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Original Article

Is lymphadenectomy necessary for low-risk endometrial cancer?

İlker Çakır [a, †], Mehmet Özeren [a]

[a] *Department of Obstetrics and Gynecology, Tepecik Education and Reseach Hospital, İzmir*

ABSTRACT

Objective: The aim of this study is to investigate the effect of lymphadenectomy on disease-free survival (DFS) and overall survival (OS) in low-risk endometrial cancer cases.

Material and Methods: Patients who were operated for endometrial carcinoma with endometrioid type, The International Federation of Gynecology and Obstetrics (FIGO) stage 1A, grade 1 or 2 histology between 1994 and 2013 were included in this study. The patients were divided into two groups as those who underwent intraoperative lymphadenectomy (LA +, n=197) and those who did not (LA -, n=133). Each group was evaluated in terms of survival times and recurrences.

Results: When the LA+ and LA - groups were compared in terms of survival, no significant difference was found between the two groups about DFS(p=0.955) and OS(p=0.937). The 5-year DFS rate was 95.1% in the LA - group and 94.9% in the LA+ group (P= 0.974). The 5-year OS rates in patients who did and did not undergo lymph node dissection were 96.8% and 97.0%, respectively, and no statistically significant difference was found between the groups (P= 0.551).

Conclusion: Performing lymphadenectomy in patients with FIGO stage 1A, grade 1 or 2, endometrioid adenocarcinoma has no effect on DFS and OS.

Keywords: endometrial cancer; lymphadenectomy; survival

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Introduction

Endometrial cancer is the most common gynecological malignancy in women [1]. It is the fourth most common malignancy in women after breast, lung, and colorectal cancer [1,2]. Endometrial cancer is usually seen in the sixth-seventh decade. Despite the lack of an effective screening method, most cases are diagnosed early due to the common symptom of vaginal bleeding. 70-80% of patients diagnosed with endometrial cancer are at stage 1, and the five-year survival rate in this patient group is over 90% [3].

Endometrial cancer is histopathologically divided into two groups. Type 1 endometrial cancer; estrogen-dependent, limited to the uterus at the time of diagnosis, hormone receptor positive, well and moderately differentiated endometrioid histology, while type 2 endometrial cancer; it has an estrogen-independent, hormone-receptor negative, poorly differentiated non-endometrioid histology (such as clear cell, serous carcinoma) [4].

Standard treatment in endometrial cancer cases is total extrafacial hysterectomy and bilateral salpingoophorectomy. There is controversy over whether to perform systematic pelvic-paraaortic lymph node dissection in all patients [5]. It has been shown that lymphadenectomy (LA) does not affect disease-free survival (DFS) and overall survival (OS), especially in low-risk endometrial cancer patients (endometrioid type, grade 1 or 2, myometrial invasion <50%, no intraoperative macroscopic spread)[6,7].

Material and methods

Patients who were operated for endometrial carcinoma with endometrioid type, The International Federation of Gynecology and Obstetrics (FIGO) stage 1A, grade 1 or 2 histology at a tertiary cancer center between 1994 and 2013 were included in this study.

The study was approved by the institutional ethics committee. Exclusion criteria from the study; endometrial cancer cases other than endometrioid type endometrial adenocarcinoma, histological grade 3 cases, cases at all stages except FIGO stage 1A and cases deviating from follow-up protocols were determined. From the medical records of patients; patients' age, comorbidities, parity, preoperative hemoglobin, platelet, white blood cell (WBC) values; the histological type and grade of the tumor in the preoperative curettage materials; postoperative histological type, grade, size, stage of the tumor; whether adjuvant therapy was given; if recurrence occurred, the time, localization, treatment modality of recurrence and survival were collected. In addition, preoperative serum cancer antigen (CA) 125 values were also examined.

Patients were divided into two groups as those who underwent intraoperative lymphadenectomy (LA+) and those who did not (LA-). In the LA- group; patients underwent only total hysterectomy with bilateral salpingo-oophorectomy (TH and BSO).

