

The Therapeutic Role and Survival Impact of Systematic Lymphadenectomy in Endometrial Cancer: A Retrospective Cohort Study

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ABSTRACT

The aim of this study was to evaluate the therapeutic and prognostic role of systematic lymphadenectomy in patients with endometrioid endometrial cancer. The study included 512 patients with FIGO 2009 stage I-III endometrioid endometrial carcinoma who underwent primary surgical treatment at a tertiary university hospital between January 2010 and May 2025. Patients were categorized according to whether lymphadenectomy was performed. Clinicopathological features, disease-free survival (DFS), and overall survival (OS) were compared. Survival outcomes were estimated using Kaplan–Meier analysis and log-rank tests, and prognostic factors were identified using Cox proportional hazards regression. Of the total cohort, 407 patients (79.5%) underwent lymphadenectomy and 105 (20.5%) did not. The lymphadenectomy group more frequently exhibited adverse pathological features, including larger tumor size, high-grade histology, deep myometrial invasion, and LVSI (all $p < 0.01$). After a median follow-up of 68 months, recurrence rates were comparable between the groups (7.9% vs. 6.7%, $p = 0.837$). The estimated 5-year DFS rates were 92.5% for the lymphadenectomy group and 92.1% for the non-lymphadenectomy group. The 5-year OS rates were 83.2% and 87.5%, respectively. Lymphadenectomy was not associated with improved DFS (HR 1.31, 95% CI 0.58–2.96, $p = 0.547$) or OS (HR 1.42, 95% CI 0.81–2.47, $p = 0.199$). Multivariable analysis identified age, tumor grade, and LVSI as independent predictors of recurrence and survival, whereas lymphadenectomy was not an independent prognostic factor. Systematic lymphadenectomy does not confer a survival benefit in endometrioid endometrial cancer. Tumor biology, rather than the extent of nodal dissection, appears to be the dominant determinant of oncologic outcomes.

Key words: Endometrial Cancer. Overall Survival. Disease Free Survival. Lymphadenectomy.

Endometriyal Kanserde Sistemik Lenfadenektominin Terapötik Rolü ve Sağkalım Üzerine Etkisi: Retrospektif Kohort Çalışması

ÖZET

Bu çalışmanın amacı, endometrioid endometriyal kanserli hastalarda sistemik lenfadenektominin terapötik ve prognostik rolünü değerlendirmektir. Çalışmaya, Ocak 2010 ile Mayıs 2025 arasında üçüncü basamak bir üniversite hastanesinde primer cerrahi tedavi uygulanmış FIGO 2009 evre I-III endometrioid endometriyal karsinom tanılı 512 hasta dahil edildi. Hastalar, lenfadenektomi uygulanıp uygulanmadığına göre kategorize edildi. Klinikopatolojik özellikler, hastalıksız sağkalım (DFS) ve genel sağkalım (OS) karşılaştırıldı. Sağkalım sonuçları Kaplan–Meier analizi ve log-rank testleri ile değerlendirildi, prognostik faktörler ise Cox orantısal risk regresyonu ile belirlendi. Toplam kohortun 407'sine (%79,5) lenfadenektomi yapılırken, 105'ine (%20,5) yapılmadı. Lenfadenektomi grubunda daha büyük tümör boyutu, yüksek dereceli histoloji, derin miyometriyal invazyon ve LVSI gibi olumsuz patolojik özellikler daha sık izlendi (tümü $p < 0,01$). Ortalama 68 aylık takip sonunda, nüks oranları gruplar arasında benzerdi (%7,9'a karşı %6,7; $p = 0,837$). Beş yıllık DFS oranları lenfadenektomi grubunda %92,5, lenfadenektomi yapılmayan grupta %92,1 idi. Beş yıllık OS oranları ise sırasıyla %83,2 ve %87,5 olarak bulundu. Lenfadenektomi, DFS (HR 1,31; %95 GA 0,58–2,96; $p = 0,547$) veya OS (HR 1,42; %95 GA 0,81–2,47; $p = 0,199$) üzerinde iyileşme ile ilişkili değildi. Çok değişkenli analizde, yaş, tümör derecesi ve LVSI nüks ve sağkalımın bağımsız öngördürücüleri olarak belirlendi; buna karşılık lenfadenektomi bağımsız bir prognostik faktör değildi. Sistemik lenfadenektomi, endometrioid endometriyal kanserde sağkalım avantajı sağlamamaktadır. Onkolojik sonuçların esas belirleyicisi, nodal diseksiyonun kapsamından ziyade tümör biyolojisi gibi görünmektedir.

