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Surgically treated early stage cervical cancer – Prognostic factors and adjuvant treatment

[*]Verneker Ruchika A[1] , Desai Arun J[2] and Patel Shilpa M[3].

[1]Consultant gynaecologist Madhuram Hospital
[2]Consultant gynaecologist Shivam Hospital ,
[3]Department of Gynaecological oncology at Gujarat cancer research institute Ahmedabad.
Correspondence Email : ruchika2103@gmail.com

ABSTRACT

Invasive cancer of cervix is considered a preventable disease as it has a long pre-invasive state. If detected in early stages i.e upto stage IIA_1 the disease is curable with good survival rates.

- *To identify the prognostic factors in surgically treated early stage cervical cancer*
- *To study if preoperative findings could accurately predict presence of poor prognostic factors such as nodal status*
- *To evaluate these histological prognostic factors in deciding the further management of patient with adjuvant treatment*

This is a prospective study of prognostic factors and adjuvant treatment in 60 cases of surgically treated early stage cervical cancer (Radical hysterectomy with bilateral pelvic lymph node dissection).Histo-pathological findings were evaluated to determine the prognosis.Result:25% patients had lymph node involvement and lymphovascular space invasion was seen in 15% of cases. Parametrium was involved in 16.6%. There were 3 patients with positive margins and 65% patients had moderate differentiation of tumor. Maximum number of nodes were positive in stage IB2. Size of the tumor more than 4 cm is an important determinant of prognosis and has an definite effect on lymph node metastasis and other poor histological prognostic factors. • Adjuvant treatment is must incase of patients with intermediate or high risk prognostic factors

Keywords: carcinoma cervix, surgically treated, risk factors.

INRODUCTION

Cervical cancer is a deadly yet a preventable and a curable disease. If detected early i.e. upto stage IIA_1 , it is operable. However to prevent recurrence adjuvant treatment in the form of radiotherapy is needed. Radiotherapy itself has its own morbidities over a period of time which includes acute complications like, a. Diarrhea b. Abdominal cramps c. Nausea d. Frequent urination e. Bleeding from bladder and bowel mucosa and chronic complications like a. Proctosigmoiditis b. Rectovaginal fistula c. Small bowel complications. To avoid this morbidities we need to rationalise which patients actually need adjuvant treatment which can be kept only on observation without adjuvant treatment. Purpose of this study is to analyse the prognostic factors based on which adjuvant treatment can be decided and rationalised.

MATERIALS AND METHODS

This is a prospective study of prognostic factors and adjuvant treatment in 60 cases of surgically treated early stage cervical cancer (Radical hysterectomy with bilateral pelvic lymph node dissection) Cases of stage IB to stage IIA_1 carcinoma cervix operated between July 2012 and February 2014 were taken Inclusion criteria:

• Operated cases of early stage cervical cancer FIGO stage IB to stage IIA_1

Exclusion criteria:
• FIGO stage IA and Advanced cervical cancer fromIIA_2/ IIB to stage IV
• Medically unfit patients of early stage cervical cancer not treated with surgery.

Histo-pathological findings were evaluated to determine the prognosis. Adjuvant treatment was individualized based on the histo-pathological prognostic factors Type of adjuvant treatment included radiotherapy, chemotherapy and concurrent chemo-radiation.

Adjuvant pelvic radiation was given in two circumstances:
I. Patients with positive nodes, parametria, or surgical margins
II. Patients with negative nodes but high-risk features in the primary tumor

Prognostic factors include
Intermediate Risk Factors
• Size of the primary tumor
• Depth of stromal invasion
• Lymph-vascular space invasion
• Histological type

High Risk Factors
• Status of the lymph nodes
• Parametrial extension
• Status of the vaginal margins

Patients with intermediate risk were given radiation therapy alone, however patients with high risk factors were given concurrent chemoradiation. These patients were followed at 3month interval after completion of treatment. Recurrence over a period of minimum 6 months to 2 years post operatively was studied. This study was done ethically at Gujarat cancer research institute.

RESULTS

Table: 1.Number of patient in each stage of disease.