† Corresponding author.
E-mail: ilkercakirdr@yahoo.com.tr
ORCID ID: 0000-0003-0245-5298

In the LA+ group patients underwent, TH and BSO and bilateral pelvic and/or para-aortic lymph node dissection and omentectomy. It was decided whether to perform lymph node dissection or not, based on intraoperative pelvic examination findings, frozen results and surgeon's decision.
Follow-up intervals of the patients were every 3 months for the first 2 years, every 6 months for up to 5 years, and annually after 5 years. Follow-up visits consisted of clinical examination, ultrasound of the pelvis and abdomen, and CA-125 testing if elevated levels were present preoperatively. Computed tomography or magnetic resonance imaging were used as imaging modalities if clinically necessary. Each group was evaluated in terms of demographic data, survival times and recurrences. Staging was performed according to the FIGO surgical staging system.

Statistical analysis
Chi-square test was used in the descriptive statistics of the data as mean, standard deviation, frequency, ratio, distribution of data in proportional analysis. The distribution of variables was tested with Kolmogorov Smirnov. Mann-Whitney U test and independent sample t test were used to compare the two groups. The Fischer test was used when the chi-square conditions could not be met. Logistic regression was used in the effect level analysis. DFS was defined as the time from the date of the primary surgery to detection of recurrence or the latest observation. OS was defined as the time from the date of primary surgery to death or the latest observation. Kaplan Meier (log-rank) analysis was used for survival analysis. SPSS 20.0 program was used in the analysis. All data were summarized in tables. The results were evaluated at the 95% confidence interval and the significance level of $p<0.05$.

Results

Among the patients included in the study, there were 197 patients in the LA+ group and 133 patients in the LA- group. Demographic data of the LA + and LA - group are given in the table 1.

Table 1: Demographic data and blood counts

	Not Undergone lymphadenectomy (n=133), mean±s.d.	Undergone lymphadenectomy (n=197), mean±s.d.	p-value
Age	57.8 ± 10.1	59.6 ± 9.6	0.120
Hemoglobin (g/dL)	12.7 ± 1.7	12.4 ± 2.0	0.157
Platelet(/mL)	277000 ± 90000	294000 ± 83000	0.078
Parity(é)	3.2 ± 2.4	3.3 ± 2.2	0.897
WBC(/mm^3)	8770 ± 3760	8260 ± 2500	0.139

é: number of births of multiparity patients
WBC:White blood cell count

The distribution of comorbid diseases of the cases is shown in table 2. There was no difference between the groups in terms of comorbid disease.

Table 2: Comorbid Disease(s)

Comorbid Disease	Not Undergone lymphadenectomy (n=133) n- %	Undergone lymphadenectomy (n=197) n-%	p-value
Diabetes Mellitus	38 (30.4%)	60 (31.6%)	0.825
Hypertension	59 (47.2%)	93 (48.9%)	0.761

It was determined that at least total hysterectomy and bilateral salpingo-oophorectomy operation were performed in all cases. No lymph node involvement was detected in the LA + group.
When the postoperative specimens of the patients were examined, there was no significant difference between the two groups in terms of tumor sizes. In addition, the percentage distributions of both groups about lymphovascular space involvement and histological grade were found to be similar (Table 3).

Table 3: Preoperative CA-125 levels and tumor diameters, histologic characteristics at postoperative specimens

		Not Undergone lymphadenectomy mean±S.D. n-%	Undergone lymphadenectomy mean±S.D. n-%	p-value
Tumor diameter		3.1 ± 1.4 cm	3.4 ± 1.7 cm	0.092
CA-125		19.5 ± 22.6	22.0 ± 27.2	0.382
LVSI	No	130 (%97.7)	188 (%95.4)	0.374
	Yes	3 (%2.3)	9 (%4.6)	
Histologic grade	1	97 (%72.9)	129 (%65.5)	0.153
	2	36 (%27.1)	68 (%34.5)	

LVSI, Lymph-vascular space invasion

NiNe patients had recurrence in the LA + group; 3 cases had peritoneal carcinomatosis, 4 cases had vaginal recurrence, 2 cases had lymph node recurrence. Six patients had recurrence in the LA – group; 2 cases had vaginal recurrence, 2 cases peritoneal carcinomatosis, 2 cases colon recurrence. There was no significant difference between two groups about recurrence and number of deaths (Table 4).

