4	0	0
Leucopenia:		
No Toxicity	27 (45.8%)	23 (40.4%)
1	25 (42.4%)	27 (47.3%)
2	7 (11.8%)	7 (12.3%)
3	0	0
4	0	0
Platelet		
No Toxicity	58 (98.3%)	56 (98.2%)
1	1 (1.7%)	1 (1.8%)
2	0	0
3	0	0
4	0	0
Nausea		
No Toxicity	5 (8.5%)	6 (10.5%)
1	17 (28.8%)	14 (24.6%)
2	34 (57.6%)	35 (61.4%)
3	3 (5.1%)	2 (3.5%)
4	0	0
Vomiting		
No Toxicity	5 (8.5%)	6 (10.5%)
1	17 (28.8%)	14 (24.6%)
2	37 (62.7%)	37 (64.9%)
3	0	0
4	0	0
Diarrhea		
No Toxicity	20 (33.9%)	8 (14%)
1	12 (20.3%)	14 (24.6%)
2	26 (44.1%)	34 (59.6%)
3	1 (1.7%)	1 (1.8%)
4	0	0
Proctitis:		
No Toxicity	25 (42.4%)	14 (24.6%)
1	10 (16.9%)	20 (35.1%)
2	24 (40.7%)	23 (40.3%)
3	0	0
4	0	0
Serum Creatinine		
No Toxicity	58 (98.3%)	56 (98.2%)
1	1 (1.7%)	1 (1.8%)
2	0	0
3	0	0
4	0	0
Cystitis		
No Toxicity	36 (61%)	30 (52.6%)
1	14 (23.7%)	14 (24.6%)

Grade	Group A (*n*=59)	Group B (*n*=57)
2	9 (15.3%)	13 (22.8%)
3	0	0
4	0	0
Dermatitis:		
No Toxicity	57 (96.6%)	53 (93%)
1	2 (3.4%)	4 (7%)
2	0	0
3	0	0
4	0	0

The *p*-value for all toxicities as anemia, acute leucocyte, nausea, vomiting, diarrhea, proctitis, cystitiswhen compared in both groups was 0.7355, statistically insignificant (Table 4).

Table 5: Response at 1st followup (6 weeks after completion of RT)

Response	Group A (*n*=59)	Group B (*n*=57)
CR	48 (81.4%)	43 (75.4%)
PR	11 (18.6%)	14 (24.6%)
SD	0	0
PD	0	0

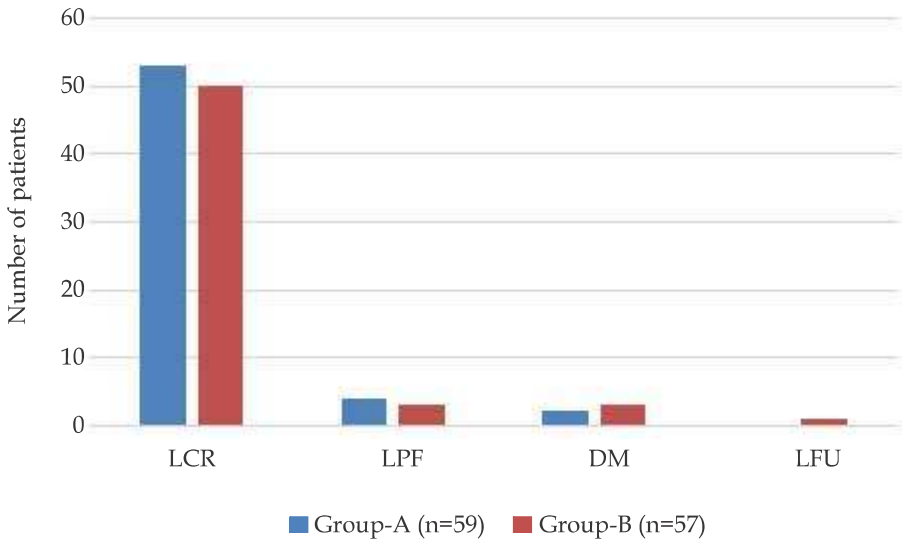
In Group A, 48 patients (81.4%) out of 59 and in Group B, 43 patients (75.4%) out of 57 showed complete response on 1st follow up as shown in the Graph 1.

No patient in both groups developed any Skin or Subcutaneous tissue toxicity. The *p*-value when compared with kidney and late bladder toxicities in both groups was 0.7962, statistically insignificant (Table 6).

