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ANALYSIS OF HISTOPATHOLOGICAL RISK FACTORS FOR NODAL METASTASIS IN INVASIVE CERVICAL CANCER TREATED WITH RADICAL HYSTERECTOMY AND PELVIC LYMPHADENECTOMY

Oncology

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ABSTRACT

OBJECTIVE:

The aim of this study was to identify the independent histopathological and clinical risk factors for pelvic lymphnodal metastasis in patients with cervical carcinoma treated with radical hysterectomy and pelvic lymphadenectomy.

METHODS:

From Jan 2012 to Dec 2017, patients with stage Ib-IIa cervical cancer who underwent upfront surgery were retrospectively studied. The relationship between pelvic lymph node metastasis and age, menopausal status , histological subtype, clinical stage, tumor size, grade of differentiation, depth of stromal invasion & lympho vascular space invasion were evaluated by univariate and multivariate analyses.

RESULTS:

Totally 603 lymph nodes were dissected in 70 patients, with an average of 8 lymph nodes in each patient. 61.4% (43/70) were belongs to age group 50 years or more.45(64.3%) patients attained menopause.63(90%) patients had squamous cell carcinoma. Grade 1 tumors were 51.4%(36/70).stage 1B1 tumors 75.7%(53/70). Laparoscopic surgery was done in 25(35.7%)patients.15.7% of the patients (11/70) had metastasized pelvic lymph nodes. Univariate analysis indicated that tumor size (P = 0.009) and stromal invasion (P = 0.049) were significantly related to pelvic lymph node metastasis. Multivariate logistic regression analysis showed that tumor size alone (p=0.038, 95%CI 1.064-22.248) was significantly related to pelvic lymph node metastasis in patients with early-stage squamous cell carcinoma of the uterine cervix.

CONCLUSION:

In early-stage cervical cancer, tumor size and stromal invasions are risk factors of pelvic lymph node metastasis.

KEYWORDS

Early stage carcinoma cervix, Pelvic lymph node metastasis, Radical hysterectomy

INTRODUCTION

Carcinoma cervix is the most common cancer worldwide. It usually present in advanced stage. Because of improved screening and availability of health services, number of patients with early stage diagnosis is increased. Survival depends on stage at presentation. Recent FIGO staging depends only on primary tumor stage. Eventhough pelvic and para aortic lymphnode metastasis adversely affect prognosis , staging does not includes regional lymphnode metastasis.

Early stage cervical cancer includes stage 1A, 1B1,IB2 and selected IIA1. The definitive treatment of early stage cervical cancer consists of concurrent chemoradiation or radical hysterectomy with pelvic lymphadenectomy1(Landoni et al,1997). Surgery is selected because it eradicates the primary disease and preserves ovarian function .It also permits planning of adjuvant therapy by accurate staging.

Lymph node metastasis is one of the important prognostic factor of carcinoma cervix. Information on lymph nodal status is necessary to determine the treatment strategy1 . For patients with Stage 1 cancer treated with radical hysterectomy had 15-20 % pelvic, and 1-5% para aortic lymphnode metastasis2,3. Five year survival is equal in both for surgery and radiotherapy (80-82%).

This retrospective study analyzed early cervical cancer managed by radical hysterectomy and pelvic lymphadenectomy .Patients clinical and pathological characteristics with pelvic lymphnode metastasis were analyzed .

Material and methods

Patients with biopsy proven carcinoma cervix who were eligible for radical surgery were included in this study . The inclusion criteria were as follows: age more than 18 years and less than 70 years, clinical FIGO stage IA2-IIA disease, procedure done with radical hysterectomy (type II or III) with pelvic lymphadenectomy and no prior chemotherapy or radiotherapy.. Laparoscopic surgery-25 (35.7%) patients and open radical hysterectomy -45(64.3%) patients - was done. Pelvic lymphadenectomy was done which included external iliac, hypogastric,obturator lymph nodal groups. Para aortic lymphadenectomy was not done.

Stage 1B1,1B2,IIA1 includes 53(75.7%),3(4.3%),14(20%) patients respectively (Table-1). Squamous cell carcinoma (SCC) includes 63 (90%) patients-of them ,subtypes invasive SCC were52(74.3%) patients, Large keratinizing carcinoma were 7(10%) patients, Large non-keratinizing carcinoma were 9(12.9%)patients. Age, menopausal state, histological sub type, grade of the tumor, FIGO clinical staging, tumor size, margin status, lympho vascular space invasion(LVSI), parametrial and deep stromal extension were correlated with pelvic lymph nodal status. Patients with rare histological subtypes, HIV positive status , incidental cancer diagnosed after simple hysterectomy were excluded from this study.

Univariate analysis and multivariate analysis using logistic regression analysis was done.