Anahtar Kelimeler: Endometriyal Kanser. Genel Sağkalım. Hastalıksız Sağkalım. Lenfadenektomi.

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Endometrial cancer is the most common gynecologic malignancy in developed countries, with a steadily increasing incidence worldwide¹. In most cases, endometrial cancer is detected while still confined to the uterus, where surgical treatment alone is often sufficient. Once the disease extends beyond the uterus, however, recurrence risk and survival outcomes are markedly affected, highlighting the critical need for precise assessment of disease spread and the provision of appropriate adjuvant therapy after surgery².

The standard surgical approach in endometrial cancer consists of total hysterectomy, bilateral salpingo-oophorectomy, and evaluation of regional lymph nodes. Lymphadenectomy may reveal occult nodal metastases, thereby providing important prognostic information, enabling more accurate staging, and facilitating the individualization of adjuvant therapy³. Nevertheless, the therapeutic value of lymphadenectomy in endometrial cancer remains a matter of considerable debate. Several retrospective and population-based investigations have suggested that removal of regional lymph nodes may contribute to improved oncological outcomes, potentially by reducing the risk of residual microscopic disease and allowing for more accurate risk stratification of patients³⁻⁶. In contrast, two large randomized controlled trials - ASTEC trial and the Italian study conducted by Benedetti Panici and colleagues - failed to demonstrate any survival benefit^{7,8}. It should be noted, however, that both trials specifically assessed pelvic lymphadenectomy, and a considerable proportion of women assigned to the no-lymphadenectomy arm-ranging from 25.2% to 33%-subsequently received pelvic radiotherapy. This crossover in treatment complicates the interpretation of the results, as the administration of adjuvant pelvic radiation in the control groups may have masked any potential survival benefit attributable to lymphadenectomy, thereby limiting the ability of these trials to definitively evaluate its therapeutic value.

The aim of our study is to compare the overall survival and disease-free survival between two groups of patients: those who underwent total hysterectomy and bilateral salpingo-oophorectomy, and those who received total hysterectomy and bilateral salpingo-oophorectomy in addition to lymphadenectomy.

Material and Method

Study Design and Patient Selection

This retrospective cohort study was conducted using clinical and histopathological data retrieved from the electronic medical records of patients diagnosed with endometrial cancer and treated in our clinic between January 2010 and May 2025. A total of 512 patients

who underwent primary surgical treatment for endometrial cancer were included in the analysis. The study protocol was approved by the Bursa Uludağ University Clinical Research Ethics Committee (Protocol No: 2025/803/14-22) and carried out in accordance with the principles of the Declaration of Helsinki.

Eligible patients were those with histologically confirmed endometrioid endometrial carcinoma, staged as FIGO (International Federation of Gynecology and Obstetrics) 2009 stage I–III, who underwent total hysterectomy, bilateral salpingo-oophorectomy, and/or pelvic and/or para-aortic lymphadenectomy. Exclusion criteria were patients who received fertility-sparing treatment, those with non-endometrioid histologic subtypes, FIGO stage IV disease, intraoperatively detected bulky metastatic lymph nodes, peritoneal dissemination, mixed histology, synchronous malignancies, or those who had received neoadjuvant therapy. All surgical procedures were performed by experienced gynecologic oncologists in accordance with international surgical standards.

