



PELVIC LYMPH NODE AND ITS SIGNIFICANCE IN TREATMENT OUTCOME IN PATIENTS WITH CARCINOMA CERVIX

Oncology

Amit Agarwal*	Assistant Professor, Department of Radiotherapy, G.R. Medical College, Gwalior, Madhya Pradesh. *Corresponding Author
Chinky Garg	Junior Resident, Dept of Surgery, Index Medical College, Indore, Madhya Pradesh.
Bhavya Patneedi	Junior Consultant, HCG Cancer Center, Mumbai, Maharashtra.

ABSTRACT

Objective: To study role of pelvic lymph nodal involvement in treatment outcome in carcinoma cervix.

Materials and methods: This was a prospective open label study conducted in patients with carcinoma cervix during July 2014 to June 2016. Enrolled patients underwent chemoradiation followed by brachytherapy. Clinical response of each patient was analysed at two timepoint; during radiotherapy and at 6 months post-radiotherapy.

Results: Total of 40 patients were enrolled and at the end of 6 months, 75%, 40%, and 20% of patients had complete response, partial response, and progressive disease, respectively. In this study, among lymph node positive patients, residual was observed in 57% (4/7) of the patients at end of 6 months after treatment. While in patients with node negative status, residual was observed in 18% (6/33) of patients. So, there is difference in disease residual as per lymph node status. This trend was statistically significant ($p=0.031$).

Conclusion: Nodal involvement has significant impact in treatment outcome of patients with carcinoma cervix.

KEYWORDS

INTRODUCTION

According to GLOBOCAN 2020, it has been estimated 19.3 million new cancer cases and 10.0 million cancer deaths were reported during 2020 worldwide. Among females, breast cancer contributed to one fourth of the total cases (24.5%) worldwide and was the leading cancer type in 2020, followed by colorectal cancer (9.4%) and lung cancer (8.4%). Cancer of the cervix uteri was the fourth most commonly diagnosed cancer type among females with 604,107 (6.5%) new cases 2020 and also the fourth leading cause of mortality due to cancer worldwide [1].

As per GLOBOCAN 2020 data, there were 678,383 new cases of cancer in Indian females of which, the most common cancer was breast cancer contributing to 26.3% cases in 2020. However, in contrast to worldwide data cancer of cervix uteri was the second leading cancer in Indian females with 123,907 (18.3%) cases [2]. According to a recent report, the projected number of patients with cancer in India are 1,392,179 for the year 2020, and the fourth leading cancer after breast, lung, mouth was cervix uteri [3].

Cervical cancer is not very common in females aged less than 30 years. It is more commonly seen in women aged more than 40 years and the incidence increase as the age progresses and advances with stage [4]. Several factors that increase the risk of cervical cancer in women have been noted. These include younger age, having multiple sexual partners or having promiscuous male partners, poor genital hygiene, history of smoking or sexually transmitted diseases.

It is a well-known fact that few viruses contribute to the development of cancers in humans. Around 15% to 20% of all the cancer cases are considered to be related with viral infections. One of such oncogenic viruses is human papillomavirus (HPV) which is generally transmitted sexually [5]. In a study it has been reported that high-risk HPV DNA was found in 99.7% of cervical cancer samples [6]. Patients who have had a high-risk HPV types infection tend to continue which increase the chances of progression to cervical cancer [5]. The squamocolumnar junction is considered the most common site for the development of cervical cancers particularly between the columnar and the squamous epithelium of the ectocervix where constant metaplastic changes happen. At the age of puberty and at the first pregnancy there are highest chances of metaplastic activity; however, post-menopause this generally decreases. Overall, the age of highest metaplastic activity matches the highest risk of HPV infection leading to increased risk of cervical cancer [7]. More than 80% of the total cervical cancers are due to squamous cells followed by adenocarcinomas; however, adenocarcinomas are four-fold more common in cervical stumps than squamous cell carcinomas [8].

Several factors are described that help in monitoring the prognosis and outcomes in cervical cancer patients. The patient related factors include age of the patient, associated comorbid conditions, status of renal impairment, hemoglobin level, and history of HPV infection. Tumor related factors include stage of the cancer, involvement lymph nodes, parametrial extension, hydronephrosis, grade and tumor size, and the treatment related factors include duration of the treatment, dose of total radiation and use of chemotherapy. In general, the 5-year survival rates are stage I – greater than 90%, stage II – 60-80%, stage III approximately 50% and stage IV – less than 30%.

The treatment of cervical cancer depends on various factors and may vary from stage to stage. The most common strategy for the management of cervical cancer is simultaneous use of radiotherapy and chemotherapy, particularly in patients with advanced disease. In the present study, we aimed to evaluate the role of pelvic lymph node and its significance in management and clinical outcomes of patients with carcinoma cervix.

METHODS

This was a prospective open label study conducted at the department of radiotherapy at SRMS, Bareilly between July 2014 and June 2016. The study included patients aged more than 18 years with biopsy proven carcinoma cervix, Karnofsky performance scale above 70, stage IA to IIIB, no history of previous malignancy, and the patient should have adequate hepatic, renal and cardiopulmonary functions. Patients with carcinoma of the cervix with FIGO stage IV, patients with metastatic disease, any other previous pelvic surgery, previous chemotherapy, or previous history of pelvic radiotherapy were excluded from study.

