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Recurrent Carcinoma Cervix–Not the End of World

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Abstract: ***Objective*: In Recurrent Cervical cancer, the impact of Interstitial brachytherapy was seen in patients who had recurrence, for whom Pelvic Exenteration was not feasible due to extensive disease. *Material & Methods*: A total of 15 patients with Recurrent Cervical cancer who developed recurrence after 1yr were treated using Interstitial Brachytherapy. They had received prior Chemoradiation and Brachytherapy. 10 Patients had received Palliative Chemotherapy (Pacli+Carbo-3 to 6 cycles). The patients had received Total Bladder dose of (60-70Gy) and Total Rectal dose received prior was (60-67Gy). Patients received Interstitial irradiation HDR-600 cGy * 3 fractions using a Transperineal Syed-Neblett template with mean tumor dose of 2900 cGY, the mean Bladder dose was 2200cGY and mean Rectal dose was 2000 cGY. *Result*: We analysed 15 patients, 9 patients are alive, 7 patients have complete response, 6 deaths were due to progressive disease. Maximal survival of 26 months was seen in 1 patient. The median average survival after ISBT is 13 months. The complication rates are 40% (GrI-II Cystitis) and 53.3%(GrI-II Proctitis) and 2 patients had Gr IV Proctitis. *Conclusion* : There was no significant differences between the stages. In Patients with Recurrent Cervical cancer who have received prior chemoradiation and having good performance status and who are not suitable for Pelvic Exenteration, reirradiation can be considered by Interstitial Brachytherapy. The total bladder and rectal doses received prior to the treatment is very important before considering Reirradiation.***

Keywords: Recurrent Carcinoma cervix, Interstitial Brachytherapy, High Dose Rate, Total Bladder Dose, Total Rectal dose.

1. Aim

In Recurrent Cervical cancer, the survival outcomes are poor. The impact of Interstitial brachytherapy was seen in patients who had recurrence, for whom Pelvic Exenteration was not feasible due to extensive disease in this study.

2. Background

Although there has been important advances in the management of cervical cancer, the optimal treatment for patients with locally recurrent and metastatic disease is still not clear and there are relatively very few randomized trials to guide treatment decisions.

A 10%-20% recurrence rate has been reported following primary surgery or radiotherapy in women with stage IB-IIA cervical tumors with no evidence of lymph node involvement, while up to 70% of patients with nodal metastases in locally advanced tumors will relapse[(1).]

Perez et al. reported a total pelvic failure rate of 10% in stage IB, 17% in stage IIA, 23% in stage IIB, 42% in stage III, and 74% in stage IVA after radiotherapy alone . The majority of recurrences occur within 2 years of diagnosis and the prognosis is poor, with most of the patients dying as a result of uncontrolled disease[(2).]

In a retrospective review of over 500 patients treated at the University of Kentucky, 31% of patients developed tumor recurrence, 58% of these recurred within 1 year and 76% within 2 years and only 6% of patients with recurrent tumor survived 3 years.

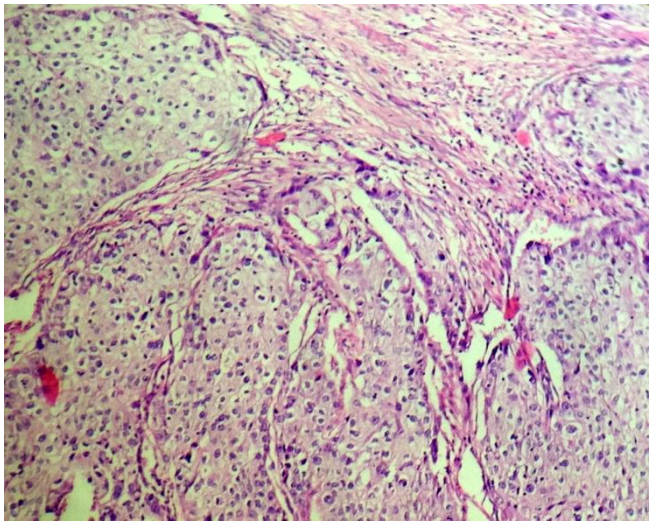
While, it is possible to identify subgroups of patients with recurrent cervical cancer who have a substantially better prognosis and in whom the objective of treatment is cure[(3)]. 50%-60% of patients have disease situated beyond the pelvis which is incurable and treatment is given with only palliative intent.

