

Original article**Value of Lower Uterine Segment Involvement as a Predictor of Lymph Node Spread in Endometrial Carcinoma**Modares Gilani M¹, Akhavan S²*1 Obstetric and Gynecology Dept., Tehran University of Medical Sciences, Imam Khomeini Hospital, Tehran, Iran**2 Obstetric and Gynecology Dept., Kurdistan University of Medical Sciences, Behsat Hospital, Sanandaj, Iran*

Abstract This retrospective study performed at Gynecology_Oncology department of Valiasr Hospital, Tehran, Iran from 2002 to 2008. All patients with endometrial cancer who underwent complete surgically staging and were evaluated for lower uterine segment involvements were included. In multivariate logistic regression model ,LVI⁺ independently predicts para-aortic node spread ,(OR= 2.05,CI95% :1.14-3.69)(*P*<0.05); In contrary ,both LUS⁺ and high grade tumors independently predicts pelvic node spread ,respectively ,(OR=3.9,CI95%:1.25-12.06 and OR=2.5,CI95% :1.09-5.87)(*P*<0.05). LUS⁺ and LVI⁺ are respectively significant predictors of pelvic and para-aortic lymph node spread in endometrial carcinoma .Thus, LUS⁺ may be regarded as another important parameter for surgical staging.

KeyWords: Endometrial cancer; Lower uterine segments (LUS); Pelvic lymph node

Introduction

Endometrial cancer is the most common female genital malignancy in the United States. [1] In general, the stage of endometrial cancer is considered the most important prognostic factor and other factors such as grade, depth of myometrial invasion, LVS invasion are involved in disease prognosis as well. Lower uterine segments (LUS) may also have a role in prognosis. [2,3] Currently, some parameters such as tumor size measured by imaging methods ,myometrial depth of invasion and intramural resistance index (RI) are used preoperatively to predict lymph node metastasis of endometrial cancer ; however , making decision for lymphadenectomy based on these parameters is not easily possible.[3] None of the preoperative methods has been replaced the surgical staging and intraoperative evaluations .[4] Herein ,there is some evidences [2,5] that proposed lower segment involvement as a good candidate for predicting lymph node spread ,but this relationship has been questioned by others [6] and needs further study to be clarified. The aim of this study was to investigate the association between lower uterine segment involvement in endometrial cancer and pelvic and para-aortic lymph node spread in fully staged patients. Then, it is

expected that intraoperative and postoperative management therapies would be affected in the case of this relationship.

Material and Methods

This retrospective study performed on 750 patients at Gynecology_ Oncology department of Valiasr hospital, Tehran, Iran from 2002 to 2008. All patients with endometrial cancer who underwent complete surgically staging and were evaluated for lower uterine segment involvement was included. So, data of 247 patients was complete and enrolled in our series. Surgical staging was defined as total abdominal hysterectomy, bilateral salpingoophorectomy, pelvic and para-aortic lymph node dissection, and cytologic washings. Patients without lymph node dissection excluded from study. Pathologic evaluation of lower uterine segment involvement (LUS⁺) consisted of thorough macroscopic and microscopic assay of available samples through transverse sections and named as absent or present. The histopathologic parameters were the same for pathologists. The medical archived files searched for pathology reports , patients age, gravidity, surgery type, lymph node dissection and the anatomic location of involved nodes (pelvic or para-aortic), histology, grade, lower uterine segment involvement, depth of myometrial invasion, lymphovascular invasion .

Statistical analysis

Categorical variables were compared using fisher's exact test and predictors of node spread compared with each other by multivariate logistic regression. Odds ratios (OR) with 95% confidence intervals were calculated. All statistical analyses were performed with SPSS.16.

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Results

Totally 247 patients with endometrial carcinoma enrolled in this study. The mean \pm sd age of patients was 54 ± 11 (25-80) years old. Most of them had 3 gravities, 36(14.6%) and nulligravida reported in 30 (12.1%). The distribution of tumor grades did not differ significantly from expected figure in each grade, ($P=0.58$); Most of the them were grade. I 88(35.6%) & grade.II 84(34%) followed by grade.III 75 (30.4%). Deep myometrial invasion (>50%) and lympho-vascular-space invasion (LVI⁺) were found respectively in 97 (39.3%) and 79 (32%) of patients. Lower segment involvement (LUS⁺) revealed to be in 141(57.1%) surgically staged patients. All of the patients were categorized in stage I, 150(60.7%) or stage III, 97 (39.3%), and we had no patients in stage II. Lower segment involvement seen in 78 (52%) of patients in stage I and 63 (65%) of patients in stage III, ($P=0.049$). Extra-uterine invasion reported by surgeons in only 11 (4.5%) of patients and positive results reported by pathologist for peritoneal cytology in 57 (23.1%). Also explored para-aortic and pelvic node in all patients detected nodes spread respectively in 73(29.6%) and 28(11.3%) of patients.

