

# Assessment of radiological prognostic factors in patients with carcinoma cervix treated with concurrent chemoradiation: A clinical study

Manraj Singh Kang<sup>1</sup>, Taranjeet kaur<sup>2</sup>, Gaurav Jaswal<sup>3</sup>, D P Singh<sup>4</sup>, Gagandeep Singh<sup>5</sup>  
Khusbu Goyal<sup>6</sup>

<sup>1</sup>Assistant Professor, Department of Radiation Oncology, GGS Medical College and hospital, Faridkot

<sup>2</sup>Senior Resident, Department of Radio-diagnosis, GGS Medical College and hospital, Faridkot

<sup>3</sup>Consultant Radiation Oncologist, Onco-LifeCare Cancer Center Hospital, Chiplun

<sup>4</sup>Professor and head, Department Radiation Oncology, Mahatma Gandhi University of Medical Sciences & Technology, Jaipur

<sup>5</sup>Senior resident, Department of Radiation Oncology, GGS Medical College and hospital, Faridkot

<sup>6</sup>Junior resident, Department of Radiation Oncology, GGS Medical College and hospital, Faridkot

<sup>2</sup>Email: loveykochhar@gmail.com

## **ABSTRACT:**

***Aims & Objective:*** The present study was undertaken for assessing the radiological prognostic factors in patients with carcinoma cervix treated with concurrent chemoradiation.

***Materials & methods:*** A total of 40 patients were included. Only those patients were included which had histological proven diagnosis of carcinoma of cervix. Patients were within the age range of 19 to 60 years. Complete demographic and clinical details of all the patients were obtained. Thorough physical examination of all the patients was carried out. Treatment planned was 3-dimensional conformal radiotherapy with concurrent chemotherapy followed by radiotherapy and follow-up for 6 months.

***Results:*** Out of 40 patients, 25 patients had NED after 6 months while in 15 patients were of residual after 6 months. Among the patients with NED, 16 patients had parametrical extension of less than lateral pelvic wall while disease dimension was more than 6 cm in 17 patients. Hyponephrosis was present in 2 patients. Among the patients with residual, 10 patients had parametrical extension of less than lateral pelvic wall while disease dimension was more than 6 cm in 15 patients. Hyponephrosis was present in 5 patients.

***Conclusion:*** Patients with higher parametrical extension upto pelvic wall, hydronephrosis and greater dimension were associated with pelvic failure of disease at follow-up.

***Key words:*** Radiotherapy, Cervix, Carcinoma

## Introduction

Cervical cancer is the third most common cancer in women worldwide, accounting for 9% of total new female cancers. Although the prognosis of locally advanced disease is poor, the introduction of concurrent chemotherapy has improved survival of these patients compared with radiation therapy (RT) alone due to the synergistic interaction between chemotherapy and RT. Concurrent chemoradiation therapy (CCRT) is therefore used as the standard treatment for locally advanced cervical cancer (LACC).<sup>1-3</sup> In early stage cervical cancer (i.e., clinical stage IA tumors with <6% chance of presenting pelvic or para-aortic nodal involvement), the treatment of choice is surgery. The selection of adjuvant therapy will depend on the risk of relapse: patients with a high risk of relapse – defined as presenting one or more of the following factors: positive pelvic nodes, parametrial invasion, positive surgical margins (parametrial/vaginal), and a probability of recurrence of 50–60% – require concomitant chemoradiotherapy.<sup>4-8</sup> The prognosis for advanced or recurrent cervical carcinoma is poor, with a 1-year survival rate between 10% and 15%. The need for effective therapy in this clinical setting is well recognized and optimal treatment has yet to be defined.<sup>7-9</sup> Hence; the present study was undertaken for assessing the radiological prognostic factors in patients with carcinoma cervix treated with concurrent chemoradiation.