Clinical and Pathological Evaluation

Demographic variables (age, body mass index (BMI)) and clinicopathological characteristics (tumor size, histologic subtype, tumor grade, depth of myometrial invasion, presence of lymphovascular space invasion (LVSI), and FIGO 2009 stage) were recorded. Patients were categorized into two groups based on the performance of lymphadenectomy (lymphadenectomy performed vs. not performed). In cases where lymphadenectomy was carried out, pelvic and/or para-aortic lymph node dissection was performed. In our cohort, para-aortic lymphadenectomy was not systematically performed in all patients. The decision was guided by intraoperative frozen section findings and surgical judgment. Specifically, para-aortic dissection was omitted in cases with technically challenging anatomy, poor general condition, or when frozen section results did not indicate high-risk features such as grade 3 endometrioid carcinoma, $\geq 50\%$ myometrial invasion, cervical stromal involvement, or tumor size ≥ 2 cm. This selective approach reflects the institutional practice during the study period and may aid in the interpretation of the study design and outcomes.

We do not perform sentinel lymph node mapping in our institution because near-infrared fluorescence imaging with indocyanine green (ICG), which is required for laparoscopic procedures, is not available.

The decision for adjuvant treatment (chemotherapy, radiotherapy, or combined chemoradiotherapy) was made by a multidisciplinary tumor board in accordance with national and international guidelines. Postoperative follow-up was scheduled every 3–6

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months during the first two years, every 6 months during the following three years, and annually thereafter. Additional imaging (CT or PET/CT) was obtained if recurrence or metastasis was clinically suspected. Findings consistent with recurrence, as confirmed by imaging or biopsy and evaluated according to RECIST 1.1 (Response Evaluation Criteria in Solid Tumors) criteria, were considered as disease recurrence.

Oncological Outcomes

The primary endpoints were disease-free survival (DFS) and overall survival (OS). DFS was defined as the interval from surgery to the date of first recurrence or disease progression, whereas OS was defined as the interval from surgery to death from any cause. Survival times were calculated in months from the date of surgery.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were compared between groups using the Mann–Whitney U test, while categorical variables were analyzed using the Chi-square test. Descriptive statistics were expressed as median (minimum–maximum) for continuous variables and as frequency (percentage) for categorical variables. A two-sided p -value <0.05 was considered statistically significant.

Survival outcomes (DFS and OS) were estimated using the Kaplan–Meier method, and survival curves were compared using the log-rank test. To identify independent prognostic factors influencing DFS and OS, Cox proportional hazards regression analysis was performed. Variables with a p -value <0.10 in univariate analysis were included in the multivariate model. Results were reported as hazard ratios (HRs) with 95% confidence intervals (CIs).

Results

A total of 512 patients with endometrial cancer were included in the study, of whom 407 (79.5%) had undergone lymphadenectomy and 105 (20.5%) had not. Within the lymphadenectomy group, in addition to pelvic lymphadenectomy, para-aortic lymphadenectomy was performed in 291 patients.

The median follow-up duration for the entire cohort was 68 months (range, 1–167 months). The median age was slightly higher in the lymphadenectomy group compared with the non-lymphadenectomy group (63 vs. 62 years, $p=0.011$). Patients who had undergone lymphadenectomy had a lower median BMI (34.0 vs. 36.1 kg/m², $p=0.007$) but significantly

larger tumor sizes (4.0 vs. 3.0 cm, $p<0.001$). Distribution of FIGO stage differed significantly between the two groups ($p<0.001$). Stage IA disease was more frequent among patients without lymphadenectomy (90.5% vs. 61.7%), whereas more advanced stages (II–IIIC) were more common in the lymphadenectomy group. Similarly, high-grade tumors (grade 3) were more prevalent in the lymphadenectomy group (17.2% vs. 6.7%, $p=0.004$). Deep myometrial invasion ($>50%$) was significantly more frequent among patients who underwent lymphadenectomy (29.7% vs. 7.6%, $p<0.001$). Lymphovascular space invasion (LVSI) was also more common in the lymphadenectomy group (26.5% vs. 8.6%, $p<0.001$).

Surgical approach differed significantly between groups: laparotomy was more common in the lymphadenectomy group (72.5% vs. 58.1%), whereas laparoscopy was more frequently performed in the non-lymphadenectomy group (41.9% vs. 27.5%, $p=0.006$). Adjuvant therapy administration also varied: in the lymphadenectomy group, radiotherapy (53.3%) and combined chemoradiotherapy (19.4%) were most common, while the non-lymphadenectomy group predominantly received no adjuvant therapy (67.6%) ($p<0.001$). Recurrence rates did not significantly differ between groups (7.9% vs. 6.7%, $p=0.837$) (Table I).

