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Comparision of Lymph Node Coverage in Conventional Versus Computed Tomography Simulation Planning For Radiotherapy Treatment in Cervical Cancer

Gerim Prasai, Bibek Acharya, Sandhya Chapagain, AmbujKarn, Sauharda Lohani, Aarati Shah
National Academy of Medical sciences, Bir Hospital, Nepal

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I. INTRODUCTION

Cervical cancer is one of the most common gynecological problems in the world. It ranks fourth in both incidence and mortality. It is the fourth common cancer in women with 85% of the cases occurring in developing countries. According to Globocan 2018, most common cancer in female in Nepal was cervical cancer accounting for 18.5%.[i]

Principle causative agent of cervical cancer is the persistent Human Papilloma Virus (HPV) infection, of which HPV types 16 and 18 have been found to be responsible for more than 70% of the cases. Other known risk factors associated with cervical cancer are early menarche, early child birth, early age of first intercourse, multiple sexual partners, multiple pregnancies, history of sexually transmitted diseases and smoking.

Locally, the tumor may spread to the adjacent vaginal fornices, paracervical or parametrial tissues or adjacent organs, including the bladder and the rectum. Most commonly involved group of lymph nodes are - the obturator, hypogastric, external iliac and common iliac nodes. The incidence of involvement of pelvic nodes in carcinoma of cervix in International Federation of Gynecology and Obstetrics (FIGO) Stage I is observed to be around 15%; stage II is 30% and stage III is 50%. Tanaka et al reported 49% 5year survival for those with involved pelvic lymph nodes, and 92% for patients with negative lymph-node involvement. Hence, for optimal therapeutic outcome, it is of utmost importance that these groups of nodes are not missed in the radiotherapy portals irrespective of the technique used.

Regional lymph node involvement is an important prognostic factor in determining the clinical outcome in patients with cervical cancer. Therefore, adequate coverage of the draining pelvic lymph nodal regions is essential, as grossly unenlarged nodes on imaging may still harbor micro metastasis.

EBRT plays an important role in the management of patients with carcinoma cervix. EBRT treats the whole pelvis, including clinically and radiologically apparent tumor, uterine corpus, upper part of vagina, parametrium and the draining lymph nodes. EBRT along with concurrent chemotherapy followed by brachytherapy is the primary treatment choice for stages IB2 to IVA disease. Patients with stages IA to IB1 may be considered for External Beam Treatment if they are deemed inoperable or prefer to avoid surgery.

EBRT simulation can be done via two techniques: Conventional or Computer Tomography simulation planning. Conventional simulation may involve either the opposed antero-posterior and posterior-anterior or 4 field box technique. They are planned using the radiologically determined bony landmarks. During treatment planning by Conventional technique, the superior border is set at the L4-5interspace, which corresponds to the aortic bifurcation and the lateral borders are placed 1.5 to 2 cm from the pelvic brim. The inferior border covers the lower margin of the obturator foramen. When there is vaginal involvement, the entire length of vagina is treated, down till the introitus.

CT simulation allows direct visualization and assessment of pelvic vessels and the draining lymph nodes. Planning is done based on Gross Tumor Volume (GTV), Clinical Target Volume (CTV) and Planning Target Volume (PTV).

In spite of the emergence of various new conformal techniques in radiation therapy, conventional techniques still hold vital importance. Majority of patients are treated with conventional techniques in Nepal, due to limited resources and lack of technical facility[x]. However, it has been observed that regional recurrence rate after conventional RT is quite high, and this can be attributed to marginal failure (indicating deficiency in target volume).

The five-year survival rate comparing conventional RT Vs. 3DCRT in cervical cancer

was observed to be 73% VS 82.3% ($p<0.007$). It was observed that cervical cancer patients treated with 3DCRT had better overall survival rate.

Various studies have been conducted to evaluate the coverage of pelvic lymph nodes in conventional treatment planning and computed tomography treatment planning. In a study by Mishra et al, they concluded that with conventional simulator-based RT planning the superior border of radiation portal should be kept above mid-vertebral level of L4 in advanced carcinoma cervix patients to adequately cover common iliac group of lymph nodes.

The relationship between conventional pelvic fields and pelvic lymph node coverage plays an important role in the treatment of cervical cancer and will give a perspective of conventional planning in comparison to CT simulation in our set up. Thus, this study was designed to compare the coverage of lymph nodes in conventional versus CT simulation planning in treatment of cervical cancer.

