Panacea Journal of Medical Sciences 2022;12(3):641–644

Content available at: https://www.ipinnovative.com/open-access-journals

Panacea Journal of Medical Sciences

Journal homepage: http://www.pjms.in/

Original Research Article

Study of radiation enteritis in cervical cancer patients treated with definitive radiotherapy and adjuvant radiotherapy – A prospective study

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ARTICLE INFO

Article history:
Received 17-07-2022
Accepted 21-10-2022
Available online 28-11-2022

Keywords:
Definitive Radiation therapy
Adjuvant Radiation therapy
Radiation enteritis
chemoradiation

ABSTRACT

Introduction: The third most frequent type of cancer in the world is cervical cancer. Traditionally cervical cancer treatment is carried by either Radiation therapy alone and/or with chemotherapy. High doses of Radiation therapy can cause gastric enteritis.
Objective: To study the incidence of radiation enteritis in cervical cancer patients of stage upto IIIA.
Materials and Methods: A total of 94 patients receiving radiation therapy (RT) for cervical cancer treatment were enrolled for the study in our hospital from August 2018 to January 2020. The 94 patients were divided into definitive RT group (64 patients) and Adjuvant RT group (30 patients). The incidences of radiation enteritis were evaluated statistically.
Results: In all cervical cancer patients, early radiation enteritis (RE) observed in 68.08%, and late radiation enteritis observed in 21.1%. Patients treated with definitive RT showed more frequent radiation enteritis than in adjuvant RT. In the group treated with definitive RT, the occurrence of early (RE) is more in the Radical radiotherapy group (RRT), whereas late RE appeared more with concurrent chemoradiotherapy (CCRT) group. The late (RE) severe cases (Grade 3,4) observed more with the definitive RT group (only RRT) than in the adjuvant RT group.
Conclusion: In the Definitive RT group, early and late RE occurrence is more than the Adjuvant RT group. The incidence of enteritis was correlated with the lengthening of total irradiation time. Methods to reduce small bowel intervention in RT and volume of irradiation will further decrease enteritis morbidity.

1. Introduction

Cervical cancer is the third and seventh most prevalent of all types of cancer in women. There are approximately 528,000 new cases and 26,000 deaths reported each year by cervical cancer.[1] Radiation treatment (RT) was long used for a curative purpose to treat pelvic malignancy. The pelvic irradiation is an important aspect of cervical cancer patient treatment during definitive and adjuvant RT. Despite the availability of advanced techniques and equipment, RE is a significant problem in patients receiving pelvic RT.[2]

Generally, either surgery, with or without the combination of RT and definitive RT, is used to treat early stages of cervical cancer (FIGO stage IB1 and IIA). FIGO Stage IIB-IIIA is contemplated as LACC and hence RT alone or chemoradiotherapy has been used as the standard treatment method.[3,4] As per the NCCN guideline version 2.2015, FIGO stage IB2 and IIA2 are under the advanced disease category and preferred treatment is done with cisplatin-based Chemoradiotherapy.[4]

In patients receiving RT targeted at pelvis, abdomen or rectum, RE can cause nausea, vomiting, diarrhoea and stomach cramp.[4] Acute enteritis of the radiation is temporary and decreases inflammation typically several

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https://doi.org/10.18231/j.pjms.2022.119

weeks after therapy is over. Chronic RE can produce complications like anemia, diarrhoea, and partial bowel obstruction. Inflammation in chronic radiation enteritis subsides even after a year of treatment. Radiation enteritis can cause serious problems in the effective treatment of cervical cancer. It is observed that almost 90% of the patients encountered permanent changes in their bowel habits after the pelvic RT.[5] The biggest problems to the effective management of these patients are correct diagnosis and proper treatment.[6]

Given the distress of radiation enteritis after pelvic RT and negative effect on the quality of life,[5] it is essential to develop a proper understanding of this important clinical aspect. Although there are few treatments for acute enteritis, late enteritis can be effectively managed by detecting the specific consequential effects of radiation, e.g., bile salt malabsorption, small intestinal bacterial overgrowth, etc., and providing specific treatments. The definite diagnosis has a significant impact on the prognosis of the disease. It is essential to assess the prevalence of radiation enteritis. Evaluating the prevalence of enteritis between the definitive and adjuvant RT group might contribute to a better protocol for the RT scheme of cervical cancer patients.