Table 6: Late toxicities in both groups of studies

Grade	Group A (*n*=59)	Group B (*n*=57)
Small Intestine/Large Intestine		
No Toxicity	53 (89.8%)	49 (86%)
1	5 (8.5%)	7 (12.3%)
2	1 (1.7%)	1 (1.8%)
3	0	0
4	0	0
Kidney Toxicity		
No Toxicity	57 (96.6%)	55 (96.5%)
1	2 (3.4%)	2 (3.5%)
2	0	0
3	0	0
4	0	0
Late bladder toxicity		
No Toxicity	47 (79.7%)	43 (75.4%)
1	10 (16.9%)	12 (21.1%)
2	2 (3.4%)	2 (3.5%)
3	0	0
4	0	0

Loco regional Control was seen in 53 patients (89.8%) in Group A and 50 patients (87.6%) in Group B. 1 patient was lost to follow up in Group B. 2 patients (3.4%) in Group A and 3 patients (5.3%) in Group B developed distant metastasis. Loco regional failure was seen in 4 patients (6.8%) and 3 patients (5.3%) in Group A and B respectively.



Graph 1: Response at median follow up

Discussion

A total of 120 patients who satisfied the eligibility criteria were enrolled in the study. The patients were randomized with 60 patients in IMRT arm as Group A and 60 patients in Conventional RT arm as Group B. Patients in both the groups planned for concomitant chemoradiation with RT dose of 50 Gy in 25 fractions at a dose of 2 Gy per fraction and cisplatin @ 40 mg/m^2. This was followed by Brachytherapy. The age range of patients in Group A was 30–65 years with a median age of 50 years and in Group B it was 32–63 years with a median age of 50 years.

This is in accordance with data from cancer registries in developing countries which suggest that about 80 to 90 percent of confirmed cervical cancers cases occur among women age 35 year or older because cervical cancer progresses slowly from precancerous condition to advanced cancer, the incidence of cancer is very low in women under the age of 25. Incidence increases at about ages 35 to 40 and reaches a maximum in women in their 50s and 60.

All the 120 cases of cervical cancer taken up for the study were of squamous cell carcinoma histology. Of these, most common was moderately differentiated squamous cell carcinoma, seen in a total of 66 patients (55%) out of total 120. It was followed by well differentiated squamous cell carcinoma seen in 40 patients (33.3%). Poorly differentiated squamous cell carcinoma was the least common subtype seen in 14 patients (11.7%). This distribution of tumour grades was also reflected in the two study groups. In both the study groups, moderately differentiated squamous cell carcinoma was the most common subtype followed by well differentiated and least common being poorly differentiated squamous cell carcinoma. The most common tumour morphology that was seen was exophytic type seen in 94 patients (78.3%) out of 120. It was followed by endophytic type of growth seen in 20 patients (16.7%) out of 120. The rest were ulcero-infiltrative type.

All the patients in both the groups received concurrent chemoradiation. This is in compliance with NCI alert. The alert was issued following the five landmark trials: Keys *et al.*,[1] Morris *et al.*,[2] Rose *et al.*,[3] Whitney *et al.*,[4] Peters *et al.*[5] All patients received chemotherapy in the form of Inj. Cisplatin at a dose of 40 mg/m2 prior to EBRT every week. Rose *et al.*[3] reported the results of GOG-120 trial in which a course of standard pelvic radiotherapy was combined with one of the three concurrent chemotherapy regimens with median follow up of 35 months, survival curves for the two cisplatin groups were almost identical and both were statistically superior to the survival curve of the hydroxyurea alone group. However toxicities were much more in the combined drug arms than in the cisplatin alone arm.

In Keys *et al.*[3] reported the results of the GOG-123 study in which 369 patients for 36 months, local recurrence and distal metastasis rates were 9% and 21% and 12% and 16% respectively, both in favour of concomitant arm. At a median follow up of 36 months, local recurrence and distal metastasis rates were 9% and 21% and 12% and 16% respectively, both in favour of concomitant arm. These trials

proved that single agent Cisplatin is as efficacious as a triple drug combination therapy with reduced toxicity. There have been controversies about the optimum timing of Cisplatin administration in relation to radiation treatment. Pre-clinical data suggests enhanced tumour response by a factor of 1.7 when Cisplatin was administered at least thirty minutes prior to radiation treatment.[6]

In our study, 49 patients out of 120 (40.8%) received four cycles of cisplatin instead of planned five cycles. The 5th cycle was omitted either due to toxicity or financial reason. About three-fourth of patients in both the groups completed treatment (EBRT and ICRT) in eight weeks (≤ 56 days). In Group A and B, the numbers were 43 (72.9%) and 42 (73.7%) respectively. The patients who completed EBRT without any treatment gaps were 29 (48.3%) in Group A and 27 (45%) in Group B. The delay in EBRT was made up by the only a small delay, 3-5 days, in ICRT for most of the patients (91.5% and 98.2% in Groups A and B respectively). The gap between EBRT & ICRT was seven days or less in all the patients who completed the treatment. This was achieved by reserving the tentative dates for ICRT at the initiation of EBRT. The treatment delay was seen in a total of 16 patients in Group A and 15 patients in Group B. It was caused due to toxicity in 5 patients (31.3%) and 3 patients (20%) in Group A and B respectively.

