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ORIGINAL ARTICLE/ORİJİNAL MAKALE

# Sentinel Lymph Node Mapping in the Surgical Management of Endometrial Intraepithelial Neoplasia: A Single-Center Experience

## Endometrial İntraepitelyal Neoplazi Cerrahisinde Sentinel Lenf Nodu Haritalaması: Tek Merkez Deneyimi

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**ABSTRACT**

**Objective:** Endometrial intraepithelial neoplasia (EIN) is a well-defined precursor lesion of endometrial cancer (EC) and is associated with a substantial risk of concurrent malignancy. The necessity of lymph node assessment in patients diagnosed with EIN remains controversial. This study aimed to evaluate the feasibility of sentinel lymph node (SLN) mapping, surgical outcomes, and clinical parameters associated with concurrent EC in patients with a preoperative diagnosis of EIN.

**Material and Method:** Thirty-three patients who underwent hysterectomy with SLN mapping for a preoperative diagnosis of EIN between January 2024 and February 2026 at our center were retrospectively analyzed. According to final pathology results, patients were divided into two groups as EC and EIN/benign pathology. Clinical, pathological, and surgical parameters were compared between the groups.

**Results:** Concurrent EC was detected in 10 of 33 patients (30.3%). The bilateral SLN detection rate was 66.7%, and unilateral SLN detection was achieved in 27.2% of patients. No lymph node metastasis was identified. All EC cases had low-grade endometrioid histology without deep myometrial invasion or lymphovascular space invasion. Two patients had pathological features indicating lymph node dissection according to Mayo criteria. Suspicion of invasive disease in preoperative pathology and higher CA-125 levels were significantly associated with concurrent EC ($p<0.05$). The perioperative complication rate was 15.2%, with only one complication requiring surgical intervention.

**Conclusion:** SLN mapping appears to be a feasible and safe approach in patients with a preoperative diagnosis of EIN. The considerable rate of concurrent EC suggests that SLN evaluation may contribute to surgical staging, particularly in patients with suspicion of invasive disease.

**Keywords:** Atypical Endometrial Hyperplasia, Endometrial intraepithelial neoplasia, Endometrium Cancer, Sentinel Lymph Nodes

**ÖZET**

**Amaç:** Endometrial intraepitelyal neoplazi (EIN), endometrium kanserinin (EK) iyi tanımlanmış prekürsör lezyonu olup önemli oranda eş zamanlı kanser riski taşımaktadır. EIN tanısı alan hastalarda lenf nodu değerlendirmesinin gerekliliği tartışmalıdır. Bu çalışmada preoperatif EIN tanısı olan hastalarda sentinel lenf nodu (SLN) haritalamasının uygulanabilirliği, cerrahi sonuçları ve eş zamanlı endometrium kanseri ile ilişkili klinik parametrelerin değerlendirilmesi amaçlandı.

**Gereç ve Yöntemler:** Ocak 2024 – Şubat 2026 tarihleri arasında merkezimizde preoperatif EIN tanısı ile opere edilen ve en az histerektomi ile birlikte SLN haritalaması uygulanan 33 hasta retrospektif olarak incelendi. Hastalar nihai patoloji sonuçlarına göre EK ve EIN/benign patoloji olarak iki gruba ayrıldı. Klinik, patolojik ve cerrahi parametreler karşılaştırıldı.

**Sonuçlar:** Toplam 33 hastanın 10'unda (%30.3) eş zamanlı EK saptandı. Bilateral SLN saptama oranı %66.7, unilateral saptama oranı %27.2 idi. Hiçbir hastada lenf nodu metastazı izlenmedi. EK saptanan olguların tamamı düşük dereceli endometrioid histolojide olup derin myometrial invazyon ve lenfovasküler alan invazyonu saptanmadı. İki hastada Mayo kriterlerine göre lenf nodu diseksiyonu gerektirebilecek patolojik özellikler mevcuttu. Preoperatif patolojide invaziv hastalık şüphesi ve yüksek CA-125 düzeyi eş zamanlı kanser ile anlamlı olarak ilişkili bulundu ($p<0.05$).Perioperatif komplikasyon oranı %15.2 idi ve sadece bir hastada cerrahi müdahele gerektirecek komplikasyon izlendi.

**Tartışma:** Preoperatif EIN tanısı olan hastalarda SLN haritalaması uygulanabilir ve güvenli bir yöntemdir. EIN olgularında eş zamanlı EK oranının yüksek olması, hastalarda SLN değerlendirmesinin cerrahi evreleme açısından katkı sağlayabileceğini düşündürmektedir. Özellikle invaziv hastalık şüphesi bulunan hastalarda SLN haritalaması daha fazla önem kazanabilir.