2. Aim

To study the incidence of radiation enteritis in cervical cancer patients receiving pelvic irradiation.

3. Materials and Methods

This prospective comparative study was conducted in the radiotherapy department from dated August 2018 to January 2020, 94 patients with cervical cancer who were receiving definite or adjuvant RT at the site hospital were enrolled for the study. The patients were in the FIGO stage of IIB and IIIB. The patients were divided into two group's, i.e. definitive RT group with 64 patients and adjuvant therapy group with 30 patients.

A total of 64 cervical cancer patients were positively treated with RT. All definitive RT patients received both external beam radiation and high dose rate (HDR) brachytherapy. In the definitive RT group, 34 patients were managed with Radiation therapy only RRT group and 30 patients were given Cisplatin (30mg/m^2) once a week along with the Radiation CCRT group. External beam RT was conducted by using ^{60}CO with the 4‑field‑box technique. The tumor of the cervix with corpus uterus, fornix, vaginal walls, parametrium and lymph nodes in the pelvis was the therapeutic goal. Definitive RT patients received a fractionation dose of 180cgy, 5 days in a week up to a total dose of 50.4Gy.

The adjuvant RT group comprises of 30 patients receiving an adjuvant RT. The patients qualified for the adjuvant RT category had low histopathological test prognostic factors. Patients received External beam RT 180cgy per fraction, 5 days in a week up to a total dose of 50.4Gy.

All the patients received HDR BRT with three fractions of 6.0 Gy, administered weekly. The dose was fixed at 0.5 cm from the applicator surface, and the diameter of the dose was adjusted to the anatomy of the patient's vagina (2.0–5.0 cm).

3.1. Assessment of patients and grading of grading of radiation enteritis

This study has adopted FIGO staging for cervical cancer (2009). Early (occurring within 3 months after RT) and late radiation enteritis (occurring later than 3 months after RT) were observed during a 1-year follow-up. All patients were scheduled for follow-up after RT, and if they missed, telephonic follow-up was done.

EORTC/RTOG scaling was used for grading radiation enteritis toxicity.[7] The mild reactions were graded as Grade 1 and 2. Whereas severe reaction was grade as Grade 3 and 4.

3.2. Data management and analysis

The questionnaires were checked for completion. The data were entered into the SPSS statistical software. For the significant difference between the expected and the observed incidence, we used the chi-squared test. $P< 0.05$ was considered significant.

4. Results

In this study, 94 patients who underwent radiotherapy for stage IIB and IIIA cervical cancer were included. In the study, 64 patients underwent definite radiotherapy and 30 patients underwent adjuvant radiotherapy. Patients treated with definite RT were significantly older than patients receiving adjuvant RT. The average age of patients receiving definitive RT was 59.24±8.24 years and 51.20±5.5 years for those receiving adjuvant RT. The study on a group of 94 patients showed a higher incidence of radiation enteritis. In the definitive RT group, 53.13% were treated with RRT and 46.87% with CCRT. In all enrolled patients (94) early RE was reported in 68.08% of patients, late RE was reported in 21.2% of patients. The occurrence of early RE in the definitive RT group was 73.4% and in the group receiving adjuvant therapy was 56.6%. (Table 1)

A higher incidence of Grade 3 and 4 enteritis in the definitive RT group (both the RRT and CCRT group) 19.15% was observed than in the adjuvant radiation group 5.9% (p-value =0.004). (Table 2)

In the definitive RT group, 17 patients had late RE, of which 47.05% were treated with RRT and 52.94% with CCRT. Severe late RE cases (Grade 3 and 4) can be seen

Table 1: Radiation enteritis between the definitive RT group (both RRT and CCRT group) and adjuvant RT group.

