

## A Study of Pelvic and Para-Aortic Lymph Node Involvement in Surgically Staged Endometrioid Carcinoma of Endometrium

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### Abstract

**Purpose** The purpose of this study was to investigate the influence of the depth of myometrial invasion and tumor grade on lymph node involvement in endometrial carcinoma.

**Methods** Patients with endometrioid carcinoma of endometrium who underwent surgical staging between January 1999 and September 2010 under the division of gynecologic oncology were studied retrospectively. Patients treated by radiotherapy or chemotherapy before surgeries were excluded.

**Results** The study group included 61 patients. Six patients had lymph node metastasis, of which 83.3 % had >50 % myometrial invasion ( $P = 0.052$ ). Grades 1, 2, and 3 were each seen in 33.3 % of them ( $P = 0.061$ ). When the study group was divided into two sets, namely, those with <50 and

>50 % myometrial invasion, the odds ratio was 10.3, which means that the chance of the prevalence of lymph node metastasis in the latter group is 10 times more.

**Conclusions** Although the  $P$  value was not significant, the odds ratio reveals that there is an increased risk of lymph node positivity with deeper myometrial invasion. Surgical staging needs to be done for all operable cases of carcinoma endometrium to determine the prognosis and further management.

**Keywords** Retroperitoneal lymphadenectomy · Endometrioid carcinoma · Myometrial invasion

### Introduction

According to the data from the National Cancer Institute during the years 2003–2007, endometrial cancer occurred at an incidence of 17.3 per 100,000 women among Asians and 24.4 per 100,000 women in the whites [1]. The Cancer statistics of the United States have estimated uterine cancer to account for 6 % of all cancer cases in women and 3 % of deaths due to cancer during the year 2010.

The National cancer registry, under the ICMR (Indian Council of Medical Research) is studying the cancer trends in India since 1981. In the report on cancer incidence trends across the country from 1982 to 2005, it is observed that the cancer of the corpus uteri showed an increase in incidence rates. The annual percentage changes were 5.8, 3.8, and 1.7 in Bangalore, New Delhi, and Mumbai, respectively. A total of 734 cases of cancer of the corpus uteri have been reported

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from five cities in the country during 2004–2006 by the NCRP, of which 55 cases were from Bangalore alone.

Endometrial cancer is known to present at an early stage compared to its ovarian counterpart because of its clinical manifestations like abnormal uterine bleeding and post-menopausal bleeding. Nevertheless, the prognosis is affected by factors like histological cell type, tumor grade, depth of myometrial invasion, occult extension to cervix, adnexal metastasis, and lymph node metastasis. A study by Yokoyama et al. [2] has reported the involvement of lymph nodes in early-stage endometrial cancer and that lymph node involvement is a poor prognostic factor for patient survival. Smith et al. [3] have reported that lymph node dissection improves both overall survival and uterine-specific survival. On the other hand, if the lymph nodes are negative, then post-operative pelvic radiation can be avoided and only brachytherapy can be given, if needed. This was studied by Berclaz et al. [4]. It is also reported by Chi et al. [5] that the lymph node involvement correlates with depth of myometrial invasion and the histologic grade of the tumor. In a study by Kondalsamy-Chennakesavan, [6] the depth of myometrial invasion was found to predict nodal involvement independently when compared with tumor-free distance (TFD). The purpose of the present study was to determine the influence of depth of myometrial invasion and tumor grade on lymph node involvement in patients with endometrioid carcinoma of the endometrium, who underwent surgical staging with pelvic and para-aortic lymphadenectomy. This will help in determining the prognosis of the disease and further management of these patients.

## Methods

This is a retrospective study which includes all women diagnosed as carcinoma endometrium and who underwent surgical staging including pelvic and para-aortic lymphadenectomy between January 1999 and September 2010 at St. John's Medical College Hospital under the division of gynecologic oncology. Surgical staging included total abdominal hysterectomy with bilateral salpingo-oophorectomy and pelvic and para-aortic lymph node dissection and cytology of peritoneal washings. The patients were staged according to the FIGO staging of 1988. Only patients with endometrioid histology were included to reduce bias arising from the more aggressive variants like papillary serous and clear cell carcinomas.