Objective:

To compare the coverage of lymph nodes between conventional and CT simulation treatment planning in treating cervical cancer by Radiotherapy.

Methodology

The study was carried out after ethical clearance was taken from IRB, NAMS. This is a Comparative Observational study. All patients of cervical cancer attending the out-patient department were staged according to the FIGO staging system. Cases for the study was selected as per the inclusion criteria.

Inclusion Criteria

1) Histological proven cervical carcinoma
2) Patients with cervical cancer (FIGO Stage IB2 to IVA) planned for radiation therapy

Exclusion Criteria

1) Post-Operative cases of cervical cancer
2) Stage IIIC2 and IV B
3) Patient not giving consent

Patient positioning: Patients were kept in supine position with arms above or on their chest. Pelvic immobilization was done using the thermoplastic cast or vac-lock. Markings were done in anterior and lateral sides, aligned with lasers to prevent rotations to ensure precise and accurate radiation delivery. Clinical examination were done in treatment position and inferior extent of tumor in vagina was marked with radio-opaque material.

Using IV contrast to outline pelvic blood vessels, CT scan was taken from D8 to Mid-thigh with 3mm CT scan cuts. Images obtained were transferred to the Treatment Planning System (TPS) and contouring was done. GTV, CTV, PTV were taken as per Consensus Guidelines for delineation of CTV for definitive treatment of Cervix cancer[xviii]and pelvic lymph nodes contouring was done as per Taylor et al[xix].

The outlines of the conventional pelvic fields were virtually drawn on TPS as per the bony landmarks. Assessment of pelvic nodal coverage were done between CT simulation and virtually outlined borders representing the standard field borders of 2D. For the anterior/posterior (AP) field, the superior border was placed at the L4-L5 interspace; the inferior border was placed at the inferior aspect of the obturator foramen, and the lateral border was placed 2.0 cm beyond the widest part of the pelvic brim. Evaluation of coverage was done in coronal view. Inclusion of lymph nodes in both planning techniques were tabulated and then compared.

Data Collection: Data collection was done on a structured proforma within a period of one year. Patient's name, age, occupation, hospital number, date of enrollment, diagnosis with FIGO staging and coverage of lymphatics by both simulation technique was recorded in the proforma.

Data Analysis: The data were entered in the SPSS 16 software on a master chart following which statistical analysis was done. Data were analyzed and the variables were correlated and tested for statistical significance. A 95% confidence interval and p value less than 0.05 was termed as statistically significant.

II. RESULTS

There were 100 patients who were the study participants in this study. The age rangeof the participants varied from 28 years to 76 years. The median age of studypopulation was 45 years. The most common stage was stage IIIC1, with 50 cases falling in this category, followed by Stage IIA with 22 cases. The most common symptom that 59% of the cases presented with was found to be menorrhagia, followed by lower abdominal pain in 26% of the cases.

In the study population, 48 of the cases did not have any lymph node involvement.

While, among those with nodal involvement, involvement of external iliac nodes was found to be the highest 22%, followed by internal iliac nodes in 18%.

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The most common level of aortic bifurcation which corresponds to the level of common iliac lymph nodes was observed to be in the upper level of L4 i.e. in 21 % of population.

In conventional planning, there was lymph node coverage in 12% of cases in superior border, 86% of cases in lateral border and 100 % in inferior border. There was 100% lymph node coverage in CT simulation planning. In 88% of cases, lymph nodes were missed in superior border while in 14% of cases, lymph nodes were missed in lateral border. (shown in Table 1)

The mean distance between superior border of the field labeled at L4-L5 and aortic bifurcation was 28.4 mm. The minimum distance observed was 5 mm while the maximum distance was 58 mm. The mean distance is 4.85 mm from lateral border of a conventional planning method (2cm from pelvic brim). (shown in Table 2)

	Covered	Missed	Chi Square P Value
Superior Border	12 (12%)	88 (88%)	P<0.001
Lateral Border	86 (86%)	14 (14%)	P<0.001
Inferior Border	100 (100%)	0 (0%)	-

Table 1: Coverage of lymph nodes in Conventional Method

Conventional vs CT simulation (in mm)		
	Superior Border	Lateral Border
Minimum	5.0	4
Maximum	58	6
Mean	28.48	4.85

Table 2: Difference in border between Conventional RT Planning vs CT Simulation based