Disease-free survival

In the univariate Cox analysis for DFS, significant predictors included age (HR 1.050, 95% CI 1.013–1.087, $p=0.007$), BMI (HR 1.14, 95% CI 1.04–1.024, $p<0.001$), LVSI (HR 2.624, 95% CI 1.393–4.943, $p=0.003$), and tumor grade (grade 3 vs. 1: HR 3.158, 95% CI 1.364–7.307, $p=0.007$). Multivariable analysis confirmed age (HR 1.048, 95% CI 1.022–1.076, $p<0.001$), presence of LVSI (HR 2.278, 95% CI 1.051–4.939, $p=0.037$), and grade 3 histology (HR 2.498, 95% CI 1.000–6.242, $p=0.050$) as independent prognostic factors for DFS (Table II).

Kaplan–Meier survival analysis revealed no significant difference in DFS between patients who had undergone lymphadenectomy and those who had not (HR 1.31, 95% CI 0.58–2.96, $p=0.547$). The estimated 5-year DFS rates were 92.5% in the lymphadenectomy group and 92.1% in the non-lymphadenectomy group (Figure 1).

Table I. Comparison of clinical and pathological characteristics between lymphadenectomy (+) and lymphadenectomy (-).

Characteristics	Lymphadenectomy (+) (n=407)	Lymphadenectomy (-) (n=105)	p ^a value
Age, y, median (range), n, (%)	63.0 (31-90)	62.0 (27-93)	0.011
BMI, kg/m2, median (range)	34.0 (18.0-65.3)	36.1 (20.0-64.5)	0.007
Tumor size, cm, median (range)	4.0 (0.2-12.0)	3.0 (0.2-10.0)	<0.001
FIGO stage ^b , n, (%)			
IA	251 (61.7%)	95 (90.5%)	<0.001
IB	66 (16.2%)	8 (7.6%)	
II	29 (7.1%)	1 (1.0%)	
IIIA	15 (3.7%)	1 (1.0%)	
IIIB	0 (0.0%)	0 (0.0%)	
IIIC1	17 (4.2%)	0 (0.0%)	
IIIC2	29 (7.1%)	0 (0.0%)	
FIGO grade			
1	185 (45.5%)	64 (61.0%)	0.004
2	152 (37.3%)	34 (32.4%)	
3	70 (17.2%)	7 (6.7%)	
Depth of myometrial invasion, n, (%)			
< %50	286(70.3%)	97 (92.4%)	<0.001
≥ %50	121 (29.7%)	8 (7.6%)	
LVSI, n, (%)			
Absent	299 (73.5%)	96 (91.4%)	<0.001
Present	108 (26.5%)	9 (8.6%)	
Surgery type, n (%)			
Laparoscopy	112 (27.5%)	44 (41.9%)	0.006
Laparotomy	295 (72.5%)	61 (58.1%)	
Adjuvant treatment, n, (%)			
None	94 (23.1%)	71 (67.6%)	<0.001
Chemotherapy	17 (4.2%)	0 (0.0%)	
Radiotherapy	217 (53.3%)	30 (28.6%)	
Chemotherapy and radiotherapy	79 (19.4%)	4 (3.8%)	
Recurrence, n, (%)			
Yes	32 (7.9%)	7 (6.7%)	0.837
No	375 (92.1%)	98 (93.3%)	

Abbreviations: BMI: body mass index; FIGO: International Federation of Gynecology and Obstetrics; LVSI: lymph-vascular space invasion; n: number; y: years. ^ap-values of age, BMI and tumor size were determined by Mann-Whitney U test and the others were determined by Chi-squared test. ^bThe disease stage was based on the 2009 FIGO staging system.

Table II. Univariate and multivariate analysis of factors affecting disease-free survival.

