Original Research Article

Analysis Of Pelvic Lymph Nodal Metastasis In Operable Cases Of Cancer Cervix-A One Year Cohort Study at a Regional Cancer Centre.

Abstract:

Objective: To study the incidence of nodal metastasis in early stage operable cases of cancer cervix and to correlate the nodal metastasis with different parameters like stage, degree of differentiation, lympho-vascular space invasion (LVSI) and deep stromal invasion.

Materials and Methods: This is an observational study conducted in Department of Gynec Oncology, Acharya Harihar Regional Cancer Centre & SCB Medical College ,Cuttack. from September 2013 to August 2014.The incidence of Lymph node positivity, Degree of differentiation, Deep Stromal invasion and Lymphovascular space invasion(LVSI) were analysed in 80 patients who underwent Wertheim's Radical hysterectomy for early stage operable cancer cervix which includes stage I A to II A. **Results:** The mean age of patients with early stage Cervical cancer was 52.5 years. Post menopausal bleeding was the most common clinical presentation . 17.5% patients had lympho-vascular invasion and pelvic lymph node involvement where as 20% had stromal invasion. None of the patients had vaginal margin involvement. Majority of cases belonged to Stage I B (57.5%) , followed by Stage II A (40%) and only 2.5% had Stage I A. Most of the cases (85%) were reported to have squamous cell carcinoma on histopathological examination

Discussion: Patients with Lymph node postivity , positive vaginal margin, parametrial positivity (1 out of 3 high risk factors) received chemo-radiation. Patients with lesion size more than 4 cm, LVSI, Deep stromal invasion (2 out of 3 intermediate risk factors) received radiation only as per all international protocols.

Conclusion: The incidence of lymph node metastasis in cancer cervix patients is quiet significant mostly found in stage IB2,IIA2 but found to be less in stage I A.We are of opinion that Wertheim's Radical hysterectomy along with bilateral pelvic lymphadenectomy is an effective mode of treatment in patient with early stage cancer cervix which is required for risk stratification as per post operative histopathological analysis to decide adjuvant therapy in form of Radiotherapy alone or combination of Radiation and Chemotherapy for the better survival rate of patients.

INTRODUCTION:

Cervical cancer is the leading cause of cancer mortality in India, accounting for 17 percent of all cancer deaths among women age 30 to 69 years. At current incidence rates, the World Health Organization (WHO) estimates that the annual burden of new cases in India will increase to nearly 225,000 by 2025[1]. Multi-factorial causation, potential for prevention, and the sheer

threat it poses make cervical cancer an important disease for in-depth studies .Metastasis to lymph nodes indicate poor prognosis[2]. According to International Federation of Gynecology and Obstetrics (FIGO) staging system for cervical cancer , [3] cervical carcinoma confined to the cervix (disregard extension to the corpus) is classified as Stage I. Invasive carcinoma diagnosed only by microscopy; stromal invasion with a maximum depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of 7.0 mm or less; vascular space involvement, venous or lymphatic, does not affect classification and is I A , further sub-classified as I A 1 and I A 2. Clinically visible lesion confined to the cervix or microscopic lesion greater than I A 2 is classified as I B further divided into I B 1 and I B 2.In Stage II ,cervical carcinoma invades beyond uterus but not to pelvic wall or to lower third of vagina .II A means tumor without parametrial invasion, and II B involves parametrium. Early stage cancer cervix includes I and II A.Lymph node metastasis develops in 15−25% of early-cervical cancer patients [4].With involvement of pelvic lymph nodes, the long term survival is considerably reduced[5]. The five year survival in this group of patients is approximately 60% [6].Patients with common iliac or para-aortic node involvement had less five year survival rate compared to patients with only pelvic node involvement (external iliac, hypogastric, or obturator). Early stage cervical cancers(IA-IIA) are treated by radical hysterectomy and bilateral pelvic lymphadenectomy .Depending on the intermediate & high risk factors for recurrence adjuvant treatment is given. 5-Year survival rate of patients with positive nodes ranges from 20% to 74%. Information on the lymph node (LN) status is necessary to determine the treatment strategy [8].Our aim of study is to evaluate the incidence of lymph node metastasis in early stage operable cases of Cervical cancer and its correlation with various risk factors.