A trial done by Bahena *et al.*[7] concluded that the use of three fractions, once per week, allowed inclusion of greater number of patients during the life span of Iridium-192 source, therebydecreasing the cost of treatment. In addition the three fractions were safe and effective in the management of patients with locally advanced cervical cancer.

The second most common toxicity was hematological toxicity in the form of anemia, 84.7% in Group A and 79% in Group B. There was no statistically significant difference between both the groups as bone marrow was not contoured as an Organ at Risk (OAR) during treatment planning. One patient in Group A and two patients in Group B developed Grade 3 anemia for which a treatment break was given. Grade 2 toxicity was seen in 61% patients in Group A and 52.7% patients in Group B. The anemia was corrected using nutritional supplements and blood transfusion when required. When compared with the study done by Chen *et al.* (2011), the Grade 3 hematologic toxicity was less, 1.7% in our study vs. 23.9% in their study. It may be due to the fact that, as per institutional protocol, patients were advised blood transfusion when the hemoglobin decreased to 9.0 g/dl.

Acute leukocyte toxicity was seen in 54.2% and 59.6% of the patients in Group A and B respectively. Out of these most of the patients had Grade 1 toxicity, 78.1% in Group A and 79.4% in Group B. The leukocyte toxicity was corrected using growth factors when required. No patient had Grade 2 or more platelet toxicity. Only one patient in each group had Grade 1 platelet toxicity.In the study done by Chen *et al.*[8] bone marrow sparing IMRT was compared with conventional box RT. They found that in IMRT arm, Grade 0, 1, 2 and 3 or more acute hematological toxicities were seen in 14, 8, 9 and 2 patients respectively.

The above comparison shows advantage of contouring bone marrow as an OAR. It resulted in lesser hematologic toxicity. Lower GI toxicities include diarrhea and proctitis. Diarrhea was seen in 39 patients in Group A and 49 patients in Group B. The most severe grade was Grade 3 which was seen in 1 patient in each group. Most of the patients, who developed diarrhea, had Grade 2 toxicity. It was 44.1% in Group A and 59.6% in Group B. Proctitis was seen in 34 patients (57.6%) in Group A and43patients (75.4%) in Group B. No Grade 3 proctitis was seen in either group. Group A, IMRT arm, had 10 (16.9%) and 24 patients (40.7%) who had Grade 1 and 2 proctitis ile in Group B, Conventional RT arm, the numbers were 20 (35.1%) and 23 (40.3%) respectively. The acute lower GI toxicity was similar to the study done by Mundt *et al.*[9] The difference was statistically significant (p=0.002). In our study also, with respect to proctitis, the difference was statistically significant (p=0.0403) but not as much as the above study.

In the study done by Chen *et al*[8] no patient had Grade 3 or 4 gastrointestinal toxicity. In their study, 33 patients were in IMRT arm. Out of these 8 (24.2%) developed Grade 2 GI toxicity and 4 developed Grade 1 toxicity. No GI toxicity was present in 21 patients (63.6%). For 3D-CRT arm,20 patients (57.14%) out of 35 developed Grade 2 toxicity which is more than that seen in the IMRT Arm. 7 patients had no GI toxicity. Like our study, this study also has much better acute GI toxicity profile of patients in IMRT arm. In another study done by Beriwal *et al.*[10] 36 patients were treated with Extended Field IMRT. Out of these, 1 patient had Grade 3 GI toxicity. 22 patients out of 36 (61%) had Grade 2 toxicity while 4 (11.1%) had Grade 1 toxicity. The systematic review and meta-analysis of 13 articles done by Yang *et al.*[11] showed that IMRT-delivered high radiation dose produced significantly less average percent volumes of irradiated rectum and small bowel than.