	Univariate Model		Multivariable Model	
	HR (95%CI)	p	HR (95%CI)	p
Age (years)	1.050 (1.013–1.087)	0.007	1.048 (1.022–1.076)	<0.001
BMI (kg/m2)	1.14 (1.004–1.024)	<0.001	1.014 (0.973–1.057)	0.509
Tumor Size (cm)	1.084 (0.935–1.256)	0.284	-	-
Lymphadenectomy, (yes)	1.19 (0.51 – 2.79)	0.681	-	-
FIGO Stage		0.023		0.324
• IB – IA (Ref.)	1.668 (0.712–3.906)	0.239	2.708 (0.681–10.770)	0.157
• II – IA (Ref.)	1.207 (0.284–5.135)	0.799	1.309 (0.286–5.990)	0.729
• ≥III – IA (Ref.)	2.301 (1.023–5.175)	0.044	2.625 (0.971–7.098)	0.057
Depth of myometrial invasion (>50%)	1.292 (0.643–2.596)	0.472	-	-
LVSI (Present)	2.624 (1.393–4.943)	0.003	2.278 (1.051–4.939)	0.037
Grade		0.043		0.062
• 2 – 1 (Ref.)	1.934 (0.904–4.135)	0.089	1.463 (0.651–3.288)	0.357
• 3 – 1 (Ref.)	3.158 (1.364–7.307)	0.007	2.498 (1.000–6.242)	0.050
Surgical type – Laparotomy	0.778 (0.385–1.573)	0.484	-	-
Adjuvant Treatment		0.001		0.056
• KT – (Ref: No)	3.002 (0.602–14.964)	0.180	2.456 (0.422–14.297)	0.317
• RT – (Ref: No)	2.207 (0.881–5.528)	0.091	1.490 (0.531–4.179)	0.449
• KRT – (Ref: No)	4.014 (1.506–10.702)	0.005	2.467 (0.637–9.557)	0.191

Abbreviations: BMI: body mass index; FIGO: International Federation of Gynecology and Obstetrics; LVSI: lymph-vascular space invasion; KT: Chemotherapy, RT: Radiotherapy, KRT: Chemotherapy and Radiotherapy, HR: Hazard Ratio, CI: Confidence Interval, Ref: Reference Category.

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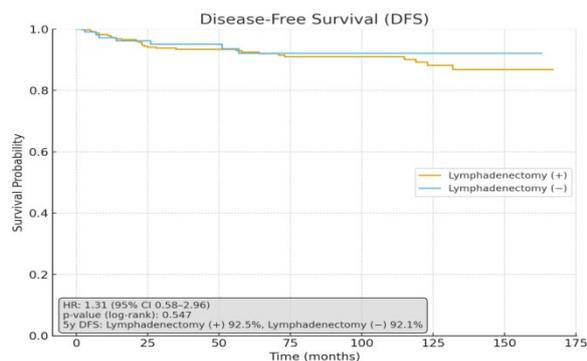


Figure 1:
Kaplan–Meier estimates of 5-year disease-free survival (DFS) in patients with and without lymphadenectomy.

Overall survival

For OS, univariate analysis revealed age (HR 1.101, 95% CI 1.074–1.129, $p < 0.001$), advanced stage (IB vs. IA: HR 2.039, 95% CI 1.217–3.415, $p = 0.007$), deep myometrial invasion (HR 2.092, 95% CI 1.371–3.193, $p = 0.001$), and tumor grade (grade 2 vs. 1: HR 2.344, 95% CI 1.435–3.831, $p = 0.001$; grade 3 vs. 1: HR 2.403, 95% CI 1.315–4.393, $p = 0.004$) as significant prognostic factors. In the multivariable model, independent predictors for OS were age (HR 1.098, 95% CI 1.069–1.127, $p < 0.001$) and grade 2 histology compared with grade 1 (HR 1.870, 95% CI 1.114–3.137, $p = 0.018$) (Table III).

Kaplan–Meier survival analysis showed that lymphadenectomy was not associated with improved

OS (HR 1.42, 95% CI 0.81–2.47, $p = 0.199$). The 5-year OS rate was 83.2% in the lymphadenectomy group compared with 87.5% in the non-lymphadenectomy group (Figure 2).