## Materials & methods

The present study was undertaken for assessing the radiological prognostic factors in patients with carcinoma cervix treated with concurrent chemoradiation. A total of 40 patients were included. Only those patients were included which had histological proven diagnosis of carcinoma of cervix. Patients were within the age range of 19 to 60 years. Patients with history of previous malignant neoplasm, hepatic or renal failure, and patients with presence of cardiac abnormalities were excluded. Complete demographic and clinical details of all the patients were obtained. Thorough physical examination of all the patients was carried out. Treatment planned was 3-dimensional conformal radiotherapy with concurrent chemotherapy followed by radiotherapy and follow-up for 6 months. All the results were recorded in Microsoft excel sheet and were analyzed.

## Results

In the present study, 40 patients were analyzed. Mean age of the patients was 42.8 years. Out of 40 patients, 25 patients had NED after 6 months while in 15 patients were of residual after 6 months. Among the patients with NED, 16 patients had parametrical extension of less than lateral pelvic wall while disease dimension was more than 6 cm in 17 patients. Hyponephrosis was present in 2 patients. Among the patients with residual, 10 patients had parametrical extension of less than lateral pelvic wall while disease dimension was more than 6 cm in 15 patients. Hyponephrosis was present in 5 patients.

Table 1: Radiological variables

Variable		Number of patients NED after 6 months (n=25)	Number of patients with residual after 6 months (n=15)
Parametrical	Present less than	16	10

extension	lateral pelvic wall		
	Present upto lateral pelvic wall	2	5
	No involvement	7	0
Disease dimension	< 4 cm	3	0
	4 to 6 cm	5	0
	>6 cm	17	15
Hyponephrosis	Present	2	5
	Absent	23	10
Grade of vascularity	Grade I	1	0
	Grade II	7	5
	Grade III	17	10

## Discussion

Cervical cancer is one of the leading causes of morbidity and mortality worldwide, despite efforts to improve treatment outcomes. It is the fourth most common cancer, with a mean incidence rate of 9.0 cases per 100,000 persons in developed countries and 17.8 cases/100,000 in developing countries. Cervical cancer is closely associated with human papilloma virus (HPV) infection. Nearly 80% of cervical cancer-related deaths occur in low income countries with inadequate screening measures. The treatment of early stage disease includes surgery and radiotherapy. The standard of care for locally advanced disease is radiotherapy in combination with cisplatin-based chemotherapy and this treatment may be curative in patients with limited metastatic involvement.<sup>6-9</sup> Hence; the present study was undertaken for assessing the radiological prognostic factors in patients with carcinoma cervix treated with concurrent chemoradiation.

In the present study, 40 patients were analyzed. Mean age of the patients was 42.8 years. Out of 40 patients, 25 patients had NED after 6 months while in 15 patients were of residual after 6 months. Endo D retrospectively reviewed records of 85 consecutive patients with cervical cancer who were treated with Concurrent chemoradiotherapy (CCRT) between 2002 and 2011, with external beam radiation therapy, intracavitary brachytherapy, and platinum-based chemotherapy. Of the 85 patients, 69 patients (81%) had International Federation of Gynecology and Obstetrics (FIGO) stage III/IV disease; 25 patients (29%) had pelvic lymph node enlargement (based on magnetic resonance imaging), and 64 patients (75%) achieved clinical remission following treatment. Median maximum tumor diameter was 5.5 cm. The 3- and 5-year overall survival rates were 60.3% and 55.5%, respectively. Cox regression analysis showed tumor diameter >6 cm, pelvic lymph node enlargement, and distant metastasis were significantly and independently related to poor outcomes. New treatment strategies should be considered for locally advanced cervical cancers with tumors >6 cm and radiologically enlarged pelvic lymph nodes.<sup>10</sup>