The material for study was obtained by reviewing the records of the patients in the division of gynecologic oncology, department of pathology and Medical case records of the hospital. The study received clearance from

the ethical board of St. John's Medical College and Hospital where the study was undertaken.

## Inclusion Criteria

- Those with diagnosis of endometrial cancer of endometrioid histology.
- Those who underwent surgical staging including pelvic and para-aortic lymphadenectomy.

## Exclusion Criteria

- Those patients who did not undergo surgical staging.
- Those who had synchronous second primary malignancy.
- Those who had undergone radiotherapy or chemotherapy before surgical intervention.

## Data Analysis

The details of the patients who underwent surgical staging for carcinoma endometrium were obtained from the records. The histo-pathological details were reviewed in detail including the histological type of carcinoma endometrium, the histological grade, depth of myometrial invasion, involvement of cervix and adnexa, and lymph nodes. The lymph node positivity was correlated with depth of myometrial invasion and tumor grade.

Data were analyzed using SPSS (Version 18) software. Descriptive statistics were reported using mean and standard deviation for continuous variables, number and percentages for categorical variables. Chi-square test was used to assess the association between lymph node metastasis with myometrial invasion and tumor grade. Unadjusted odds ratio was reported for the association between the lymph node positivity and myometrial invasion. Level of significance was set as 5 %.

## Results

A total of 88 cases of carcinoma endometrium were treated during the study period. Sixty-seven patients underwent surgical staging according to FIGO staging system. Of these 67 patients, one patient had a synchronous second primary in the ovary, three patients had papillary serous histology; one had received neo-adjuvant chemotherapy and one patient had received radiotherapy before surgery, and hence, they (6 patients) were excluded from the study. Thus, a total of 61 patients who underwent surgical staging and were of endometrioid histology were included in the study group.

Of the 61 study patients, two patients (3.28 %) had no myometrial invasion, 36 patients (59.01 %) had less than 50 % myometrial invasion, and 23 patients (37.7 %) had more than 50 % myometrial invasion.

The distributions of grades among these patients were 27 (44.26 %), 29 (47.54 %), and 5 (8.20 %) with grade 1, grade 2, and grade 3, respectively.

Among the study patients, six patients (9.8 %) had lymph node metastasis. Five patients (83.3 %) had more than 50 % myometrial invasion, and one patient (16.7 %) had less than 50 % myometrial invasion ( $P = 0.052$ ) (Table 1). No lymph node involvement was observed in the absence of myometrial invasion. The incidence of lymph node involvement in relation to tumor grade was as follows: grade 1: two (33.3 %), grade 2: two (33 %), and grade 3: two (33 %) ( $P = 0.061$ ) (Table 2). The tumors with deeper myometrial invasion and higher grade showed a trend toward higher lymph node involvement, though, in this study, the association did not reach statistical significance.

Of the six patients with lymph node metastasis, three had only pelvic lymph node involvement and three had both pelvic and para-aortic lymph node involvement. In the latter group, two patients had tumor of grade 1. However, no case was seen with para-aortic lymph node involvement when pelvic lymph nodes were negative. When the depth of myometrial invasion of more than 50 % and lymph node involvement were compared, the odds ratio was 10.3 (95 %

**Table 1** Comparison of lymph node involvement with myometrial invasion

Variable	Lymph node		<i>P</i> value
	Positive Lymph nodes	Negative Lymph nodes	
Myometrial invasion			
Absent	0	2	0.052
<50 %	1	35	
>50 %	5	18	
Total	6	55	–

**Table 2** Comparison of tumor grade with lymph node involvement

Variable	Lymph node		<i>P</i> value
	Positive Lymph nodes	Negative Lymph nodes	
Grade			
1	2	25	0.061
2	2	27	
3	2	3	
Total	6	55	

CI). In other words, with deeper myometrial invasion, the probability of lymph node involvement increased 10 times (Table 3).