**Anahtar Kelimeler:** Atipili endometrial hiperplazi, Endometrial intraepitelyal neoplazi, Endometrium kanseri, Sentinel lenf nodu

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## INTRODUCTION

Endometrial cancer (EC) is the most common gynecologic malignancy in developed countries. Endometrial intraepithelial neoplasia (EIN), also referred to as atypical endometrial hyperplasia, is a well-defined precursor lesion of EC (1). These lesions carry both a risk of progression to cancer and a significant probability of concurrent EC at the time of diagnosis (2). The reported risk of concurrent EC in patients diagnosed with EIN ranges between 10% and 50% in the literature (3-5). Due to this risk, hysterectomy is considered the standard treatment for EIN, with bilateral salpingo-oophorectomy recommended in appropriate patients.

Lymph node assessment represents an important part of surgical staging in EC; however, its necessity in EIN patients remains controversial. Most EC cases detected in the setting of EIN are early-stage, low-grade endometrioid tumors confined to the uterus, and the risk of lymph node metastasis is generally considered low (4). Therefore, the benefit of systematic lymphadenectomy in these patients has been questioned (6). Nevertheless, cases of lymph node metastasis have been reported among patients undergoing surgery for EIN, suggesting that nodal evaluation should not be completely disregarded (4, 6).

Sentinel lymph node (SLN) mapping has been demonstrated to be an effective and minimally invasive method for surgical staging in early-stage EC (7). Compared with systematic lymphadenectomy, SLN biopsy provides similar staging accuracy with lower surgical morbidity (8). Because of the relatively low risk of nodal metastasis, many surgeons have adopted SLN mapping in patients with EIN (9). Recent studies have demonstrated an increasing use of SLN mapping in EIN and atypical hyperplasia patients without a significant increase in perioperative morbidity (10). However, despite its minimally invasive nature, SLN mapping may still expose patients without concurrent cancer to procedure-related risks and potential overtreatment. Therefore, the routine use of nodal assessment in this population remains controversial (11).

In this study, we aimed to evaluate the feasibility of SLN mapping in patients with a preoperative diagnosis of EIN and to present our single-center experience. Additionally, we investigated clinical parameters that may be associated with concurrent EC in EIN patients.

## MATERIALS AND METHODS

This retrospective study included patients who underwent surgery with at least hysterectomy and SLN mapping for a preoperative diagnosis of EIN at our institution between January 2024 and February 2026. Patients were divided into two groups according to final pathology results as EC or EIN/benign pathology. Clinical and pathological characteristics were compared between groups.

The need for lymph node dissection was determined retrospectively using the Mayo criteria based on final histopathological findings (12). Intraoperative frozen section evaluation was not included in the study. Preoperative pathology reports including statements such as “invasive disease cannot be excluded” or “suspicious for invasive disease” were considered as suspicion of EC. Suspicion of invasive disease on imaging was based on magnetic resonance imaging and/or computed tomography findings, when available. Imaging was not routinely performed in all patients and was obtained selectively according to clinical indication. If the tumor was present only as

microscopic foci in the final pathology, tumor size was accepted as 1 mm.

Complications occurring within the first 30 days after surgery were considered perioperative complications and were graded according to the Clavien–Dindo classification (13).

Statistical analysis was performed using SPSS software. Continuous variables were expressed as mean ± standard deviation, and categorical variables were presented as number and percentage. Appropriate parametric or non-parametric tests were used for comparisons between groups. Chi-square analysis was performed for categorical comparisons, and Fisher's exact test was applied when necessary. A p-value <0.05 was considered statistically significant.

## RESULTS

A total of 33 patients were included in the study. The mean age was 50.4 ± 8.3 years. Final pathology revealed concurrent EC in 10 patients (30.3%). Indocyanine green (ICG) was the most commonly used tracer for SLN mapping (78.8%). Bilateral SLN detection was achieved in 66.7% of patients (n=22), while SLN mapping failed in 6.1% of patients (n=2) **(Table 1)**.

All EC cases were endometrioid adenocarcinoma with grade 1 histology. No nodal metastasis was detected. According to final pathology results, two patients had pathological features indicating lymph node dissection based on Mayo criteria **(Table 2)**.

CA-125 levels were significantly higher in patients with EC compared to those with EIN/benign pathology (27.5 ± 18.2 vs 13.2 ± 7.8; p=0.039). Suspicion of invasive disease in preoperative pathology was also significantly associated with the presence of EC (p=0.036). No statistically significant differences were observed between groups for other clinical variables **(Table 1)**.

