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Original Research Article

Failure of radical hysterectomy in early invasive cancer cervix: an A. H. regional cancer centre experience

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ABSTRACT

Background: Early invasive invasive carcinoma of cervix is adequately treated by surgery,radiotherapy or by combination of both.The disease-free and overall survival varies from centre to centre. Recurrence of the disease is a reflection of failure in treatment.
Methods: A total of 541 cases of Radical hysterectomy with pelvic lymphadenectomy, for early stage cancer cervix performed during the period 2006 April - 2017 March at A. H. Regional Cancer Centre Cuttack, were retrospectively analysed, with an objective to identify the risk factors responsible for treatment failure. All cases were followed-up for 5 years or more.
Results: Radiotherapy was supplemented in 27% of cases. Recurrence occurred in 17.18% cases. The incidence of recurrence increased from 13.9% in Stage IB to 26.3% in Stage IIB. Younger patients showed a higher recurrence of 19.16% compared to older group. Poorly differentiated squamous cell carcinoma showed 15.9% recurrence and adenocarcinoma showed 15.38% recurrence. Only 3.7% of recurrence occurred in growths <2cms which increased to 20.6% in tumors >5cms diameter. Infiltrating growths were responsible for treatment failure, recurring in 52.4%. Nodal involvement in >2 groups showed increased recurrence (30%) in contrast to 15.65% in node negative patients. Maximum recurrence occurred in the first year of treatment and beyond three years it looked safe. Adjuvant radiotherapy given in 27%, encountered 18.3% recurrence in comparison to the overall treatment failure.
Conclusions: Age, stage, nature of growth, node-involvement, tumor-bulk and histo-pathological grading, combinedly altered the prognosis in early invasive cervical carcinoma treated with radical hysterectomy and selectively supplemented by radiotherapy.

Keywords: Cancer, Cervix, Radical- hysterectomy, Radiotherapy, Recurrence

INTRODUCTION

Worldwide cervical cancer is the third most common malignancy and the second most common cancer in women.[1] Early invasive cervical carcinoma can be treated by radical hysterectomy or radiotherapy, with similar effectiveness. Radical hysterectomy with bilateral lymphadenectomy is an effective treatment option for early invasive cervical carcinoma.[2] Interest in developing a surgical cure for cancer of the uterine cervix, predates from 20th century.[3] Clark, Rumpf and Ries, described radical hysterectomy with lymphnode dissection in the mid-1890s.[4] Wertheim designed radical hysterectomy with selective pelvic lymphadenectomy, as a treatment for early invasive cancer cervix, in the year 1898. This was followed by Schauta's radical vaginal hysterectomy in 1902. Again, there was revival of radical hysterectomy with selective pelvic lymphadenectomy by Wertheim.

This was finally modified by Meigs, who advocated more extensive removal of the parametrium with complete pelvic lymphadenectomy and obtained good disease-free survival results. Appropriate selection is critical when considering whether surgical therapy would be most beneficial to a patient with cancer cervix. The choice of treatment depends upon a number of factors like age of the patient, co-morbidities, experience of the gynaecologist and availability of institutional facilities. When surgery is chosen as the primary therapy, it is supplemented with radiotherapy, if adverse clinicopathological factors are present. These adverse factors are, large volume lesions, deeply invasive tumors, parametrial involvement, positive surgical margins and positive lymphnodes. The aim of postoperative radiotherapy is to prevent recurrence.[5] Therefore early invasive carcinoma of cervix is adequately treated by surgery and radiotherapy, independently or in combination of both. But in spite of the best efforts the results of survival vary between 60%-90%, leading to a failure of treatment in the range of 10%-40%; as stated by Alvarev RD, Soon SJ, Kinney WK et al 1989 and Figge DC, Tamimi HK et al 1981.[6,7] Many factors influence the disease-free survival. Factors like, advanced age, tumor load, histopathologically adenocarcinoma, close resection of clear margins and lymph-node involvement, may modify the result of treatment. Thus, a clear high-risk group and low risk group should be identified for additional adjuvant therapy. Many other studies worldwide also show, the 5-year survival rates for early stage cervical cancer treated by radical surgery to be within 80% to 85% range and these figures drop to 3.2% to 13% when there is recurrence.[8]

METHODS

A total number of 541 patients in Stage IB, IIA and a few in Stage IIB were subjected to Primary Radical Surgery in the form of Wertheim's Hysterectomy, during the period 2016 January to 2016 January, in A. H. Regional Cancer Centre Cuttack. Out of these 146 patients required adjuvant radiotherapy because of specific factors like, lymph-node involvement and difficult dissectibility. There were recurrences in 91 cases during 1-5 years period following surgery. The factors like age, histopathological types, morphology of the growth, size of the tumor, nodal status were analysed in relation to the recurrences.