The study protocol and all the relevant documents were reviewed and approved by the institutional ethics committee. The study was conducted in accordance with the Good Clinical Practice guidelines and Declaration of Helsinki. All the study participants provided written informed consent for participation in the study.

All patients received a radiotherapy dose of 50 Gy in 25 fractions at 200cGy/day through a three-Dimensional Conformal radiotherapy using four field box technique. According to departmental protocol, this radiotherapy was followed by intracavitary brachytherapy (four applications of 6Gy/fraction or three applications of 7Gy/fraction each). This treatment was completed in less than two months of duration. Intravenous administration of cisplatin 35 mg/m² weekly intravenous for a total of 5 cycles or 75 mg/m² triweekly for two cycles was received in all patients.

Assessment of clinical response was done as per WHO criterion at different study timepoints; during radiotherapy and at follow-ups in the intervals of one month until 6 months after radiotherapy. Statistical

analysis was done using SPSS software and chi-square test was used to determine association between presence of nodes and clinical outcomes. A p-value of <0.05 was considered as statistically significant.

RESULTS

Total of 40 patients with carcinoma cervix were enrolled in this study. Of these, at the study endpoint (6 months follow-up), majority of patients had complete response (n=30; 75%) followed by patients with partial response (n=8; 20%); while two (5%) patients showed progressive disease (Figure 1).

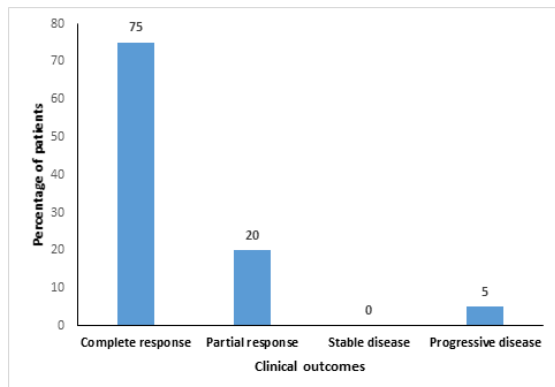


Figure 1: outcome of treatment of patients at the end of 6 months

Among the patients with lymph node positive status, residual was observed in 57% (4/7) of the patients at end of 6 months after treatment. While in patients with node negative status, residual was observed in 18% (6/33). The difference in the proportion of disease residual according to the lymph node status was significant ($p=0.031$) (Table 2).

Table 1: Lymph node vs response at 6 months

Lymph node status	Total Number of Patients	No. of Patients disease-free at 6 months follow-up, n (%)	p-value
Node Positive	7	3(43)	0.031
Node Negative	33	27(82)	

DISCUSSION

A study evaluating impact of lymph node density on prognostic outcomes in patients with lymph node-positive cervical cancer reported a significant association of lymph node density with disease-free survival ($p=0.01$) and overall survival ($p<0.05$). Further, the lymph node density higher than 10% was suggested as an independent prognostic marker for impaired disease-free survival and overall survival outcomes [9].

Node -positive patients could be divided into low risk group (without common iliac node involvement) and high-risk group (with common iliac node involvement). A study by Xiong Y, et al. reported a relationship of common iliac node involvement with the prognosis of patients with cervical carcinoma and pelvic lymph node metastasis. They observed a significantly reduced 5-year disease free survival in patients with common iliac node involvement than those without common iliac node involvement (24.5% vs. 69.4%; $p=0.003$) [10]. Further, Agarwal A, et al. reported that in patients with stage IIB to IVA cervical cancers, a 5-year disease-free survival was lower in patients with node involvement (pelvic-node positive, 34% and para-aortic node positive, 12%) as compared to node negative status (57%) [11].

Impact of lymph-node involvement on a 3-year disease-free survival was reported in few studies. Patients of stage IB-IIA with node negative status had 100% disease-free survival and those with node positive status had 67% of disease-free survival. On the other hand, patients from stage IIB-IVA with node negative status had 56% and those with node positive status had 24% of disease-free survival [12, 13]. Most notably, the FIGO system is oblivious to the lymph node status.

In the present study lymph node positivity was observed in 17.5% of patients. In these node positive patients, two had para-aortic nodes. One patient with para-aortic node had bilateral pelvic nodes. Out of patients with node positive status, residual was observed in 57% of the

patients. While in patients with node negative status, residual was observed in 18% of patients. So, there is difference in disease residual as per lymph node status. This trend is statistically significant ($p=0.031$). Similar to other studies, in this study lymph node involvement was observed to be a major risk factor for poorer survival outcomes in patients with cervical cancer.

In a retrospective study including records of 85 patients, pelvic lymph node enlargement, and distant metastasis were significantly and independently related to poor outcomes [14]. In a study of Jung-Woo Park, medical records of 163 patients were retrospectively reviewed and reported that poor survival outcomes in patients with carcinoma cervix is significantly associated with the number of lymph node metastases ($p=0.021$) [15].

CONCLUSION

Lymph node involvement of patients in cancer cervix appeared to be one of the strongest factors to impact on disease free survival in the present study.

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