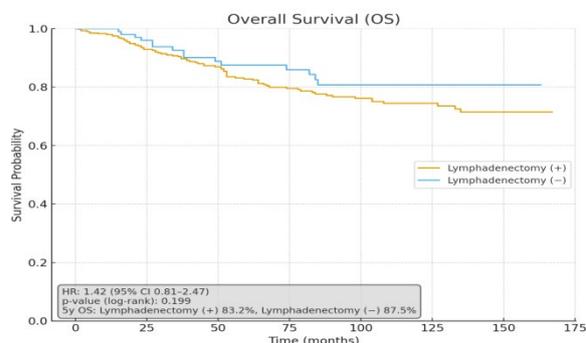


Figure 2:
Kaplan–Meier estimates of 5-year overall survival (OS) in patients with and without lymphadenectomy.

Discussion and Conclusion

In this retrospective cohort study, we investigated the therapeutic and prognostic impact of retroperitoneal lymphadenectomy in 512 patients with endometrioid endometrial cancer. Our findings demonstrated that although patients who had undergone lymphadenectomy more frequently presented with adverse pathological features, including larger tumor size, higher tumor grade, deep myometrial invasion,

Table III. Univariate and multivariate analysis of factors affecting overall survival.

	Univariate Model		Multivariable Model	
	HR (95%CI)	p	HR (95%CI)	p
Age (years)	1.101 (1.074–1.129)	<0.001	1.098 (1.069–1.127)	<0.001
BMI (kg/m ²)	1.010 (0.984–1.037)	0.464	-	-
Tumor Size (cm)	1.064 (0.963–1.176)	0.223	-	-
Lymphadenectomy, (yes)	1.38 (0.76–2.51)	0.296	-	-
FIGO Stage		0.012		0.124
• IB – IA (Ref.)	2.039 (1.217–3.415)	0.007	0.690 (0.271–1.757)	0.437
• II – IA (Ref.)	1.321 (0.528–3.308)	0.552	0.796 (0.277–2.286)	0.672
• ≥III – IA (Ref.)	1.663 (0.922–3.002)	0.091	1.004 (0.448–2.251)	0.992
Depth of myometrial invasion (>50%)	2.092 (1.371–3.193)	0.001	2.089 (0.904–4.830)	0.085
LVSI (Present)	1.511 (0.972–2.349)	0.067	-	-
Grade		0.001		0.021
• 2 – 1 (Ref.)	2.344 (1.435–3.831)	0.001	1.870 (1.114–3.137)	0.018
• 3 – 1 (Ref.)	2.403 (1.315–4.393)	0.004	1.767 (0.921–3.390)	0.087
Surgical type – Laparotomy	1.759 (0.955–3.241)	0.070	-	-
Adjuvant Treatment		0.044		0.654
• KT – (Ref: No)	1.279 (0.382–4.286)	0.690	0.833 (0.210–3.306)	0.795
• RT – (Ref: No)	1.406 (0.844–2.341)	0.191	0.790 (0.431–1.447)	0.444
• KRT – (Ref: No)	1.840 (1.012–3.347)	0.046	0.950 (0.383–2.355)	0.911

Abbreviations: BMI: body mass index; FIGO: International Federation of Gynecology and Obstetrics; LVSI: lymph-vascular space invasion; KT: Chemotherapy, RT: Radiotherapy, KRT: Chemotherapy and Radiotherapy, HR: Hazard Ratio, CI: Confidence Interval, Ref: Reference Category.

and the presence of lymphovascular space invasion, the procedure did not provide any significant improvement in disease-free survival or overall survival.

In our study, the estimated 5-year DFS rates were 92.5% in the lymphadenectomy group and 92.1% in the non-lymphadenectomy group. The 5-year OS rate was 83.2% in the lymphadenectomy group compared with 87.5% in the non-lymphadenectomy group. No statistically significant differences were observed between the groups with respect to either DFS or OS. The survival rates observed in our study are consistent with those reported in the literature⁹. These results suggest that the therapeutic benefit of systematic lymphadenectomy may be limited, and its primary role lies in accurate staging and prognostic assessment rather than direct improvement of oncologic outcomes.