III. DISCUSSION

According to Globocan 2018, most common cancer in female in Nepal was cervical cancer accounting for 18.5%.**Error! Bookmark not defined.**Concurrent chemo-radiation has shown promising results in treatment of cervical cancer especially in stage IB2 to stage IVA. It was found that an optimal external irradiation to prevent the loco-regional relapse required an adequate coverage of pelvic lymph nodes.**Error! Bookmark not defined.**

Approximately 5%~50% of patients with radiotherapy would relapse ultimately in their pelvis.**Error! Bookmark not defined.** This loco-regional failure may be caused by inadequate pelvic radiation. The radio-therapeutic fields of patients with cervical cancer in Nepal are mostly planned conventionally by bony landmarks due to unavailability of CT simulator, financial constraints and technical issues.**Error! Bookmark not defined.** By using CT simulation, we found that the conventional radiation fields usually did not have adequate coverage of pelvic lymph nodes, and most of the inadequate coverage were located at common iliac lymph nodes. In the present study, we found that the relationship between conventional pelvic fields and the location of pelvic lymph nodes in Nepalese patients was like that observed in other populations.

Complete coverage of common iliac group of lymph nodes is essential in treatment of carcinoma cervix patients as chances of pelvic lymph node metastasis increases with stage.**Error! Bookmark not defined.** Some studies have shown that most of the marginal recurrences after radiation in treatment of carcinoma cervix occur in the common iliac nodal region. This may be attributed to inadequate coverage of lymph nodes.

In a study by Mishra et al, out of 90 patients evaluated, the median age observed was 50 years. In our study 100 patients were evaluated and the median age was 45 years. The age group is quite similar to this study.

In our study, most common site of aortic bifurcation was upper level of L4 vertebrae i.e. in 21% of cases followed by L3-L4 interspace (19%), mid-level of L3 (16%), lower level of L3 (15%). In the study by Rai et al, the most common site was upper L4 in 31% of cases followed by mid L4 (17.4%), L4-L5 junction (17.2%), Mid L3 (6.9%), Lower L4 (6.9%).**Error! Bookmark not defined.** Most common level of aortic bifurcation of our study was similar to the reference studies. In the study by Mishra et al, mid vertebral level of L4 was the most common site of aortic bifurcation observed i.e. in 45.6% of cases while in the study by Ponni et al, the division of abdominal aorta into common iliac arteries occurred at the level of L3-L4 intervertebral space in 53.84%.

In the study by Beadle et al, in patients with centrally controlled cervical cancer, the most common site of regional recurrence was just above the superior border of the radiation treatment field indicating in an inadequate target volume.**Error! Bookmark not defined.** This emphasizes the importance of adequate target volume coverage. External beam radiation therapy to the pelvis with adequate volumetric coverage of the tissues at risk for dissemination of disease is an essential component of the curative treatment for locally advanced cervix cancer.

Our study showed that in 88% of cases, lymph nodes were missed in superior border while in 14% of cases, lymph nodes were missed in lateral border.

In the study by Gulia et al in 2013, the distance of the target volume from the edges of the field was measured using the Beam's Eye View. They concluded that the median miss at superior border of the fields from aortic bifurcation to L4-L5 junction was 29.5 mm.**Error! Bookmark not defined.** In our study, the mean miss at superior border of the field from aortic bifurcation to L4-L5 was 28.4mm. The minimum distance observed was 5mm while the maximum distance was 58mm.

LAG by Pendlebury et al demonstrated that the most frequently altered fields were the lateral margin in 34% of patients. This is in contrary to our study which showed the most frequent altered field is the superior border. They concluded that to cover pelvic lymph nodes in 90% of patients, the margin required would be 2.5 cm lateral to the pelvic brim. In the study by Tuli D et al, they concluded that the width of the AP: PA portal needs to be increased by 3.6 cm to cover the distal external iliac nodes adequately. In our study the mean distance missed in lateral border was 4.85mm. Hence our study showed the lateral margin required to adequately cover lymph nodes would be 2.5 cm lateral to pelvic brim.

Despite best efforts, several limitations must be considered. First, the retrospective nature of the study introduces inherent biases, such as selection bias and incomplete data capture. Additionally, our analysis is based on data from a single institution, potentially limiting the generalizability of the findings to other patient's populations and healthcare settings.

IV. CONCLUSION

There is inadequate lymph node coverage in conventional treatment planning as compared to CT planning. CT planning is better regarding lymph node coverage during radiotherapy treatment planning and treating cervical cancer.

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