RESULTS

Table 1: Stage.

Stage	Number	Failures	Failure%
IB	393	55	14
IIA	104	24	23.7
IIB	44	14	31.8
Total	541	93	17.2

The percentage of failures were higher in the advanced stages of 11A and 11B group.

The chi-square statistic is 11.9643. The p-value is 0.002523. The result is significant at $p < 0.05$.

Table 2: Age.

Age in Yrs	Number	Failures	Failure%
20-29	11	0	0
30-39	124	25	20.2
40-49	368	63	17.1
50+	38	5	13.1
Total	541	93	17.2

The chi-square statistic is 1.8437. The p-value is 0.605482. The result is not significant at $p < 0.05$.

Majority of the patients were in the age group of 30-49 years. It was interesting to find few young girls under 29 years in the series.

Table 3: Histopathology.

Histopathology	Number	Failures	Failure%
PD. SCC	471	75	15.9
MD. SCC	5	3	66.66
WD. SCC	32	7	21.8
Adenoca	31	5	15.7
Carcino-sarcoma	2	2	100
Grand Total	541	92	17

The chi-square statistic is 7.5973. The p-value is 0.055111. The result is not significant at $p < .05$. The Chi-square is calculated ignoring

Two cases of Carcinosarcoma had undergone radical hysterectomy had 100% treatment failure.

Table 4: Morphology of lesion.

Type and Size	Number	Failures	Failure%
Exo>2cms	189	8	4
Exo2-4cms	270	46	17
Exo>4cms	33	7	21.2
Infiltrating	49	25	51

The chi-square statistic is 65.4073. The p-value is < 0.00001. The result is significant at $p < 0.05$.

Majority of the lesions were small (<4cms diameter). Lesions >4 cms showed higher failure rates. Infiltrating lesions also showed higher failure rates as compared to exophytic lesions.

The chi-square statistic is 12.5525. The p-value is 0.013682. The result is significant at $p < 0.05$.

Node negative case showed lower failure rates as compared to node positive cases. Even with adjuvant radiotherapy the failure rate was considerable.

Table 5: Nodal status.

Nodal-metastasis	Number	Failures	Failure%
Negative	346	52	15
Reactive hyperplasia	11	3	27
Sinus-histocytosis	22	6	27
1group+ve	92	12	13
2/more+ve	70	21	30

Table 6: Adjuvant R. T.

Number	Failures-No	Failure%
146 (27%)	26	17.8

Table 7: Recurrence period.

Period	Number	%
< 1 year	60	11.1
1-3 years	27	5
3-5 years	2	0.4
>5years	2	0.4

Majority of the recurrences occurred within one year of treatment. After three years the recurrence rate was negligible.

DISCUSSION

As seen from Table 1, there were 393 cases in Stage IB, of which 14% had recurrence in contrast to 23.7% and 31.8% in Stage IIA and IIB lesions respectively. The overall recurrence was 17.2% in all stages. Obviously the earlier the stage, the better is the survival. Majority of the cases were in the age group 40-40 years and there was recurrence in 17.1% of cases in that group. There were 124 cases in the younger group of 30-39 years. The recurrence in this group was a little higher i.e. 20.2%%. Higher the age group, more is the risk factor, as observed by Smiley LM, Burke WT' 91.[9] In this study, the younger patients seem to have a higher risk.

Squamous carcinoma of the poorly differentiated type comprised the largest group and showed a recurrence rate of 15.9%, with an overall recurrence rate of 16.7%. Adenocarcinoma was seen in 32 cases and the recurrence rate was 15.7% (Table 3).

