Original Research Paper

Volume - 10 | Issue - 9 | September - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Oncology

COMPARISON OF LATE COMPLICATIONS FOLLOWING CONFORMAL FOUR FIELD RADIOTHERAPY AND WHOLE PELVIC RADIOTHERAPY IN CANCER CERVIX PATIENTS

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ABSTRACT

Objective: Late complication rates of four-field conformal pelvic radiotherapy using CT simulation were compared with those of whole pelvic radiotherapy using parallel opposed fields in cancer cervix patients in a non-randomized study.

Materials and methods: From March 2013 to December 2013, 74 patients who underwent radical chemoradiotherapy for clinical stage I, II or III squamous or adenosquamous cell carcinoma of the uterine cervix were treated with radiotherapy consisting of 50 Gy in 25 fractions in 5 weeks followed by 8Gy in 2 fractions of HDR brachytherapy. Thirty-four patients were treated with four-field 3D conformal technique following computed tomography (CT) simulation using beam's eye view and three-dimensional treatment planning with 15 MV photons on Linear accelerator. Forty patients received the conventional two-field technique, with CT simulation in 13 patients and X-ray simulation in 27 patients.

Results: The actual 5-year pelvic control rate was 94% for the two-field technique and 100% for the four-field conformal technique. The incidence of bowel complications in the four-field conformal technique group (4/34 ,12%) was significantly lower than that in the two-field technique group (12/40 patient , 30 %) ($p < 0.05$). The incidence of bladder complications in the four-field conformal technique group (3/34 ,9%) was significantly lower than that in the two-field technique group (20/40 patient , 50 %) ($p < 0.0123$).

Conclusions: Four-field conformal pelvic radiotherapy using CT simulation appears to be as effective as parallel opposed whole pelvic radiotherapy with a lower incidence of bowel complication and bladder complications.

KEYWORDS : uterine cervix cancer, radiotherapy, CT simulation, four-field conformal radiotherapy

INTRODUCTION

Radiation therapy plays a vital role in the management of carcinoma of the cervix. Carefully planned and executed radiation therapy yields excellent pelvic control and survival rates (1,2). Many stage IB1 cancers are treated equally effectively with radiation or radical surgery; most more advanced lesions are best treated with radiation. However, treatment modality and technique must be individualized on the basis of clinical, anatomic, and social factors. Optimal treatment selection always requires close cooperation between the patient's referring physician, gynecologic oncologist, and radiation oncologist. Radiation therapy for intact carcinoma of the cervix usually involves a combination of EBRT and brachytherapy. The goal of treatment is to balance EBRT and brachytherapy in a way that maximizes the likelihood of local-regional tumor control while minimizing the risk of treatment complications.

The degree of tissue penetration achieved by a radiation beam is related to the energy of the x-rays delivered from the radiation source. One of the earliest sources used for EBRT was Co 60, which produced a relatively deeply penetrating beam. However, linear accelerators now provide higher energy photon beams (15–25 MV) that are better suited for EBRT because they permit more homogeneous delivery of radiation to deep tissues with relative sparing of superficial tissues. If a four-field technique is used, the anterior border of the field usually includes the anterior tip of the pubis; to cover the tumor, presacral nodes, and uterosacral ligaments, the posterior border usually includes S3 . Custom blocks may be used to shield anterior small bowel, soft tissue, and, in some cases, low rectum on the lateral fields. However, care must be taken not to shield potential sites of disease. Because the inguinal nodes drain the lower third of the vagina, they should be included in the treatment volume whenever the distal vagina is involved with tumor. Whole-pelvis EBRT fields typically are designed with an upper border placed either at the L4-5 interspace. However, the fields may be extended superiorly if the para-aortic nodes are known to be involved or are believed to be at high risk for involvement. Because cervical cancer typically follows an orderly progression along the lymph node chain, the upper border is selected by balancing an estimate of the risk of disease at a given level against the expected morbidity from large-volume EBRT. In general, the upper border is placed at least 4–6 cm above known disease. This is probably sufficient if the patient has had a lymph node dissection with negative nodes above the level of involvement. Bulky or multiple nodes probably warrant greater extension of the fields, particularly if the patient has not had surgical evaluation of the nodes. Although the survival rate of patients with aortic node metastases is significantly less than that of patients with similar-stage disease who do not have this finding, about 20– 40% of patients with aortic node metastases are curable with radiation alone, depending on the extent of pelvic disease.

Complications of radiation therapy are usually characterized as acute (occurring during or shortly after treatment), or late (occurring more than a few weeks and sometimes many years after radiation therapy). The acute complications of radiation therapy usually resolve within 2–3 weeks after completion of treatment. Pelvic irradiation may cause acute proctosigmoiditis. Two to three weeks after the beginning of treatment, patients may develop diarrhea; on rare occasions, this may be associated with passage of blood and mucus or tenesmus. These symptoms usually subside shortly after the completion of EBRT. Rarely patients develop chronic proctosigmoiditis that may lead to stricture or obstruction. In less than 5% of patients, radiation injury to the rectosigmoid may result in progressive ischemia leading to necrosis and occasionally stricture or fistula formation. Approximately 5–10% of patients treated with pelvic radiation develop symptoms of dysuria and urinary frequency during EBRT for carcinoma of the cervix. Although late radiation complications involve the bladder less frequently than the bowel, a small proportion of women will develop symptoms of radiation cystitis one or more years after radical radiation therapy. Some women will have only one or two episodes of sterile dysuria or mild hematuria. Other complication are cervicovaginal necrosis etc.