Our findings are in agreement with the ASTEC and Italian randomized trials, both of which showed no survival advantage with pelvic lymphadenectomy^{7,8}. However, it should be noted that in these studies, a substantial proportion of patients in the control groups received adjuvant pelvic radiotherapy, which may have masked a potential benefit of lymphadenectomy. Similarly, Zheng et al., in their analysis of 11,603 patients with stage IA G3–4 endometrial cancer using the SEER database, initially suggested that lymphadenectomy might improve survival; however, this effect disappeared after adjustment for age and comorbidities¹⁰. Ignatov et al. also reported that systematic pelvic and para-aortic lymphadenectomy did not provide a survival benefit in patients with stage I–II endometrioid endometrial cancer at intermediate or high risk of recurrence¹¹. Furthermore, an Australian national study confirmed that lymphadenectomy had no survival impact in patients with stage IA G3, IB G1–3, and II G1–3 tumors¹². Conversely, the Japanese SEPAL study demonstrated that combined pelvic and para-aortic lymphadenectomy significantly improved survival compared with pelvic lymphadenectomy alone, particularly in patients with intermediate- and high-risk disease^{3,13}. These conflicting results highlight the challenges in assessing the therapeutic value of lymphadenectomy, which is heavily influenced by patient selection, surgical extent, and adjuvant treatment strategies.

In our analysis, age, tumor grade, and LVSI emerged as independent prognostic factors for recurrence and survival, whereas lymphadenectomy itself was not an independent predictor. This underscores the dominant role of tumor biology over surgical extent in determining oncologic outcomes. The most recent ESGO/ESTRO/ESP 2025 guidelines emphasize that routine systematic lymphadenectomy is not recommended in clinically early-stage endometrial

cancer; instead, sentinel lymph node (SLN) mapping should be preferred. This approach ensures accurate staging while minimizing morbidity associated with extensive lymph node dissection, such as lymphedema, lymphocyst formation, and prolonged operative time¹⁴.

Our findings regarding the lack of survival benefit must also be interpreted in the context of surgical morbidity. In our study, lymphadenectomy was more frequently performed via laparotomy, reflecting both surgical complexity and historical practice patterns. Currently, minimally invasive surgery combined with SLN mapping is increasingly adopted, offering a safer, less morbid, and oncologically reliable alternative to systematic dissection¹⁵.

With the Cancer Genome Atlas (TCGA) project, a molecular classification of endometrial cancer was established, defining four subgroups: POLE-ultramutated (POLEmut), mismatch repair-deficient (MMRd), p53-abnormal (p53abn), and no specific molecular profile (NSMP). The 2025 ESGO/ESTRO/ESP guidelines have fully adopted a molecular-based classification system. In this framework, disease stage and additional biological features are integrated to define low, intermediate, high-intermediate, high, and indeterminate risk categories. Each risk group is now associated with specific adjuvant treatment recommendations tailored according to molecular profile and complementary prognostic factors¹⁴.

The strengths of this study include the relatively large single-institution cohort, the availability of detailed clinicopathological data, and the long median follow-up period of 68 months. Nonetheless, several limitations must be acknowledged. The retrospective design and lack of randomization carry the risk of selection bias, as patients undergoing lymphadenectomy tended to present with higher-risk disease and were more frequently treated with adjuvant therapy. In addition, perioperative complications related to lymphadenectomy were not systematically recorded, precluding a full assessment of treatment-related morbidity. Finally, the focus on endometrioid histology limits the generalizability of our findings to non-endometrioid subtypes. The absence of SLN use in the study represents another limitation.

In conclusion, systematic lymphadenectomy does not confer a survival benefit in patients with endometrioid endometrial cancer. Age, tumor grade, and LVSI remain the most important independent prognostic factors for recurrence and survival. However, sentinel lymph node mapping has emerged as the most rational and guideline-concordant approach. Future prospective trials with standardized surgical and adjuvant treatment protocols are needed to more

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clearly define the patient subgroups that may derive benefit from lymphadenectomy.

Researcher Contribution Statement:

Idea and design: Y.Y., K.O.; Data collection and processing: Y.Y.; Analysis and interpretation of data: Y.Y.; Writing of significant parts of the article: Y.Y., K.O

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