LUS⁺ was associated with positive para-aortic nodes in 40

(54.8%) in comparing with negative para-aortic 101 (58%), ($P=0.67$); While positive pelvic nodes 24 (85.7%) versus negative 117 (53.4%) were associated with LUS⁺, ($P=0.001$). (Table.1,2) The analysis of other predictors of lymph node (para-aortic and pelvic nodes) spread was done that consisted of LVI⁺, deep myometrial invasion (>50%), and high-grade tumors (grade.III). The LVI⁺ and deep myometrial invasion were significantly associated with para-aortic node spread ($P<0.05$). In contrast, high grade tumors were significantly associated with pelvic node spread ($P<0.05$). (Table.1,2) The predictors with significant association with para-aortic or pelvic node spread entered in a logistic regression model to evaluate their combined effect. In this multivariate logistic regression, LVI⁺ independently predicts para-aortic node spread, (OR= 2.05, CI95% :1.14-3.69) ($P<0.05$); In contrary, both LUS⁺ and high grade tumors independently predicts pelvic node spread, respectively, (OR=3.9, CI95% :1.25-12.06 and OR=2.5, CI95% : 1.09-5.87) ($P<0.05$). (Table3) However LUS⁺ had higher odds ratio in comparing with high grade tumor. Further analyses revealed that LUS⁺ is significantly associated with high grade tumors, deep myometrial invasion and lympho-vascular invasion in both stage I and stage III tumors ($P<0.05$).

Table 1

Predictors of para-aortic nodes spread

Cases	Para-aortic node		P-value
	Absent n=174	Present n=73	
LUS ⁺	101(58%)	40(54.8%)	0.67
LVI ⁺	46(26.4%)	33(45.2%)	0.005
Deep Myo	60(34.5%)	37(50.7%)	0.02
High grade	47(27%)	28(38.4%)	0.09

Table 2

Predictors of pelvic nodes spread

Cases	Para-aortic node		P-value
	Absent n=219	Present n=28	
LUS ⁺	117(53.4%)	24(85.7%)	0.001
LVI ⁺	67(30.6%)	12(42.9%)	0.2
Deep Myo	81(37%)	16(57.1%)	0.06
High grade	59(26.9%)	16(57.1%)	0.002

Discussion

Uterine corpus cancer is the most common gynecologic cancer in the United States and the fourth most common cancer in women. The American Cancer Society estimated that there will be 40,100 new cases of endometrial carcinoma in 2008 and that 7,470 women will die from this disease.[7] Pathologically, the endometrium comprises two distinct areas, the uterine corpus proper (UC) and the lower uterine segment (isthmus; LUS).[8] The mucosal layer of the lower uterine segment (LUS) is thin compared with the corpus mucosa and is much less responsive to hormonal stimulation.[9]

It has been well established that patients with high grade tumors, deep myometrial invasion or lympho-vascular invasion are at increased risk for lymph node metastasis, and surgeons perform lymphadenectomy when it is technically possible.[10,11] However, the predictive power of lower uterine segment involvement of lymph node spread have shown by Some previous studies [2,5] Our results indicates that LUS⁺ and LVI⁺ are respectively predictors of pelvic and para-aortic lymph node metastasis in endometrial adenocarcinoma. Congruent with those studies, LUS⁺ significantly predicts pelvic node spread but para-aortic node spread is predicted by LVI⁺. Also, another study [6] with its small sample size has raised the question about the significance of lower uterine segment involvement in endometrial carcinoma. Beside these studies, there are some others [12,13-16] that debate the impact of LUS⁺ on outcome and try to justify the need for adjuvant postoperative radiotherapy in the case of lower uterine segment involvement.

Although, we found Lympho-vascular-space invasion as a good predictor of para-aortic invasion but may be inaccurately de-

Table 3
Predictors of para-aortic node and pelvic spread in a multivariate logistic regression

		OR(CI:95%)	P-value
Predictors of para-aortic node spread	LVI ⁺	2.05(1.14-3.69)	0.016
	Deep Myo	1.7(0.96-3.01)	0.07
Predictors of pelvic node spread	LUS ⁺	3.9(1.25-12.06)	0.018
	High grade	2.5(1.09-5.87)	0.03

terminated by pathologist at the time of intraoperative frozen section. So, lower uterine segment involvement as a good alternative may be assessed at the time of operation for pathologic gross and frozen section.

In our study, the prevalence of LUS⁺ endometrial carcinomas reported 57% among women who had undergone hysterectomy for endometrial carcinoma, this is congruent with the wide frequency of LUS⁺ mentioned in different studies (4 to 58%) [12-14,16,2]. In this study, LUS⁺ was associated with high grade carcinoma, deep myometrial involvement, and LVI⁺ among patients with stage I endometrial cancer. This finding has been advocated by Hachisuga et al.6 and Irwin et al.14 and also rejected by two rather small studies [12,16]

The retrospective nature of this study and selection bias was two limitations of ours; according to our exclusion criteria, patients who had not node dissection because of technical problems or rather short duration of operation excluded.

Conclusion

Based on our findings and other similar studies, LUS⁺ is a reflection of a potentially more advanced endometrial carcinoma and as an independent predictor of pelvic node spread should be considered as a significant risk factor by surgeons, so patients with endometrial cancer and LUS⁺ will rationally undergo lymph node dissection. Albeit other predictors are important to be considered but among them LVI⁺ was also an independent predictor of para-aortic lymph node spread which would help surgeons to decide for para-aortic dissection and avoid adjuvant treatment.

Aknowlegement

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