## Discussion

In this study, the incidence of lymph node involvement was obtained, and its relation to tumor grade and depth of myometrial invasion was studied. We observed an incidence of 9.8 % lymph node involvement in endometrioid adenocarcinoma of the endometrium which is in accordance with the rates observed in the literature [2, 6].

In the study by Chi et al. [5], 8 % of patients had positive lymph nodes when the depth of myometrial invasion was <50 % and 20 % patients had positive lymph nodes when the depth of myometrial invasion was >50 %. In our study, the same was 2.7 % and 21.3 %, respectively. (Table 4).

Chi et al. did not observe any lymph node involvement in grade 1 tumors, but in grade 2 and grade 3 tumors the incidence of lymph node metastasis was 10 and 13 percent. In the present study, the incidence rates of involvement of lymph nodes were 7.4, 6.9, and 40 percent in grades 1, 2, and 3, respectively. In the present study, the higher grade tumors had greater incidence rates of lymph node involvement (Table 5).

Yokoyama et al. [2] reported lymph node involvement in early stage of carcinoma endometrium which is seen in 2.7 % of our cases, i.e., in those with less than 50 % myometrial invasion (Table 1). They also reported a greater incidence of lymph node involvement with increasing depth of myometrial invasion and higher tumor grade, more so for para-aortic lymph node involvement. In their study, of the 14 patients with pelvic lymph node metastasis, 8 (57 %) patients had para-aortic lymph node

**Table 3** Odds ratio when myometrial invasion is more than 50 %

	B	<i>P</i> value	Exp B	95 % C.I.	
				UL	LL
Myometrial invasion	2.33	0.04	<b>10.3</b>	1.12	94.6

**Table 4** Lymph node positivity percentage according to myometrial invasion

Myometrial invasion	Number of cases	Number of lymph node positive cases	Percentage of lymph node positive cases in each category
None	2	0	0
<50 %	36	1	2.7
>50 %	23	5	21.7
Total	61	6	–

**Table 5** Lymph node positivity percentage according to tumor grade

Tumor grade	Number of cases	Number of lymph node positive cases	Percentage of lymph node positive cases in each category
Grade 1	27	2	7.4
Grade 2	29	2	6.9
Grade 3	5	2	40
Total	61	6	–

metastasis, which means approximately 50 % of the patients with pelvic lymph node metastasis also have para-aortic lymph node involvement. This observation is similar to the rates observed in our study (Table 5).

The results of our study show that patients with deeper myometrial invasion and higher grade tumor have a higher rate of lymph node involvement, which translates as adverse effect on the prognosis for the patient. However, the presence of lymph node disease in grade 1 tumors seen in this study and as reported by Yokoyama further signifies the need for pelvic and para-aortic lymphadenectomy in all cases of carcinoma endometrium. After surgical staging, adjuvant radiotherapy can be withheld for patients with grade 1 tumors, having no myometrial invasion or lymph node involvement. Those patients with less than 50 % myometrial invasion and no lymph node involvement can be subjected to only intracavity radiation instead of external pelvic radiotherapy, thus reducing the long-term side effects of the latter therapy. That this mode of management does not reduce the disease-free survival was shown in a study conducted by Berclaz et al. [4] where brachytherapy without external radiotherapy was associated with excellent disease-free survival when lymph nodes were negative.

## Conclusion

Pelvic and para-aortic lymph node involvements in endometrial carcinoma are related to the depth of myometrial invasion and grade of tumor. However, since lymph node involvement can be seen even in early stage and grade 1 tumors, it is advisable to perform complete surgical staging in all cases of carcinoma endometrium to plan further course of management of the patients and obtain better survival and longer disease-free interval.

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