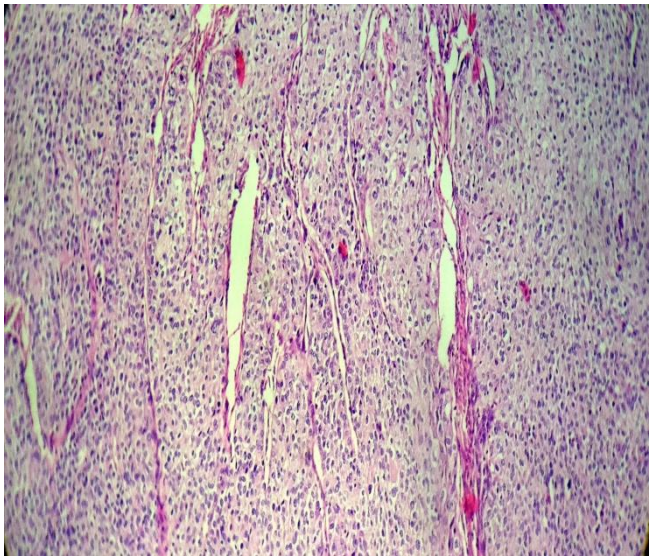
Despite a careful preoperative work-up to exclude distant metastases, about one-third of cases are found to be unsuitable for exenteration at the time of laparotomy due to peritoneal spread, para-aortic node involvement or pelvic side wall involvement.
Interstitial Brachytherapy has the advantage of treating the complete parametrium and to treat the involved parametrium by insertion of the needles. By dosimetric analysis, the dose to tumor can be increased and decreased to the normal tissues, thereby providing better local control.

3. Material & Methods

A total of 15 patients with Recurrent Cervical cancer who developed recurrence after 1yr were treated using Interstitial Brachytherapy. Patients could not undergo Pelvic Exenteration as they had extensive Central and Parametrial disease and were not willing for pelvic exenteration. They had received prior Chemoradiation and Brachytherapy. 10 Patients had received Palliative Chemotherapy (Pacli+Carbo-3 to 6 cycles)[(4).] All had good Performance status. The patients had received Total Bladder dose of (60-70Gy) and Total Rectal dose received prior was (60-67Gy).
Patients received Interstitial irradiation HDR-600 cGy * 3 fractions using a Transperineal Syed-Neblett template with mean tumor dose of 2900 cGY, the mean Bladder dose was 2200cGY and mean Rectal dose was 2000 cGY.

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Histopathology: Carcinoma Cervix- Invasive moderately differentiated Squamous cell carcinoma (non keratinizing type).

Statistical analysis: statistical analysis was done using 'R' software. The survival was analysed by Kaplan Meiers curve.

Table 1: Patient's characteristics
Stage Distribution

Stage	No	%
IIB	4	26.7
IIIA	2	13.3
IIIB	9	60
Total	**15**	**100**

Table 2: Bladder toxicity
Cystitis Distribution

Grade	No	%
0	9	60
1	2	13.3
2	4	26.7
Total	15	100

Table 3: Rectal toxicity
Proctitis Distribution

Grade	No	%
0	5	33.3
1	2	13.3
2	6	40
4	2	13.3
Total	15	100

Table 4: Dose statistics
Summary Statistics Death VS Alive

Variable	Mean	SD	Mean	SD	P-value	Mean	SD
IN_Point_A	30	0	30	0	1	30	0
IN_TBD	16	3.7	18	1.5	0.1743	16.9	3.2
IN_TRD	13.9	2.1	14.3	2.9	0.7365	14.1	2.4
R_Dose	27.4	2	28	2	0.6078	27.7	2
R_TBD	19.4	2.1	18.7	1.2	0.4346	19.1	1.8
R_TRD	15.6	2	17.5	2.8	0.1403	16.3	2.5

Table 5: Response evaluation
Response Status

Response	No	%
Alive	9	60
Death	6	40
Total	15	100

4. Results

Out of the 15 patients, 9 patients are alive, 7 patients have complete response, 6 deaths were due to progressive disease. Maximal survival of 26 months was seen in 1 patient. The median average survival after ISBT is 13 months. The complication rates are 40% (GrI-II Cystitis) and 53.3%(GrI-II Proctitis) and 2 patients had Gr IV Proctitis.

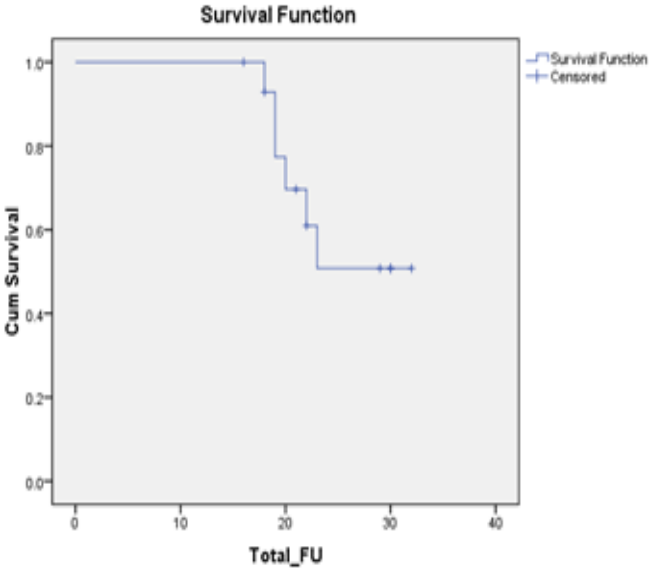


Figure 1: Overall survival before Reirradiation.