The perioperative complication rate was 15.2% (n=5). Only one patient experienced a Clavien–Dindo grade 3 complication (ureteral injury), which required surgical repair. The remaining complications were managed medically. The most common complication was the need for blood transfusion (n=2).

## DISCUSSION

In this study, we evaluated the outcomes of SLN mapping in patients who underwent surgery with a preoperative diagnosis of EIN. In our series of 33 patients, the rate of concurrent EC was 30.3%. Previous studies have reported that the prevalence of concurrent EC in patients diagnosed with EIN ranges between 10% and 50% (1, 4, 6). The rate observed in our study is consistent with the existing literature. Variations in reported rates across studies may be explained by differences in patient demographics, histopathological evaluation criteria, and inter-institutional diagnostic variability.

In our study, the rates of bilateral and unilateral SLN mapping were 66.7% and 27.2%, respectively. No statistically significant difference in mapping success was observed between patients diagnosed with EC and those with EIN/benign pathology. No nodal metastasis was detected in our cohort. Previous studies have reported nodal metastasis rates ranging between 1% and 6% in patients operated on with a preoperative diagnosis of EIN (6, 9). In a study by Matanes et al., the nodal metastasis rate was reported as 3.3% (9), while Touhami et al. reported a rate of approximately 6% (6). Notably, these studies included patient populations with higher mean age and a

**Table 1.** Clinical and surgical characteristics of patients with a preoperative diagnosis of EIN

| Parameters | Total (n:33) | EC (n:10) | EIN/Benign (n:23) | p value |
|---|---|---|---|---|
| Age (years) | 50.4 ± 8.3 | 48.8 ± 10.3 | 51.1 ± 7.5 | 0.539 |
| BMI (kg/m²) | 32.5 ± 4.3 | 31.7 ± 5.9 | 32.9 ± 3.5 | 0.638 |
| Menopausal status | | | | |
| Postmenopausal | 10 (30.3%) | 4 (40%) | 6 (26.1%) | 0.424 |
| Premenopausal | 23 (69.7%) | 6 (60%) | 17 (73.9%) | |
| Parity | | | | |
| Nulliparous | 3 (9.1%) | 0 (0%) | 3 (13.0%) | 0.295 |
| 1-2 | 24 (72.7%) | 7 (70%) | 17 (74.0%) | |
| ≥3 | 6 (18.3%) | 3 (30%) | 3 (13.0%) | |
| Suspicion of invasive disease on preoperative pathology | | | | |
| Yes | 8 (24.2%) | 5 (50%) | 3 (13.0%) | **0.036** |
| No | 25 (75.8%) | 5 (50%) | 20 (87.0%) | |
| Suspicion of invasive disease on imaging | | | | |
| Yes | 9 (27.3%) | 3 (30%) | 6 (26.1%) | 0.549 |
| No | 7 (21.2%) | 3 (30%) | 4 (17.4%) | |
| Not available | 17 (51.5%) | 4 (40%) | 13 (56.5%) | |
| CA-125 (U/mL) | 19.4 ± 14.9 | 27.5 ± 18.2 | 13.2 ± 7.8 | **0.039** |
| Endometrial thickness (mm) | 12.2 ± 6.8 | 12.6 ± 8.8 | 12.1 ± 5.7 | 0.842 |
| Surgical approach | | | | |
| Laparotomy | 1 (3.0%) | 0 (0%) | 1 (4.3%) | 0.426 |
| Laparoscopy | 29 (87.9%) | 9 (90%) | 20 (87.0%) | |
| V-notes | 3 (9.1%) | 1 (10%) | 2 (8.7%) | |
| Sentinel dye | | | | |
| ICG | 26 (78.8%) | 8 (80%) | 18 (78.3%) | 0.648 |
| Methylene blue | 7 (21.2%) | 2 (20%) | 5 (21.7%) | |
| Operative time (minutes) | 165.3 ± 35.4 | 176.8 ± 31.9 | 161.3 ± 36.3 | 0.292 |
| SLN detection | | | | |
| Bilateral | 22 (66.7%) | 6 (60%) | 16 (69.6%) | 0.736 |
| Unilateral | 9 (27.2%) | 3 (30%) | 6 (26.1%) | |
| Not detected | 2 (6.1%) | 1 (10%) | 1 (4.3%) | |
| Number of SLNs removed | 3.9 ± 3.1 | 4.6 ± 3.4 | 3.7 ± 3.0 | 0.451 |
| Perioperative complications | | | | |
| Yes | 5 (15.2%) | 1 (10%) | 4 (17.4%) | 0.515 |
| No | 28 (84.8%) | 9 (90%) | 19 (82.6%) | |

