

ORIGINAL ARTICLE

A Study of the Relationship between Histopathological Tumor Grade and Depth of Myometrial Invasion with Pelvic Lymph Node Metastasis in Patients with Endometrial Cancer

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ABSTRACT

Understanding the risk factors for lymph node metastasis in endometrial cancer is necessary for optimal treatment of such patients. This study is aimed at determining the risk of Lymph Node Metastasis (LNM) based on the depth of myometrial invasion and tumor grade in endometrial cancer. This is a retrospective study in which pathologic findings related to 170 patients with endometrial cancer had been evaluated who underwent surgical staging including pelvic lymphadenectomy with or without para-aortic lymphadenectomy in the years 1994 to 2009. The data was analyzed using SPSS 20 and the level of statistical significance was considered to be $p < 0.05$. From 170 patients evaluated in this study, 29 patients (17.1%) had lymph node metastasis, among which 3 cases (3.6%) were classified as Grade I, 8 patients (15.1%) as Grade II and 18 patients (52.9%) as Grade III. Among 29 patients (17.1%) who had lymph node metastasis, in those patients with non-myometrial invasion, there was no lymph node metastasis (0%); while in patients with myometrial invasion $< 50\%$, 24 patients (28.6%) had lymph node metastasis; meanwhile, among 24 patients (14%) with histopathological Grade III and myometrial invasion $> 50\%$, 15 patients (62.5%) had lymph node metastasis. Patients with endometrial cancer, histopathological Grade I and II and without myometrial invasion are considered to have low risk of lymph node metastasis. While for other groups in surgical staging, complete pelvic and para-aortic lymphadenectomy should be performed.

Keywords: myometrial invasion, endometrial cancer, Lymph Node Metastasis, Histopathological Tumor Grade

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INTRODUCTION

Endometrial carcinoma is the most common malignancy in the female genital tract, accounting for nearly half of all gynecologic cancers in the United States. Endometrial carcinoma is the fourth most common cancer in women after breast, lung and colorectal cancers and is the eighth leading cause of death due to malignancy in women [1-3].

In recent years, certain factors have increased the understanding of endometrial cancer and have emphasized on its diagnosis and treatment; the factors include reduced (cervical cancer) ? incidence and associated mortality, increased life expectancy, using hormone therapy and early diagnosis. Availability of easy to use diagnostic tools and better understanding of the premalignant lesions of the endometrial has also led to an increase in the number of women diagnosed with endometrial cancer [5-8].

The treatment of endometrial cancer also has evolved, and intrauterine or pelvic radiation method performed preoperatively and the following hysterectomy has changed to an approach in which the decision is made on a case-by-case basis given the characteristics of individual patients. In this approach, hysterectomy is performed as initial treatment and additional treatments will be performed postoperatively and based on the findings and pathological assessment. Further analysis and research is needed to determine whether initial surgical approach and postoperative targeted therapy improves survival rate and reduces morbidity or not [9, 10].

Endometrioid carcinoma comprises approximately 80% of cases of endometrial carcinoma. Staging of endometrial cancer was converted from clinical staging to surgical staging in 1988 by FIGO. In surgical staging, the importance of grading, histological type, depth of myometrial invasion and spread of tumor to

lymph nodes, adenex and peritoneal cavity have been identified as factors influencing prognosis. Lymph node status is one of the most important predictors of endometrial metastasis [10,11].

In many studies, there has been found a significant relationship between myometrial invasion and metastasis to lymph nodes and also between histological tumor grade and lymph nodes metastases, the incidence rate and the level of which varies, however [11, 12].

Given that no study has been conducted in Iran on patients with endometrial cancer regarding the relationship between the grade of disease and depth of myometrial invasion by endometrial cancer with lymph node involvement, and since knowing such relationship and its level can be useful for follow-up of these patients after surgical treatment, this study was performed to determine the relationship.

MATERIAL AND METHOD

This is a retrospective study in which pathological findings related to 170 patients with endometrial cancer who underwent surgical staging had been evaluated. Surgical staging of the patients was carried out in women's department, Imam Hossein Hospital, or in other centers and the patients were treated and followed up in Radiation Oncology department of this hospital.

Surgical staging of these patients include pelvic lymphadenectomy with or without para-aortic lymphadenectomy performed from 1994 to 2009. In accordance with FIGO staging classification, the patients were at various stages [1, 2, 3 and 4] and in terms of tumor pathologic types included endometrioid, mucinous, papillary serous, clear-cell, squamous cell and undifferentiated carcinomas.

The data of age of the patients, pathological type of tumor, histopathological grade of tumor, surgical stage and depth of myometrial invasion and pelvic lymph node metastasis were determined according to the pathologic findings after surgical staging of patients and the patients' medical records, and the data analysis was carried out using SPSS 20. To describe data, the mean, standard deviation, frequency and percentage were used. To find the relationship, the Fisher's exact test, Spearman's correlation coefficient and Mann-Whitney test were used. P-Value of less than 0.05 was considered to be statistically significant.