Group	Total cases	Early Radiation Enteritis	Late Radiation Enteritis	Age (Years)
Definitive Patients	64	47 (73.4%)	17 (26.6%)	59.24 ±8.24
Adjuvant radiotherapy patients	30	17 (56.6%)	3 (10%)	51.20 ±5.5

Table 2: Incidence of early radiation enteritis between the definitive RT group (RRT/CCRT) and adjuvant RT group.

Group	Grade 0	Grade 1 and 2	Grade 3 and 4
RRT	6 (23.1%)	15 (57.7%)	5 (19.2%)
CCRT	11 (52.4%)	6 (28.6%)	4 (19.0%)
Adjuvant radiotherapy patients	14 (82.4%)	2 (11.8%)	1 (5.9%)

Table 3: Incidence of late radiation enteritis between the definitive RT group (RRT/CCRT) and adjuvant RT group.

Group	Grade 0	Grade 1 and 2	Grade 3 and 4
RRT	6 (75.0%)	1 (12.5%)	1 (12.5%)
CCRT	7 (77.8%)	2 (22.2%)	0
Adjuvant radiotherapy patients	2 (66.7%)	1 (33.3%)	0

in the definitive RT group (RRT treated only). Whereas no severe case (grade 3, 4) was observed in the adjuvant RT group (p value=0.726). (Table 3)

5. Discussion

RT is a widely used method for the treatment of cancer and cures almost 25% of all cancers.[8] The study aimed to assess RE incidence in cervical cancer patients treated with definitive RT and adjuvant RT.

Evaluation of the data of all cervical cancer patients (94) enrolled for the study showed a statistically higher percentage of patients who had developed both early and late RE in definitive RT than in the adjuvant RT group. Early RE accounted for 68.08%, whereas late RE accounted for 21.1% of all patients. The above findings are similar to as reported by Wang et al.[9] This might be due to more physical and biological doses given to organ under risk. Patients receiving definitive RT were older and this group showed more incidence of RE (whether early or late), which might due to the more vulnerability of high age patients to RT. Age is another factor that might influence treatment intolerance. These results are in accordance with those reported by van den Aardweg, et al.[10]

Patients receiving RT only (RRT group) had a higher rate of early radiation enteritis than patients receiving CCRT and adjuvant RT. However, Eifel et al. reported more serious adverse effects in concurrent chemotherapy (CCRT) and adjuvant RT than in the definite RT.[11] In our study, the higher occurrence of radiation enteritis in the definite RT group might be due to patients' high clinical stage of the disease, old age, performance status and other socioeconomic factors.

In the definitive RT group, only 1 incidence of higher grade (Grade 3, 4) of late radiation enteritis was observed in the RRT group. Whereas no higher grade incidence (Grade 3, 4) of late radiation enteritis was observed in groups receiving CCRT and adjuvant RT. This might be due to the low dose of radiation and better irradiation regime followed in our study.

Total radiation doses are not the only variable that can affect RE occurrence in patients treated with RT. Factor including age, metabolic disorders, concomitant renal dysfunction, and intestinal diseases can also be vulnerable to enteritis through radiation.[12,13]

6. Conclusion

To conclude, RE was high in cervical cancer patients in underwent radiotherapy. RT interruptions over 7 days were often observed in patients undergoing definitive RT rather than adjuvant RT because of adverse radiation effects, which resulted in increases in patients' overall treatment time. The rate of adverse effects was linked to an increased overall irradiation period due to required RT interruptions. The strategies for reducing RT interruptions and the volume of irradiated small bowels further minimize RE's likelihood.

7. Acknowledgement

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references to this manuscript

8. Source of Funding

None.

9. Conflicts of Interest

There is no conflict of interest.

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Cite this article: Vijayakumar S. Study of radiation enteritis in cervical cancer patients treated with definitive radiotherapy and adjuvant radiotherapy – A prospective study. *Panacea J Med Sci* 2022;12(3):641-644.