Table-1 Patients and tumor characteristics:

Patients &tumor characteristics	Number(%)
Age(years) <50	27(38.6%)
>=50	43(61.4%)
Premenopause	25(35.7%)
postmenopause	45(64.3%)
Squamous carcinoma	63(90%)
Adenocarcinoma	7(10%)
Invasive SCC	52(74.3%)
Large keratinizing	7(10%)
Large non-keratinizing	9(12.9%)
others	2(2.9%)
Grade G1,	36(51.4%)
G2	26(37.1%)
G3	8(11.4%)
Stage 1B1	53(75.7%)
1B2	3(4.3%)
IIA1	12(17.1%)

Laparoscopy Open	25(35.7%) 45(64.3%)
Tumor size <=2cm >2 cm	55(78.6%) 15(21.4%)
Stromal invasion Present Absent	15(21.4%) 55(78.6%)
Lymphovascular invasion Present Absent	6(8.6%) 64(91.4%)
Pelvic nodes Positive Negative	11(15.7%) 59(84.3%)

Results

Total number of patients included in the study were 70, of them 50 years or more comprised 43(61.4%) patients. Forty five patients(64.3%) were post menopausal. Sixty three (90%) patients had squamous cell carcinoma . In developed countries, the incidence of squamous cell carcinoma is 80% of cervical cancer and the remaining 20% are adenocarcinoma.

Low grade tumors comprised 36 (51.4%) patients. Fifty three(75.7%) patients were stage IB1. Fifty five (78.6%)patients had tumor size of 2 cm or less. Stromal invasion were present in 15(21.4%) patients. Lymph vascular invasion were present in 6 (8.6%) patients.

Total lymph nodes dissected were 603. Pelvic lymph nodes were positive in 11(15.7%) patients.

Pelvic lymph nodes were positive only in squamous cell carcinoma patients. Of the high grade tumours, only 5out of 34 patients had positive lymph nodes.

Tumor size of greater than 2 cm is an important predictor of lymph node metastasis. Of the 9 patients, 6 had positive pelvic lymphnodes(p value=0.009). Stromal invasion is an another factor predicting nodal metastasis. Of the 15 patients with stromal invasion, 5 patients had nodal positivity (p value=0.049).(table-2). Nine patients with absent lympho vascular invasion had nodal positivity.(p value=0.236).

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Table-2 Analysis of patients and tumor factors with pelvic lymph nodal status:

Variables	Negative nodes (No.of pts)	Positive nodes (No.of pts)	P value
Age >=50	37	6	0.739
<50	22	5	
Premenopause	20	5	0.506
postmenopause	39	6	
Squamous carcinoma	52	11	0.587
Adenocarcinoma	7	0	
Grade G1,	30	6	1.000
G2, G3	29	5	
Tumor size <=2cm	50	5	0.009
>2 cm	9	6	
Stromal invasion Present	10	5	0.049
Absent	49	6	
Lymphovascular invasion Present Absent	 4 55	 2 9	0.236

Table-3 Multivariate logistic regression analysis

	95% confident interval		P value
	lower	upper	
Tumor size	1.064	22.248	0.038
Stromal invasion	0.384	10.586	0.329
Lymphovascular invasion	0.149	11.952	0.797

Multiple logistic regression analysis (table-3) showed tumor size is an important factor predicting pelvic lymphnode metastasis.(95% CI 1.064-22.248). The other factors such as stromal invasion and lympho vascular invasion are not predictor of lymph node metastasis

DISCUSSION

Pelvic lymph node metastasis is an important route by which cervical carcinoma can spread. Systematic lymphadenectomy is needed because 20–50% of lymph nodes involved with micrometastasis.

Lymphnode status will not alter staging but very important for radiotherapy planning. Incidence of pelvic nodal metastasis in our study was 15.7%.

GOG study revealed that independent risk factors for Pelvic lymph node metastasis by multivariate analysis were capillary-lymphatic space involvement, depth of invasion, parametrial involvement, and age. Another study by Sun JR4 observed that depth of cervical stromal invasion is an independent risk factors of pelvic lymph node metastasis in early stage cervical cancer In our study, univariate analysis showed tumor size and stromal invasion were independent predictor of pelvic lymph node metastasis.

Pelvic lymph node metastasis were observed only in squamous cell carcinoma.Not even single case of adenocarcinoma had pelvic nodal metastasis. The reason is unknown .It could be due to predominant hematogenous spread of adenocarcinoma or could be due to low incidence of disease(10%of adenocarcinoma) in this study.

Roman et al reported a correlation between LVSI and incidence of lymph node metastasis5.The other factors such as grade of the tumor and lymphovascular invasion are not influencing pelvic lymphnode metastasis. This colud be due to small sample size.
Pelvic lymphadenectomy is warranted for patients undergoing radical hysterectomy .The detection of microscopic common iliac and para aortic lymphnode involvement nay identify patients who will benefit from extended field radiation , but lymphadenectomy can also add to morbidity of treatment.

Conclusion

Tumor size and depth of invasion are important predictor of pelvic lymph node metastasis in early stage cervical cancer. The other factors such as histologic subtype , grade and lympho vascular invasion needs further large number study.

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