Stage	n = 60	Percentage
IB_1	29	48.3%
IB_2	26	43.3%
IIA_1	5	8.3%

Table: 2.Overall histologic prognostic factors analysed

Histological prognostic factors	Present study	
	N = 60	%
Tumour cell type		
Squamous cell carcinoma	52	86.7
Adenocarcinoma	6	10
Others	2	3.3
Depth of stromal invasion		
< $2/3^{rd}$ invasion	37	61.6
>$2/3^{rd}$ invasion	23	38.3
Lymphovascularspace invasion		
Present	9	15
Absent	51	85
Parametrial involvement		
Present	10	16.6
Absent	50	83.4
Lymph node involvement		
Present	15	25
Absent	45	75
Differentiaton		
Well	2	3.3
Moderate	39	65
Poor	19	31.6
Margins		
Positive	3	5
Negative	57	95

Table: 3.Stage and lymph node involvement

Stage	n=60	Present study	
		Lymph node positive n=15	%
IB_1	N=29	6	20.6
IB_2	N=26	8	30.7
IIA_1	N=5	1	20

Table: 4.Size of tumor and lymphnode involvement

Size of tumor	Lymph node involved (%)
< 4 cm	20
> 4 cm	32

Table:5.Depth of stromal invasion and lymph node involvement

Depth of invasion	Lymph node positive (%)
$<2/3^{rd}$	13.51
$>2/3^{rd}$	43.47

Table:6.Lymphovascular space invasion and lymph node metastasis.

LVSI	Lymph node positive (%)
Present	55.5
Absent	19.6

Table:7. Stage and number of associated risk factors

Stage	High risk	Intermediate risk	Low ris k	Intermediate risk + high risk
IB_1	3.4	51.7	20.6	24.1
IB_2	3.8	42.3	3.8	50
IIA_1		40		60

Table: 8. Adjuvant treatment

Adjuvant treatment		Percentage of patients
RT		53.3
CT-RT		23.3
Observation		15
Lost to follow up	Adjuvant treatment not taken	6.6
	Incomplete adjuvant treatment	1.6

Table :9 Stage and adjuvant treatment

Stage	RT %	CT-RT %	Observation %	Lost to follow up%
IB_1	51.7	17.2	24.1	6.8
IB_2	65.3	23	7.6	3.8
IIA_1		80		20

Table: 10 Follow up

Follow up	Duration - one year
Free of disease n=52	86.6%
Alive of disease n=8	13.3%

Table: 11 Recurrence in relation to treatment

Recurrence	Total Number n=8	Over all Percentage 13.33%
After treatment	3	5%
Lost to follow up/incomplete treatment	5	8.33%

Table:12 High risk factors in recurrence after completing adjuvant treatment

Recurrence	High risk factors	Intermediate risk factors
Recurrence 1	Lymph node involved	>½ stromal thickness ,moderate differentiation, uterus involved
Recurrence 2	Lymph node involved	>½ stromal thickness, moderate differentiation
Recurrence 3	Lymph node involved	>½ stromal thickness, poor differentiation

DISCUSSION

Carcinoma of cervix is a clinically staged cancer[1]. According to studies upto figo stage IIA1 of ca cervix is considered operable. Above IIA1 the treatment of choice is primary radiotherapy[2]. However all operated cases need to be evaluated thoroughly to avoid recurrence and to give a disease free survival for the patient. Presence of high risk histological prognostic factors for recurrence in the tumor such as a) Positive or close margins[3] b) Positive lymph nodes[4] c) Microscopic parametrial involvement. Or else intermediate risk factors such as a) Large tumor size b) Cervical stromal invasion to the middle or deep 1/3rd c) Lymph vascular space invasion makes the patient appropriate candidate for adjuvant treatment[5]. Through this study we shall study these factors so as to rationalise the need for adjuvant treatment thus avoiding the long term morbidity of these treatment. In this study it is seen that size of the tumour plays an important role in deciding prognosis. Stage IB2 where size of the tumour is more than 4 cm is associated with poor prognostic factors and all these patients including IIA1 were given combination of chemotherapy plus radiotherapy instead of radiotherapy alone. Limitation of these study is the sample size and the short duration of follow up (1 year). Recurrence was seen in 8 patients out of which 3 patients had completed adjuvant treatment and 5 patients were defaulters. These 3 patients had associated high risk factors. It is also seen in this study that patients with low risk can be safely kept on observation without adjuvant treatment, thus avoiding morbidity.

CONCLUSION

Thus we conclude that size of the tumor more than 4 cm is an important determinant of prognosis and has an definite effect on lymph node metastasis and other poor histological prognostic factors. Adjuvant treatment is must in case of patients with intermediate or high risk prognostic factors. Such high risk patients who did not take adjuvant treatment, have very early recurrence. Most important histological and clinical prognostic factors include, a) Size of the tumor b) Lymph node metastasis c) Parametrial involvement d) Positive margins. Adjuvant treatment is must in such cases. However patients with intermediate risk factors also require adjuvant treatment. Only low risk cases can be kept for observation with successful outcome.

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