MATERIALS AND METHODS:

This is an observational cohort study, conducted in Acharya Harihar Regional Cancer Centre,Cuttack , a recognized regional cancer center affiliated to government medical college at Cuttack in the state of Orissa, India. After obtaining approval from the regional ethics and research committee , Lymph node positivity, Degree of differentiation , Deep Stromal invasion and LVSI were analysed in 80 patients who underwent Wertheim's Radical hysterectomy for early stage cancer cervix, from September 2013 to August 2014. Patients were appropriately staged by clinical and radiological examination before surgical procedure. Routine chest radiographs were taken and assessed. Pearson chi square test with yates correction for continuity and Fischer exact test were used to analyse the data in SPSS Version 20.

RESULTS:

Among the 80 patients in the study group ,the mean age of patients was 52.5 and ranged from 31-68 years. Both lymph node positivity and cancer cervix incidence were highest in the (51-60) years age group(Table 1). Multiparous patients had a higher lymph node involvement and vascular invasion.

Table -1: Correlation of various variables with lymph node metastasis

PATHOLOGICAL STAGE	NO OF PATIENTS (N=80)	LYMPH NODE POSITIVE(N=14)	P value
IA	2(2.5%)	0	
IB	46(57.5%)	8(17.3%)	Stage IB vs IIA<0.0001
IIA	32(40%)	6(18.7%)	
AGE(in years)	NO. OF PATIENTS	NO. OF LYMPH NODE METASTASIS	
31-40	8(10%)	11(13.75%)	
41-50	12(15%)	12(15%)	
51-60	36(45%)	45(56.25%)	
61-70	24(30%)	12(15%)	
HISTOLOGY	NO. OF PATIENTS	NO. OF LYMPH NODE METASTASIS	
SQUAMOUS 1)WDSCC *	10	2(20%)	NOT SIGNIFICANT
2)MDSCC **	56	9(16%)	
3)PDSCC ***	2	1(50%)	

4)ADENO	**12**	**2(16.6%)**	
SURGICAL FINDINGS	**NO. OF PATIENTS**		
POSITIVE VAGINAL MARGIN	**0**		
POSITIVE PELVIC LYMPH NODES	**14(17.5%)**		
LYMPHOVASCULAR INVASION	**14(17.5%)**		
STROMAL INVASION	**16(20%)**		

* well differentiated squamous cell carcinoma

** Moderate differentiated squamous cellcarcinoma

*** poorly differentiated squamous cell carcinoma

The presenting complaints in decreasing order of frequency were Post menopausal bleeding(47.5%),white discharge(22.5%),irregular bleeding per vaginum(22.5%) and postcoital bleeding(7.5%).

Table 2:Correlation Of Metastatic Lymph Nodes With LVSI and Deep stromal invasion

PARAMETERS	**LYMPHNODE METASTASIS (POSITIVE)**	**TOTAL NUMBER OF PATIENTS WITH LYMPH**	**Pvalue**

		NODE POSI TIVE	
LVSI(Lymphovascular Space Invasion) **Absent (66)** **Present (14)**	 **4(6%)** **10(71.4%)**	**14**	**P<0.005**
DEEP STROMAL INVASION **Absent (64)** **Present (16)**	 **8(12.5%)** **6(37.5%)**	**14**	**P<0.0001**

DISCUSSION:

Cervical cancer is the most common cause of death among all gynecological cancers worldwide. It is the most common gynecological cancer among Indian women.[9] In-spite of being a developing nation, screening of cervical cancer by pap smear is on a steady rise over past years resulting in increasing detection of early cervical cancer in India. The patients with early detection of cervical cancer are ideal candidates for primary surgical treatment with radical hysterectomy and pelvic lymphadenectomy [10]with fair survival without needing any adjuvant therapy. Ernst Wertheim was the pioneer of radical hysterectomy , which included the removal of Uterus, cervix, parametrium and adequate tumor margin with pelvic lymph nodes, which he described in the year1898. Time and again with many modifications suggested that the procedure remains the treatment of choice for early cervical cancer[11]. But there are also some early cases with various risk factors like tumor size,Lymphovascular Space Invasion,Stromal Invasion and lymph node status where positivity demands adjuvant treatment in form of Radiation alone or Chemo radiation in spite of radical surgery so considered as poor prognostic factors[12,13,14]

Radical hysterectomy with pelvic lymphadenectomy is indicated in Stage I. Lymph nodal involvement is significant in Stage IA2 or Stage IB1 cervical cancer [6,7] Though Chemo radiation or combined therapy is suggested for Stage IB2 or Stage IIA2 cervical cancer, Radical hysterectomy with pelvic lymphadenectomy is performed in selected cases[15,16,17].Radical hysterectomy, in combination with adjuvant therapies, is an efficient mode of treatment for pelvic lymph nodal metastatic patients with stage IB-IIA cervical cancer.[18] Locally advanced

cervical cancer, FIGO stage equal or more than IB1 is treated with chemotherapy and external beam radiotherapy followed by brachytherapy.[19] In metastatic para-aortic nodal involvement radiotherapy is extended ,therefore accurate assessment of the extent of the disease is very important for planning the most appropriate treatment.