MATERIALS AND METHODS:

From March 2013 to December 2013, 74 patients who underwent radical chemoradiotherapy for clinical stage I, II or III squamous or adenosquamous cell carcinoma of the uterine cervix were treated with radiotherapy consisting of 50 Gy in 25 fractions in 5 weeks followed by 8Gy in 2 fractions of HDR brachytherapy. Thirty-four patients were treated with four-field 3D conformal technique following computed tomography (CT) simulation using beam's eye view and three-dimensional treatment planning with 15 MV photons on Linear accelerator. Forty patients received the conventional two-field technique, with CT simulation in 13 patients and X-ray simulation in 27 patients. The details of the patients were collected & analysed from the patient medical records. Late complications were graded as grade I, II, III and IV for no requirement for medication, requirement for medical treatment, requirement for surgical treatment and death due to complications, respectively. The Kaplan–Meier method and chi-squared test were used for the comparison of late complications between groups. The mean follow-up period was 108 months for the two-field technique and 55 months for the fourfield technique.

RESULTS

The mean follow-up period was 108 months for the two-field technique and 55 months for the fourfield technique .Bladder complication was observed in 50% (20/40) of the patients in the two-field technique group; 25% (10/40) were grade I and 25% (10/40) were grade II and no patients experienced grade III complication (Table 2). Bladder complication was observed in 9% (3/34) of the patients in the

conformal four-field technique group; 6% (2/34) were grade I and 3% (1/34) were grade II. The incidence of bladder complications in the four-field conformal technique group (3/34 ,9%) was significantly lower than that in the two-field technique group (20/40 patient , 50 %) ($p < 0.0123$) (Table 2). The time of onset of chronic bowel complication was difficult to determine, so the incidence of bowel complication after 6 months was compared without consideration of the time of its onset .The incidence of bowel complications in the four-field conformal technique group (4/34 ,12%) was significantly lower than that in the two-field technique group (12/40 patient , 30 %) ($p < 0.05$) (Table 2). No other late complication was detected during the study period. In the two-field technique group, no difference was demonstrated in survival rates or pelvic control rates.

Table 1: Characteristics of patients:

	Two-field	Four-field	Total
No. of patients	40	34	74
Mean age	52 (31-78_	50(29-62)	51(29-78)
FIGO Stage			
Ia	0	0	0
Ib	10(25%)	6(18%)	16(22%)
IIa	1(3%)	6(18%)	7(9%)
IIb	18(45%)	19(56%)	37(50%)
IIIa	0	0	0
IIIb	11(28%)	3(9%)	14(14%)

Table 2: Late Complications after Radical pelvic radiotherapy for uterine cervix carcinoma:

Bladder complications	**Grade 1**	**Grade2**	**Grade 3**	**Total**	**P value**
Two field (%)	10(25%)	10(25%)	0	20(50%)	P=0.012
Four field (%)	2(6%)	1(3%)	0	3(9%)	
Bowel complications	**Grade 1**	**Grade2**	**Grade 3**	**Total**	
Two field (%)	5(13%)	3(8%)	4(10%)	12(30%)	P<0.046
Four field (%)	4(12%)	0	0	4(12%)	

DISCUSSION

Pelvic radiotherapy for cervical cancer has been associated with high morbidity (12,13). The present study suggests that conformal four-field radiotherapy is useful for reducing the complication rate. The conclusion of this study is consistent with previous reports about pelvic radiotherapy for uterus and prostate cancers (14–17). However, the present study is still an interim report in terms of late complications because the follow-up period is shorter for patients with four-field technique. Further follow-up is required to judge whether the superiority of fourfields technique is real. The lower incidence of bowel complications following irregularly shaped four-field radiotherapy was consistent with the well-known fact that bowel complications can be reduced by minimizing the volume of bowel structure that receives doses higher than about 45 Gy (18).

Anatomical landmarks are not optimal to cover the lymphatics and may be suboptimal for a significant percentage of patients and could be a contributing cause of failure to control cervical cancer (14,20). Zunino et al. have confirmed that using the anterior border of the lateral fields over the anterior edge of the pubic symphysis and the posterior at the S2–3 interspace as the anatomic border of the lateral fields is inadequate in radical radiotherapy for uterine cervix cancer (10). X-ray simulation following pelvic organ opacification using contrast media was shown to be effective for conformal therapy, but the technique is time consuming and uncertainty is caused by bony landmarks (2). Kim et al. have suggested that CT simulation is required to decrease the potential geographic miss when using the four-field technique in radical radiotherapy for uterine cervical cancer (21). With the irregularly shaped four-field technique, the anterior border and posterior border can be determined using internal anatomy rather than bony structure in CT simulation. In the present study, it was not possible to analyze whether CT simulation was useful for reducing geographic miss because of the low incidence of pelvic relapses in both techniques. However, the high pelvic control rate of the irregularly shaped four-field technique in our series may be due to accurate coverage of the clinical target volume. Recent advances in the multi leaf collimator on linear accelerators and 3D radiotherapy planning systems have made it practical to use more conformal fields than were employed with the technique used in this study (22). A further reduction of complication without deterioration in the tumor control rate can be expected using conformal fourfield pelvic radiotherapy with a multileaf collimator. In conclusion, conformal four-field pelvic radiotherapy using CT simulation appears to be as effective as parallel– opposed whole pelvic radiotherapy, with a lower incidence of bowel complication and bladder complication.

CONCLUSIONS:

Four-field conformal pelvic radiotherapy using CT simulation appears to be as effective as parallel opposed whole pelvic radiotherapy with a lower incidence of bowel complication and bladder complications.

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