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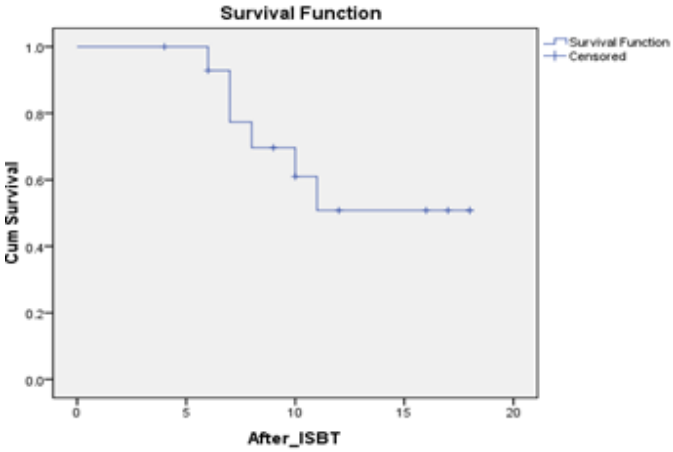


Figure 2: Survival post ISBT.

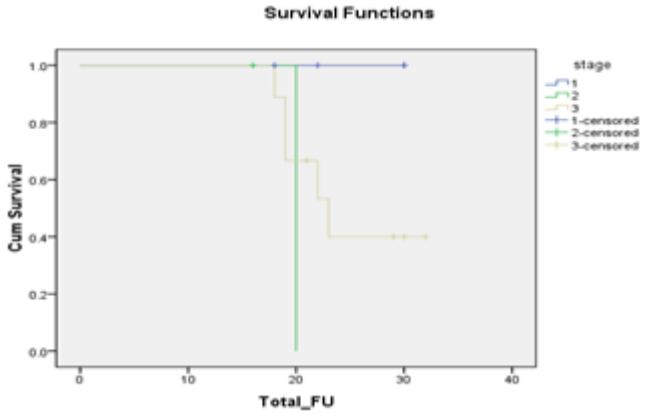


Figure 3: Overall survival, Stage grouped after Re-irradiation.

5. Conclusion

There was no significant differences between the stages, it may be due to less number of cases or events. In Patients with Recurrent Cervical cancer who have received prior chemoradiation and having good performance status and who are not suitable for Pelvic Exenteration, Re-irradiation can be considered by Interstitial Brachytherapy. The total bladder and rectal doses received prior to the treatment is very important before considering Re-irradiation. Future goals of therapy are to increase efficacy of treatment options while decreasing toxicity.

6. Discussion

Treatment decisions should be based on the performance status of the patient, the site of recurrence, the extent of metastatic disease and prior treatment. The prognosis is better for patients with a disease-free interval greater than 6 months, recurrent tumor size <3 cm in diameter and having no pelvic side wall fixation.

With the advent of Image guided Brachytherapy, higher doses of radiation can be delivered to the tumor and increase the likelihood of local control for patients with small volume central recurrences. The bladder and rectal toxicity can be reduced, giving good Quality of life to patients who have very limited options of treatment.

Patients with large volume central or pelvic side wall recurrences have very poor prognosis and efforts should be made to detect pelvic recurrences at the earliest to enhance the chance for long-term survival. A number of chemotherapeutic agents (e.g. Paclitaxel, Vinorelbine, Irinotecan, and Gemcitabine)[5] have been combined with Cisplatin in phase II studies in patients with either locally advanced and/or recurrent cervical cancer[6,7].

Future trials are necessary, not only to compare combinations of existing chemotherapeutic agents but also to incorporate biological agents (monoclonal antibodies or other molecules) in order to improve the treatment results of advanced, persistent or recurrent cancer cervix.

The coordinated efforts of a team of professionals is required to cater to the needs of the patient, to tackle particular problems faced by the individual and decide the goals of treatment. The team should include Radiation Oncologists, Gynecologic Oncologists, Medical Oncologists, Palliative care Physicians, Nursing staff, Psychologists, Stomatherapists and a specialized pain management team.

7. Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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