Radical surgery alone has low morbidity, enables more accurate prediction of prognosis and may be the sufficient in most patients with lymph node-negative early stage cervical cancer.[6]With a primary radical hysterectomy, stage IB1 cervical cancer patients have a significantly better survival rate than those with stage IB2.[20] In about two-thirds of pelvic lymph node positivity with stage IB cervical cancer cases, surgery alone could provide equal or better survival (without the toxicity of chemoradiotherapy), than any kind of multimodality treatment alternatives.[21] Para-aortic node metastasis appears to occur secondarily to wide-spread pelvic lymph node metastasis. [22,23] Terada KY et al stated that,for patients undergoing radical hysterectomy as primary treatment, postoperative adjuvant radiotherapy did not significantly improve survival. [7]. Radical hysterectomy with modifications has currently achieved lower morbidity due to its frequent usage and advancement of surgical equipments and techniques like Laparoscopy and Robotics.

Table -3: Comparison with other studies

Patient Characteristics	**Our Study N=80**	**Schorge *et al*** [24] **N=171**	**Landoni *et al*** [15] **N=343**	**Jena, Amitabh, et al** [25]	**Rajshekar S., et al.**[26] **N=601**
Median age (Years)	52.5	46	47	49.5	49
Clinical stage					
I A	2.5%	-	-	6.3%	-
I B	57.5%	91%	88%	30%	88.4%
II A	40%	9%	12%	51.2%	11.6%
Cell type					
Squamous	85%	73%	83%	91%	87%

Adeno Small cell Clear cell Adenosquamous	15%	16%	14% 3%	2.5%	10%
Pelvic nodes positive	17.5%	_	13%	12.5%	18.5%
Lymphovascular invasion	17.5%	45%	_	7.5%	17%
Deep stromal invasion	20%	42%	_	3.75%	70%

In our study, a significant number of patients in IB(17.3 %) and IIA(18.7%) had lymph node metastasis which correlated well with that of other studies.But the number of lymph node metastasis was more in well differentiated carcinoma rather than moderately differentiated which was not significant which may be due to proper lymph node dissection in those moderately differentiated carcinoma patients.Also the highest incidence of lymph node metastasis was found in age group 51-60 years where the maximum number of patients present.We had 14 patients with lymphovascular space invasion but there were 4 patients who didn't have lymphovascular space invasion but had lymph node metastasis.Same was also for deep stromal invasion where 8 patients had lymph node metastasis without stromal invasion(Table 2). But patients with risk factors(LVSI and stromal invasion) have significant node positivity which was the aim of our study and so the management varied accordingly. According to Sartori E et al, post-operative radiotherapy is controversial in node-negative pathologic stage IB cervical cancer. Radical surgery alone has low morbidity, enables more accurate prediction of prognosis and may be the sufficient therapy in the majority of patients with lymph node-negative early stage cervical cancer[27] Our study has similar results with various results of other studies(Table 3)

Our patients with lymph node postivity ,positive vaginal margins, parametrial positivity (1 out of 3 high risk factors) received chemo-radiation. Patients with lesion size more than 4 cm,

Lymphovascular Space Invasion(LVSI), Deep stromal invasion (2 out of 3 intermediate risk factors) received radiation only. The post-operative hospital stay was 8-12 days with a mean of 11 days. Except for one individual who developed urinary incontinence , none of the other cases had major complication. Superficial wound infection was noted in three cases.

CONCLUSIONS:

To conclude, the incidence of lymph node metastasis in cancer cervix patients is significant and is mostly found in stage IB2 and IIA2 which is evident in this study.This is due to large volume of tumor with early metastasis to lymphovascular channels then to nearby pelvic nodes. Wertheim's hysterectomy with its various modifications with bilateral pelvic lymphadenectomy is the most safe and cost effective mode of treatment in patient with early stage Cervical cancer .In most of cases radical surgery is sufficient without any addition of adjuvant therapy.In other early cases it helps in risk stratification as per post operative histopathological parameters to decide the need of adjuvant therapy in form of radiation or chemo radiation for the better survival of patients.

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