Table 4: Number of cases with recurrence and exitus in study groups

	Not Undergone lymphadenectomy n(%)	Undergone lymphadenectomy n(%)	p-value
Recurrence	6 (%4.5)	9 (%4.6)	0.973
Exitus	4 (%3.0)	4 (%2.0)	0.718

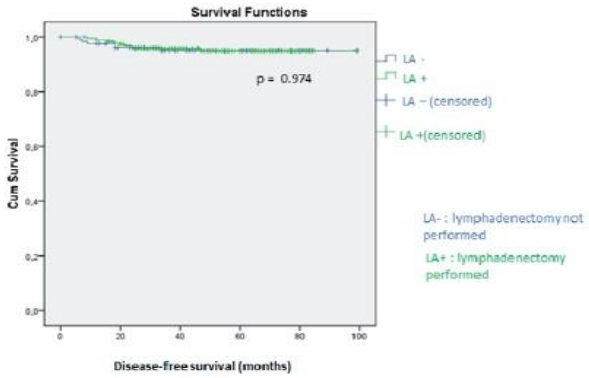
When the LA+ and LA - groups were compared in terms of survival, no significant difference was found between the two groups about DFS and OS (Table 5).

Table 5: Survival Times

	Not Undergone lymphadenectomy (n=133) (mean±S.D.)	Undergone lymphadenectomy (n=197) (mean±S.D.)	p-value
Disease-free survival (month)	51.9±24.6	52.1±20.9	0.955
Overall survival (month)	53.1±23.6	52.9±20.2	0.937

The 5-year DFS rate was 95.1% in the LA - group and 94.9% in the LA+ group (P= 0.974) (Figure 1). The 5-year OS rates in patients who did and did not undergo lymph node dissection were 96.8% and 97.0%, respectively, and no statistically significant difference was found between the groups (P= 0.551) (Figure 1).

Figure 1. Kaplan-Meier DFS and OS in the study groups



Discussion

For endometrial cancer, after the systemic surgical staging recommendation of FIGO in 1988, the issue of lymph node dissection for which patient group has become controversial [8]. In retrospective studies, it has been shown that low-risk endometrial cancer patients have a low risk of lymph node involvement [9–11]. In our study, the effect of lymph node dissection performed in low-risk endometrial cancer patients on OS and DFS was investigated.

It was shown in the study of Trimble et al. that lymph node dissection was performed in 2831 patients, lymph node dissection was not performed in 6363 patients, only stage 1 endometrial cancer patients were included, and that lymphadenectomy did not appear to convey a survival benefit [12]. Likewise, in the ASTEC study and in the randomized study by Panici et al., it was shown that lymphadenectomy does not provide a survival advantage in early stage endometrial cancer [3,13]. Same with the literature, in our study there was no difference between LA + and LA - group about DFS and OS rates.

Primary tumor size has been defined as an indicator of lymph node involvement in endometrial cancer [14]. The risk of lymph node metastasis increases with the increase in tumor size. Schink et al. detected lymph node metastasis in 4% of patients with clinical stage 1 endometrial cancer with a tumor size of ≤ 2 cm compared with lymph node metastasis in 15% of patients with a tumor size of >2 cm[15]. Mariani et al., in 2004, revised the Mayo criteria by adding tumor size (≤ 2cm) [16]. In our study, tumor sizes were similar in both groups. Contrary to the literature, although the mean tumor diameter of the patients who underwent lymphadenectomy was >2 cm, no lymph node metastasis was detected. The reason for this may be that grade 3 cases and patients with non-endometrioid endometrial cancer were not included in our study.

In our study, no significant difference was found between the LA + group and the LA - group in terms of recurrence. This may be an evidence that lymphadenectomy has no effect in low-risk endometrial cancer patients and that the recurrences are related to tumor genetics. Today, studies on cancer genetics continue.

The limitations of our study are that our study was single-centered, the number of patients was limited, its retrospective design and the data on postoperative morbidity were insufficient.

As a conclusion; in accordance with the literature, performing lymphadenectomy in patients with FIGO stage 1A, grade 1 or 2, endometrioid adenocarcinoma has no effect on DFS and OS. These results need to be supported by larger, randomized clinical trials in the future.

Disclosure

Authors have no potential conflicts of interest to disclose.

References

[1] Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011;61:69–90. https://doi.org/10.3322/caac.20107.