**Table 2.** Pathological characteristics of patients diagnosed with endometrial cancer (n=10)

| Parameter | n |
|---|---|
| Histological subtype | |
| Endometrioid | 10 (100%) |
| Non-endometrioid | - |
| Grade | |
| 1 | 10 (100%) |
| 2-3 | - |
| Myometrial invasion | |
| Superficial | 5 (50%) |
| <50% | 5 (50%) |
| ≥50% | - |
| Tumor diameter | |
| <20 mm | 8 (80%) |
| ≥20 mm | 2 (20%) |
| Cervical stromal involvement | |
| No | 10 (100%) |
| Yes | - |
| Lymphovascular space invasion | |
| No | 10 (100%) |
| Yes | - |
| FIGO 2023 stage | |
| 1A1 | 5 (50%) |
| 1A2 | 5 (50%) |
| 2 | - |
| Indication for lymph node dissection | |
| No | 8 (80%) |
| Yes | 2 (20%) |

greater proportion of high-grade tumors. The absence of nodal metastasis in our series may be explained by the limited sample size (10 EC cases), relatively younger patient population (mean age 48.8 years), and the fact that all EC cases demonstrated low-grade endometrioid histology. Furthermore, the absence of deep myometrial invasion and lymphovascular space invasion (LVSI) in our cohort also supports the low risk of nodal metastasis observed in our study.

Several clinical and pathological parameters have been investigated as predictors of concurrent EC in patients diagnosed with EIN (3-5). In our study, the presence of suspicion of invasive disease in preoperative pathology was significantly associated with an increased risk of EC (p=0.036). Similarly, Touhami et al. reported that patients with atypical hyperplasia in whom carcinoma could not be excluded

had significantly higher rates of EC in final pathology (6). In the same study, cases with suspicion of invasive disease were associated with higher tumor grade, increased rates of deep myometrial invasion, and higher rates of lymph node metastasis. These findings suggest that suspicion of invasion in preoperative pathological evaluation should be considered during surgical planning.

Another parameter evaluated in relation to the risk of concurrent EC was the CA-125 level. We found that CA-125 levels were significantly higher in patients diagnosed with EC (p=0.039). Although elevated CA-125 levels are known to be associated with advanced-stage and high-risk EC, evidence regarding its predictive value in EIN patients remains limited (3, 14-16). Therefore, our findings should be confirmed in larger patient cohorts.

Perioperative morbidity was another important parameter evaluated in this study. Complications requiring surgical or medical intervention occurred in 5 patients (15.2%). Only one patient required surgical intervention due to ureteral injury (Clavien–Dindo grade 3). Mueller et al. reported a complication rate of 9% in a series of 161 patients with EIN who underwent SLN mapping (17). In that study, the majority of complications did not require major surgical intervention. In a large study including 10,266 patients, Dioun et al. reported complication rates of 5.2% in patients who underwent SLN mapping and 6.8% in those who did not undergo nodal assessment, with no statistically significant difference between the groups (10). These findings support the safety of SLN mapping in patients with EIN.

The main limitations of our study include its retrospective design and relatively small sample size. Larger prospective studies are needed to better evaluate rare outcomes such as nodal metastasis and to further clarify the role of SLN mapping in patients with EIN.

## CONCLUSİON

SLN mapping appears to be a feasible and safe approach in patients with a preoperative diagnosis of EIN. Considering the substantial rate of concurrent EC, SLN evaluation may contribute to surgical staging. However, this potential benefit may be limited to selected patients due to the low incidence of lymph node involvement in EIN. SLN mapping may be particularly informative in patients with higher-risk features, such as suspicion of invasive disease on preoperative pathology or elevated CA-125 levels. Larger prospective studies are needed to further clarify the role of SLN biopsy in EIN.

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### Ethics Committee Approval

This study was conducted retrospectively and ethics committee approval was not required.

### Author Contributions:

HVE, CH: Conceptualization, Methodology, HNO, NÖ, GE: Data Curation, HVE,GE: Investigation: HVE: Formal Analysis, HVE: Visualization, HVE, HNO, NÖ, GE: Writing, Original Draft, All authors: Writing, Review & Editing.

All authors have read and approved the final manuscript.

### Conflict of Interests

The authors declare no conflict of interest.

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