RESULTS

170 patients with endometrial cancer were evaluated in this study. The patients were in the age range between 26 to 92 years old and the mean and standard deviation of age of the patients were 56.3 ± 14.6 years. From 170 patients evaluated, 29 patients (17.1%) had lymph node metastasis. Among these, 83 patients (48.8%) were classified as Grade I, 53 cases (31.1%) as Grade II and 34 patients (20%) as Grade III. From 83 patients of histopathological Grade I, 3 patients (3.6%) had pelvic lymph node metastases, while from 53 patients of Grade II, 8 patients (15.1%) and from 83 patients of Grade III, 18 patients (52.9%) had such metastases. As histopathological grade increased, the percentage of lymph node metastasis was also significantly increased ($p < 0.001$). (Table 1).

In the group of patients with no myometrial invasion ($n=19$, 11%), no patient had lymph node metastasis (0%); in the group of patients with myometrial invasion less than or equal to 50% ($n=67$), 5 patients (7.5%) had lymph node metastasis; meanwhile in the group of patients with myometrial invasion greater than 50% ($n=84$), 24 patients (6.28%) had lymph node metastasis. Thus, with increase of the depth of myometrial invasion, the probability of lymph node involvement and metastasis showed a significant increase ($p < 0.001$). (Table 1)

Table 1: The Depth of myometrial invasion and LNM based on the histopathological tumor grade

	Grade I N (%)	LNM* N (%)	Grade II N (%)	LNM N (%)	Grade III N (%)	LNM N (%)
No myometrial invasion	14 (8%)	0 (0%)	3 (1.7%)	0 (0%)	2 (1.1%)	0 (0%)
Myometrial invasion \leq 50%	40 (23.5%)	1 (0.5%)	19 (11%)	1 (0.5%)	8 (4.7%)	3 (1.7%)
Myometrial invasion $>$ 50%	29 (17%)	2 (1.1%)	31 (18%)	7 (4%)	24 (14%)	15 (8%)

* LNM: lymph node metastasis

DISCUSSION

In this study, we investigated that how clinico-histopathological variables can be predictive for LNM. Tumor grade and myometrial invasion were among these variable. Findings of this study are consistent with previous findings on the LNM risk assessment based on these variables (17-19).

According to our findings, regarding the lymph node metastasis rate based on 2 factors, i.e. histopathological grade of tumor and the depth of myometrial invasion, it was observed that with increased grade and depth of myometrial invasion, the probability of lymph node metastasis also increased. An interesting and important issue in this study is that in the group of patients with no

myometrial invasion, for none of the histopathological grades (I, II or III) a case of pelvic lymph node metastasis was observed. Therefore, it can be concluded that myometrial invasion is an important factor in determining lymph node metastasis. Thus, the results of other studies are confirmed considering that in patients with low risk endometrial cancer (no myometrial invasion and pathological grade I and II), lymph node metastasis probability is very low so that lymphadenectomy in these patients can be abandoned and lymphadenectomy-related complications can be avoided in them.

However, in our study in the high-risk group, i.e. Grade III with depth of invasion of greater than 50%, lymph node metastasis rate was 62.5%. So, the importance of lymphadenectomy in patients other than those with low risk endometrial cancer is emphasized. Moreover, with increased tumor grade and the depth of myometrial invasion, lymph node metastasis probability also increases.

In the present study, for all patients without myometrial invasion in all three histopathological grades (I, II or III), no pelvic lymph node metastasis has been reported. It can be understood that myometrial invasion is an important determining factor for predicting lymph node metastasis. While in the other subgroups, the risk of pelvic lymph node metastasis was higher.

In other conducted studies, it has been reported that the patients with low risk of lymph node metastasis include the patients without myometrial invasion and histopathological grades I and II [13-16]. In our study, even in cases of myometrial invasion in Grade III, no pelvic lymph node metastasis was observed and due to the small sample size in our study, further studies are needed in this field. These finding suggests that in patients at low-risk of endometrial cancer, lymphadenectomy can be removed from their surgical staging [14, 15].

To identify patients with a low risk of metastasis in preoperative and intraoperative stages, some procedures have been suggested in other studies, including preoperative MRI to determine the depth of myometrial invasion and endometrium sampling to determine histopathological tumor grade, and further studies are need to be performed in this field [15-17].

Apart from the groups with low-risk of metastasis, in our study, the risk of lymph node metastasis obviously increased in other groups, as for the patients with histopathological Grade III and deep myometrial invasion (the risk of pelvic lymph node metastasis) was 63% and so lymphadenectomy is necessary for them.

In patients with endometrial cancer, lymph node metastasis risk increased for higher histopathological grades and deeper myometrial invasions. The level of such invasion is an important **predictive** factor in lymph node metastasis, up to the point that based on our study, in the absence of myometrial invasion, no lymph node metastasis was found in all three grades.

CONCLUSION

Given these results, it can be proposed that in low risk patients, i.e. lower grades and especially in patients without myometrial invasion, lymphadenectomy can be removed from the surgical staging; however, other groups need complete pelvic and para-aortic lymphadenectomy for surgical staging.

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