In the present study, among the patients with NED, 16 patients had parametrical extension of less than lateral pelvic wall while disease dimension was more than 6 cm in 17 patients. Hyponephrosis was present in 2 patients. Lee YY et al reviewed the electronic medical

records to find patients with primary ECC (FIGO stages IB-IIA) who underwent type III radical hysterectomy and adjuvant CCRT due to pelvic LN metastasis. Among 75 patients, 34 received weekly cisplatin. Combination chemotherapy was performed without consolidation in 21 patients and with consolidation in 20 patients. The mean follow-up period was 59.0 months and the five-year survival rate was 84.4%. In multivariate analysis, combination chemotherapy with and without consolidation was associated with improved disease-free survival [hazard ratio (HR)=0.23, 95% confidence interval (CI)=0.06-0.88,  $p=0.032$ , and HR=0.29, 95% CI=0.09-0.91,  $p=0.034$ , respectively]; combination chemotherapy with consolidation significantly improved overall survival (HR=0.11, 95% CI=0.02-0.87,  $p=0.037$ ) when compared to weekly cisplatin. They found that platinum-based combination chemotherapy during adjuvant CCRT after surgery promoted better survival than a weekly cisplatin regimen in ECC patients with pelvic LN metastasis.<sup>11</sup>

In the present study, among the patients with residual, 10 patients had parametrical extension of less than lateral pelvic wall while disease dimension was more than 6 cm in 15 patients. Hyponephrosis was present in 5 patients. Wang CC et al identified the prognostic factors for locally advanced cervical cancer patients treated by intensity-modulated radiotherapy (IMRT) and concurrent cisplatin-based chemotherapy. A total of 125 patients with stage IB2–III cervical carcinoma were treated with IMRT and concurrent cisplatin-based chemotherapy, plus high dose rate (HDR) brachytherapy between January 2004 and November 2010, in our institution. All patients received external irradiation of 45–54 Gy with the IMRT technique and concurrent cisplatin-based chemotherapy monthly or weekly. HDR brachytherapy of 20–30.5 Gy was prescribed to point A, as a local boost. Prognostic factors including age, histology, stage, lymph nodes metastasis, pretreatment hemoglobin level, serum squamous cell carcinoma antigen (serum SCC-Ag), chemotherapy regimens and the cumulative dose of weekly cisplatin, were analyzed. The endpoints were overall survival (OS), local failure-free survival (LFFS) and disease-free survival (DFS). The median follow-up time was 42 months. The 4-year OS, LFFS and DFS were 73.8%, 77.9% and 67.2%, respectively. Four (3.2%) patients developed  $\geq$ grade 3 acute gastrointestinal (GI) toxicity and 29 (23.2%) patients developed  $\geq$ grade 3 acute hematological toxicity. Five (4.0%) patients developed  $\geq$ grade 3 late GI toxicity and seven (5.6%) patients developed  $\geq$ grade 3 late genitourinary system toxicity. On univariate analysis, adenocarcinoma was a poor prognostic factor for OS ( $p = 0.05$ ), LFFS ( $p = 0.01$ ) and DFS ( $p = 0.006$ ). Patients with lymph nodes metastasis at diagnosis had worse OS ( $p = 0.02$ ). The high cumulative dose of cisplatin ( $>180$  mg/m<sup>2</sup>) had better OS ( $p = 0.03$ ) and tended to have better survival on LFFS ( $p = 0.13$ ) and DFS ( $p = 0.10$ ). On multivariate analysis, adenocarcinoma was a significant independent prognostic factor for OS ( $p = 0.001$ ), LFFS ( $p = 0.005$ ) and DFS ( $p < 0.001$ ). Initial lymph nodes metastasis was an independent predictor of OS ( $p = 0.013$ ). Cumulative dose of weekly cisplatin significantly affected OS ( $p = 0.041$ ), and high cumulative dose of cisplatin tended to have better LFFS. Adenocarcinoma and lymph nodes metastases were poor prognostic factors for patients with locally advanced cervical cancer.<sup>12</sup>

## Conclusion

Patients with higher parametrical extension upto pelvic wall, hydronephrosis and greater dimension were associated with pelvic failure of disease at follow-up.

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