[2] Bessho A, Tabata M, Kiura K, Takata I, Nagata T, Fujimoto N, et al. Detection of occult tumor cells in peripheral blood from patients with small cell lung cancer by reverse transcriptase-polymerase chain reaction. Anticancer Res 2000;20:1149–54. https://doi.org/10.3322/caac.20121.Available.

[3] writing committee on behalf of the ASTEC study group T. Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. Lancet 2009;373:125–36. https://doi.org/10.1016/S0140-6736(08)61766-3.

[4] Mendivil A, Schuler KM, Gehrig PA. Non-endometrioid adenocarcinoma of the uterine corpus: A review of selected histological subtypes. Cancer Control 2009;16:46–52. https://doi.org/10.1177/107327480901600107.

[5] Zhang H, Jia L, Zhang Q, Zhang Y, Yang X, Kong B. Therapeutic role of systematic retroperitoneal lymphadenectomy in endometrial cancer. Bull Cancer 2012;99. https://doi.org/10.1684/BDC.2011.1536.

[6] Cragun JM, Havrilesky LJ, Calingaert B, Synan I, Secord AA, Soper JT, et al. Retrospective analysis of selective lymphadenectomy in apparent early-stage endometrial cancer. J Clin Oncol 2005;23:3668–75. https://doi.org/10.1200/JCO.2005.04.144.

[7] Hidaka T, Nakashima A, Shima T, Hasegawa T, Saito S. Systemic Lymphadenectomy Cannot Be Recommended for Low-Risk Corpus Cancer. Obstet Gynecol Int 2010;2010:1–5. https://doi.org/10.1155/2010/490219.

[8] Mariani A, Webb MJ, Keeney GL, Haddock MG, Calori G, Podratz KC. Low-risk corpus cancer: is lymphadenectomy or radiotherapy necessary? Am J Obstet Gynecol 2000;182:1506–19. https://doi.org/10.1067/MOB.2000.107335.

[9] Convery PA, Cantrell LA, Di Santo N, Broadwater G, Modesitt SC, Secord AA, et al. Retrospective review of an intraoperative algorithm to predict lymph node metastasis in low-grade endometrial adenocarcinoma. Gynecol Oncol 2011;123:65–70. https://doi.org/10.1016/j.ygyno.2011.06.025.

[10] Milam MR, Java J, Walker JL, Metzinger DS, Parker LP, Coleman RL. Nodal metastasis risk in endometrioid endometrial cancer. Obstet Gynecol 2012;119:286–92. https://doi.org/10.1097/AOG.0b013e318240de51.

[11] Shah C, Johnson EB, Everett E, Tamimi H, Greer B, Swisher E, et al. Does size matter? Tumor size and morphology as predictors of nodal status and recurrence in endometrial cancer. Gynecol Oncol 2005;99:564–70. https://doi.org/10.1016/j.ygyno.2005.06.011.

[12] Trimble EL, Kosary C, Park RC. Lymph node sampling and survival in endometrial cancer. Gynecol Oncol 1998;71:340–3. https://doi.org/10.1006/gyno.1998.5254.

[13] Panici PB, Basile S, Maneschi F, Lissoni AA, Signorelli M, Scambia G, et al. Systematic pelvic lymphadenectomy vs no lymphadenectomy in early-stage endometrial carcinoma: Randomized clinical trial. J Natl Cancer Inst 2008;100:1707–16. https://doi.org/10.1093/jnci/djn397.

[14] Kamura T, Yahata H, Shigematsu T, Ogawa S, Amada S, Kaku T, et al. Predicting pelvic lymph node metastasis in endometrial carcinoma. Gynecol Oncol 1999;72:387–91. https://doi.org/10.1006/gyno.1998.5288.

[15] Schink JC, Miller DS, Lurain JR, Rademaker AW. Tumor size in endometrial cancer. Cancer 1991;67:2791–4. https://doi.org/10.1002/1097-0142(19910601)67:11<2791::AID-

CNCR2820671113>3.0.CO;2-S.
[16] Mariani A, Dowdy SC, Keeney GL, Long HJ, Lesnick TG, Podratz KC. High-risk endometrial cancer subgroups: Candidates for target-based adjuvant therapy. Gynecol Oncol 2004;95:120–6. https://doi.org/10.1016/j.ygyno.2004.06.042.