Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 01, 2024

Original research article

PROPHYLACTIC PARA-AORTIC LYMPH NODE IRRADIATION IN PATIENTS WITH CERVICAL CANCER: A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background: Para - aortic node involvement in cervical cancer is associated with relapses. Prophylactic para-aortic irradiation with conventional methods was associated with acute and chronic toxicities. With evolvement of radiation techniques, the adverse effects associated with para-aortic radiation have reduced.

Materials and Methods: 30 patients with cervical cancer were managed with chemo-radiotherapy and followed up till a mean period of 15 months. Post para-aortic irradiation associated toxicities were observed.

Results: Grade 1 acute gastro-intestinal toxicity was common than grade 2. No bone marrow constraints or grade 3 toxicities were observed in present study.

Conclusion: conventional radiotherapy methods have higher rates of toxicities than compared to volumetric modulated arc therapy.

Keywords: cervical cancer, para-aortic lymph nodes, arc therapy.

Introduction

Cervical cancer is the fourth most common cancer in women. Chemo-radiation is well validated line of management for locally advanced cervical cancer. Radical pelvic chemo-radiation followed by brachytherapy has significantly improved the overall survival rates. However, many patients had distant relapses or relapse at para-aortic region. The rate of metastasis to para-aortic lymph node (PALN) was <5 per cent in early cervical cancer with a small lesion, without vaginal or parametrial involvement, while the incidence was 5-45 per cent in locally advanced cervical cancer (LACC). Tumours larger than 3.5 cm, parametrial invasion, metastasized pelvic lymph node

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(LN) size >1 cm, multiple pelvic LN metastases and common iliac LN metastasis are independent predictors of PALN involvement. The previous FIGO staging had not taken nodal status into account; hence the question of para-aortic lymph nodal irradiation (PALNI) remained undefined. However, with the recent advances in imaging technology as well as the treatment techniques, FIGO included prophylactic PALNI in the stage III C1of cervical cancer [1, 6].

Involvement of PALN in LACC is assessed using various cross-sectional imaging such as CECT scan, contrast-enhanced magnetic resonance imaging (MRI) and PET-CECT with or without histo-pathological proof of which PET-CECT has the highest specificity of all imaging modalities. Maximum standardized uptake value (SUV Max) of the involved PALN is a significant factor in overall survival with higher SUV Max having detrimental outcomes [7, 9].

With the use of conventional 2D radiation techniques, the therapeutic index could not be maintained due to treatment related toxicities. However, over the past two decades, the radiation techniques have improved to the extent of availability of highly conformal radiation delivery techniques like Volumetric Modulated Arc Therapy (VMAT) [10].

VMAT is a novel treatment technology that combines inverse planning, intensity modulation, and arc therapy for radiation delivery. VMAT is an alternative to fixed gantry angle IMRT delivery with the primary advantage of decreased treatment times [11]. With this method, it is now possible to achieve a favorable therapeutic index by reducing the doses to organs at risk [12].

The purpose of this study is to look into the acute and late toxicities of patients receiving prophylactic para-aortic irradiation with pelvic RT in carcinoma cervix patients.

Materials and Methodology

This prospective observational study was conducted in the department of radiotherapy and oncology, NRI medical college, Mangalagiri, Andhra Pradesh, India. 30 patients with biopsy confirmed FIGO (2018) stage IIIC1 cervical cancer who presented to the opd between September 2022 to May 2023 were included in the study. Eligibility criteria into the study were positive pelvic lymph nodes, positive common iliac lymph nodes and negative para- aortic nodes, Karnofsky performance scale >70, normal renal function tests. Patients with uncontrolled medical co-morbidities, previous history of chemo radiation to the pelvis and postoperative status were excluded from the study. A written informed consent was taken from all patients. Institutional ethics committee approval was obtained before stating the study. All patients were subjected to pre-treatment workup which included a pelvic examination followed by complete staging workup, complete hemogram, liver function tests, kidney function tests, chest X-ray, ECG (Electrocardiogram) and MRI abdomen and pelvis or CECT abdomen & Pelvis.

All patients received EBRT dose of 45 Gy in 25 fractions over 5 weeks, at 1.8 Gy per fraction to pelvic and para-aortic regions, with a simultaneous integrated boost of 55 Gy- 57 Gy in 25 fractions over 5 weeks at 2.25 Gy per fraction to the involved pelvic nodes. Concurrent chemotherapy with weekly injection Cisplatin at 40 mg/ m2 was given to all patients. After completion of external radiotherapy, intra-cavitary brachytherapy was given at a dose of 7 Gy HDR (High-dose-rate) to HR-CTV in four

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 01, 2024

fractions 3- 4 days apart. The dose of HR CTV D90 should be 85 Gy + /-10%.
Pelvic treatment volume delineation was in accordance with published guidelines [13, 14]. Bladder, rectum, sigmoid, femurs, kidneys and spinal cord were delineated as organs at risk (OAR) as per the RTOG (Radiotherapy oncology group) guidelines, and all the potential space for bowel loops in the abdomen was delineated as bowel bag.