The poorer the differentiation, the more is the chance of recurrence. Smiley LM, Burke WT et al, observed increased recurrence with poor differentiation in a series of 349 cases of Stage I disease.[9]

Exophytic growth >5cms diameter showed higher recurrence of 21.2% as compared to 4% with growths <2cms. (Table 5). Exophytic growth accounted for 91% of cases, whereas the incidence of infiltrating growth was 9.1%. A recurrence of 51% was noticed with infiltrating growth. Smiley LM, Burke WT et al, had about 22% recurrence in the infiltrating variety.[9]

Lymphnode metastasisa was absent in 346 out of 541 cases (Table 5). In this node, negative group there was recurrence in 15% of cases in comparison to 17.26% overall recurrence. The risk of recurrence increased to 30% with >2 groups nodes showing metastasis. Peculiarly nodes showing simple reactive hyperplasia and sinus histiocytosis, also show 25% recurrence. This shows that recurrence does not strictly depend on nodal status. In a study by Papanicolau et al, patients with pelvic node metastasis had a 5-year survival of 50% compared to 78% of those without.[10]

Radiotherapy as an adjuvant to surgery was given in27% of cases (Table 4). Inspite of surgery and radiotherapy combination there was recurrence in 18.03% of cases in this group. This probably correlates with the view of Morrow GP '80 and Fuller AF, Elliot N et al'82, who opined that there is no evidence to show improvement in survival by pot-operative radiotherapy.[11,12] In a study, conducted by Thomas WB, William J Hoskins; the authors discovered that despite postoperative whole pelvis radiation therapy in 88% of patients, 13(34.2%) developed recurrence.[13]

All patients with nodes or margins who recurred, died of disease. Patients with pelvic node or surgical margin involvement, clearly constitute a high-risk group and should considered candidates for some form of adjuvant therapy. The interval of treatment and recurrence is shown in Table 7. The maximum number of treatment failures (11.06%), were encountered in the first year of post-treatment period. The recurrences were far low (0.44%), as the patients went beyond three to five years after treatment. A study by Morley GW et al showed that 13% of the patients developed a recurrence in 5 years, with 70% occurring in the first 3 years of treatment.[14] This shows that multiple risk factors responsible for recurrences work very fast and those which are to be contained show excellent treatment pattern. The identification of various pathological risk factors after primary surgical management of early stage cervical carcinoma portends a higher rate of relapse and decreased survival.

Historical attempts to improve outcome focussed mainly on the use of adjuvant pelvic radiation with overall limited success. Wui-JinKoh, Kathryn Panwala et al 2000, retrospectively analysed the patterns of failure after radical hysterectomy.[15] They concluded that, analysis of patterns of failure of radical hysterectomy, led to better stratification of patients into risk groups and incorporated testing of systemic agents, in those considered at high risk of distant failure. In patients with positive nodes, the use of combined adjuvant chemotherapy and radiation, significantly improved the relapse-free survival and overall survival, as compared to radiation alone.

However, for node negative patients, with other primary tumor risk factors, pelvic radiation significantly improves relapse-free survival, compared to no further therapy.

CONCLUSION

A study of 541 cases undergoing Wertheim's hysterectomy for cancer cervix is presented. Surgery was supplemented with radiotherapy in27% of cases, the overall recurrence rate of the disease was 17.18% during 1-5 years post-treatment period. Surgery was limited to stage IB mainly, except for a few cases of stage IIA and IIB, where the tumor load was heavy. Majority of the case were 40- 49 years of age, but recurrence was higher 19.6% in the younger age group of 30-39 years. Squamous cell carcinoma of poorly differentiated type showed recurrence in 15.9% and adenocarcinoma recurred in 15.38% of cases. The larger the tumor load, more was the recurrence 20.6% as compared to smaller lesions, where the incidence of recurrence was only 3.7%. Recurrence was very high in infiltrating lesions, which are extremely misleading, so far as surgical decisions are concerned. More than two groups of node involvement were associated with more (30%) recurrence. Interestingly, 15.65% of recurrence, took place where nodes were negative. The maximum recurrences occurred in the first year of treatment itself, irrespective of the mode of treatment or nodal status or any other factor described earlier. A good number of failures of (8.03%), in the combined treatment group raised doubts about the efficacy of routine postoperative radiotherapy.

So, younger age, adenocarcinoma, poor differentiation, large tumor load and infiltrating lesions and multiple lymphnode involvement, seems to be the high-risk factors, in the management of carcinoma cervix, where subsequent adjuvant therapy may be warranted.

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