In our study, 23 patients (39%) out of 59 and in Group B, 27 patients (47.4%) out of 57 developed cystitis. No patient in either group had Grade 3 or more toxicity. 14 (23.7%) and 9 patients (15.3%) in Group A and 14 (24.6%) and 13 patients (22.8%) in Group B had Grade 1 and 2 toxicity respectively. The difference was not statistically significant (p=0.5383). The results are similar to the study done by Mundt *et al*.,[9] where 4 patients (10%) developed Grade 2 toxicity in IMRT arm in comparison to 7 patients (20%) in 3D-CRT arm. Grade 1 toxicity was seen in 8 patients (20%) and 7 patients (20%) in IMRT and 3D-CRT arm. The difference was not statistically significant (p=0.22) [91]. In the study done by Chen *et al*.,[8] no patient had Grade 3 or 4 genitourinary toxicity. However the number and percentage of patients who had Grade 2 toxicity or Grade 1 toxicity was almost twice in 3D-CRT arm then in IMRT arm.[9] {(25.7%) and 12 patients (34.2%) in 3D-CRT arm vs. 4 (12.1%) and 6 patients (18.2%) in IMRT arm with Grade 2 and Grade 1 toxicity respectively}. It is in contrast to the results from our study and the study done by Mundt *et al*.[9] The meta-analysis by Yang *et al*.[11] also showed no advantage of IMRT over 3D-CRT in regard to bladder toxicity. 6 patients in our study developed Grade 1 skin toxicity, 2 in IMRT arm and 4 in 3D-CRT arm. Rest of the patients had no skin toxicity. It is due to the skin sparing effect of the high energy photons being used in treatment on Linear Accelerator. Similarly no late skin or subcutaneous tissue toxicity was seen in patients of either group.

In our study, IMRT had a slightly better response than Conventional RT at 1st follow up with 81% complete response in IMRT arm and 75.4% in Conventional RT arm. The follow up in our study was short and ranges from 6 months to 1 year. The late toxicities were evaluated for all the patients in regular follow up. In addition to EBRT, ICRT also has a major role to play in late toxicities. With this short follow up the late toxicities that were evaluated included Gastrointestinal (Small Intestine/Large Intestine) and Genitourinary (Kidney and Bladder). No patient had any skin or subcutaneous toxicity. 2 patients in each group had Grade 1 late kidney toxicity. None had Grade 2, 3 or 4 late kidney toxicity. In our study, late GI toxicities were seen in 6 patients (10.2%) and 8 patients (14.1%) in Group A and B respectively. Grade 1 was seen 5 (8.5%) and 7 (12.3%) patients and Grade 2 in 1 patient each in Group A and B respectively. In the study done by Mundt *et al*.,[9] the chronic GI toxicity was seen in 4 patients (11.1%) in IMRT arm, 3 patients had Grade 1 and 2 patients had Grade 2 toxicity. No Grade 3 or 4 toxicity was reported in IMRT arm. In contrast, in 3D- CRT arm, 15 patients (50%) had chronic GI toxicity. In these, 9 patients had Grade 1, 5 patients had Grade 2 and 1 patient had Grade 3 toxicity. The difference was statistically significant (p=0.001). The study done by Chen *et al*. also had similar results with IMRT having much less late GI toxicity than Non IMRT arm, 2 (6.1%) vs. 12 (34.3%) patients. The result contrast between our study and the above referenced study may be due to the fact that the late toxicities are affected by dose given by brachytherapy. The duration of follow up was also short in our study.

Chen *et al*.[8] had results similar to our study. Grade 2 or higher rectal toxicity was seen in 7.2% patients in IMRT arm and 11.4% in non-IMRT arm. (p=0.24). They concluded that the both arms had similar treatment related toxicity. In our study, in Group A, 12 patients (20.3%) out of 59 and in Group B, 14 patients (24.6%) out of 57 developed late bladder toxicity. No patient in either group had Grade 3 or 4 toxicity. In the study done by Chen *et al*.[8] 1 patient in both arm had severe late GU toxicity (Grade 3). But the number of patients who had late GU toxicity was much less in IMRT arm (9%) as compared with 3D-CRT arm (22.8%). The contrast between our study and the above referenced study may be explained by the same reasoning for GI toxicity: Brachytherapy dose plays a role in late toxicity. Chen *et al*.[8] had results similar to our study. Grade 2 or higher bladder toxicity was seen in 9.6% patients and 13.5% patients in IMRT and non-IMRT arms respectively. The p-value was not significant (p=0.25). Distant metastasis was seen in a total of 5 patients in our study. The most common site of metastasis was supraclavicular node.

From the discussion above, it was observed that IMRT has less acute gastrointestinal toxicity then Conventional RT. Though IMRT showed a slightly better response than Conventional RT, it may be due to short follow up. The late toxicities could not be compared very well due to short duration of follow up, less than 12 months for many patients. Randomized control trials with larger sample size and longer follow up periods are required to have better comparison between the two modalities of treatment.

Conclusion

Concurrent chemoradiation using IMRT is routinely practiced, in addition to conventional treatment, at our institute. We randomised the patients to two groups to compare the toxicities and assess the response by the two modalities. All patients in both

groups received concurrent chemotherapy. From our study, we conclude that toxicity between the two modalities was comparable with advantage of IMRT in reducing the acute lower gastrointestinal toxicity. The loco-regional control was comparative in both groups. However the limitation of this study was short duration of follow up. As a result, the late toxicity could be assessed only for a short period. So, there is need for long term follow up.

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