Results

30 patients with biopsy proven cervical cancer were included in this study. After treatment completion, the patients were evaluated every 3 months for the first 2 years, and every 6 months thereafter. Acute toxicity as per CTCAEv4 (Common Terminology Criteria for Adverse Events Version 4.0), was defined as toxicity occurring between the initiation of treatment and 90 days after completion. Acute toxicity was assessed weekly during the course of radiotherapy, at the completion of RT and after 1 month. Late or delayed toxicity was defined as adverse events for >90 days after the treatment completion. The late toxicity were graded according with the Radiation Therapy Oncology Group (RTOG) late radiation morbidity scoring system.
Weekly toxicity evaluation was done and the highest reported toxicity grade from the date of EBRT initiation to 6 weeks after treatment completion was recorded as worst acute toxicity. Rapid arc was well tolerated in all the patients with predominant occurrence of Grade 1 and 2 toxicities.
2 patients didn't receive brachytherapy post EBRT. Six patients had grade 1 diarrhoea, four patients developed grade 2 diarrhoea and three of them had grade 3 diarrhoea during treatment period. There were no RT interruptions because of acute toxicity. Three patients in the group needed chemotherapy deferral owing to grade 2 neutropenia. The occurrence of vomiting as toxicity increased with increase in the volume of bowel bag receiving 45 Gy. The median volume of PTV in the patient cohort was 2889 cc (range 2421-2996 cc).

Delayed toxicity and clinical response

The median follow up period was 15 months (range 3-21 months). Delayed toxicity predominantly manifested as grade 1 pain abdomen which was seen in 15 of 30 patients and there was isolated delayed grade 1 cystitis in the 4 patients cohort. During 1st follow up, 5 patients had residual disease. Follow up at 6 months revealed persistent local disease in 4 patients and 5 patients with bulky nodes had persistent pelvic nodal disease. Isolated PA nodal recurrences were not observed in any patient. No patient had local failure as their only site of recurrence.

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Table 1: Toxicities

Acute toxicity	Grade 1 (%)	Grade 2 (%)	Grade >=3(%)
Diarrhoea	6 (20%)	4(13.3%)	3(10%)
Neutropenia	5 (16.7%)	3(10%)	-
Late toxicities	Grade 1	Grade 2	Grade >=3(%)
Pain abdomen	15 (50%)	-	-
Cystitis	4 (13.3%)	-	-

Discussion

A prospective observational study was conducted in the Department of radiation oncology which involved 30 patients with biopsy proven cervical cancer. Previously, the incidence rates of grade 3 bowel and hematologic toxicities with extended field irradiation delivered using conventional 4 field technique were 2-25% and 20-80% respectively [15]. With the advent of concurrent chemo-irradiation and rapid arc, despite using a large field and no bone marrow constraints no grade 3 toxicities were observed in present study. Despite the use of a SIB to boost the involved pelvic lymph nodes, there wasn't any increase in acute toxicities attributable to the volume of high dose regions surrounding the SIB. This finding is consistent with those in the study by Vargo *et al.* [16] and Gerstzen *et al.* [17] where they used a similar dose to boost involved pelvic lymph nodes. They reported that SIB was well tolerated and did not report any increased toxicity due to SIB.

Jin Hee Kim *et al.* [18] had compared toxicities with external field irradiation (EFI) and pelvic only radiation (PRT). 57 patients with biopsy proven cervical cancer were allotted into each group. Acute gastrointestinal and haematological toxicities were lower with EFI when compared to PRT, however they were not significant. The EFI group had a significantly higher frequency of grade 3-4 thrombocytopenia than the PRT group.

Jason *et al.* [19] compared outcomes of 96 patients with cervical cancer. There was no significant difference in rates of grade 3 acute or late toxicities between the pelvic nodal radiotherapy group and para- aortic nodal radiotherapy group.

Conclusion

The present study revealed that prophylactic para-aortic irradiation using rapid arc combined with chemotherapy to treat PALN metastasis can be used with more tolerable toxicities when compared with conventional radical pelvic radiation and chemotherapy.

The main shortcoming of our study was the sample size. A larger sample size and longer median follow up would probably be better.

Acknowledgment: The authors would like to thank the staff in department of radiation oncology for providing with all the facilties to carry out this study.

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 01, 2024

Conflicts of Interest: Nil.

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ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 01, 2024

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