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Correspondence to

Sang Wun Kim

Women's Cancer Center, Yonsei Cancer Center, Institute of Women's Life Medical Science, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
Email: san1@yuhs.ac

*Dahye Lee and Yoo-Na Kim have contributed equally to this work.

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ORCID iDs

Dahye Lee <https://orcid.org/0000-0003-4637-2224>
Yoo-Na Kim <https://orcid.org/0000-0002-0202-3228>
Sang Hyun Cho <https://orcid.org/0000-0002-7849-1829>
Hye soo Yoon <https://orcid.org/0000-0002-4830-894X>

Comparison of progression-free survival outcome of sentinel node biopsy without ultrastaging versus lymphadenectomy in endometrial cancer: a propensity-matched analysis

Dahye Lee ^{1,*}, Yoo-Na Kim ^{1,*}, Sang Hyun Cho ², Hye soo Yoon ¹,
Young Tae Kim ¹, Sunghoon Kim ¹, Sang Wun Kim ¹

¹Department of Obstetrics and Gynecology, Women's Cancer Center, Yonsei Cancer Center, Institute of Women's Life Medical Science, Yonsei University College of Medicine, Seoul, Korea

²Department of Obstetrics and Gynecology, Seoul St. Mary's hospital, The Catholic University of Korea, Seoul, Korea

ABSTRACT

Objective: We aimed to investigate the oncologic outcomes of patients with endometrial cancer who underwent sentinel lymph node (SLN) biopsy without ultrastaging compared with that of those who underwent lymphadenectomy (LND).


Methods: Patients with endometrial cancer who underwent staging with SLN biopsy or LND during 2006 – 2021 were analyzed using propensity score matching (PSM). SLN metastasis was examined using hematoxylin and eosin staining, without ultrastaging. Progression-free survival (PFS) was compared between the two groups before and after PSM using age, histology, and stage as covariates. Clinical variables such as recurrence patterns and lymphatic complications, were assessed.


Results: After excluding 213 patients who underwent validation LND with SLN biopsy, 902 were identified. The demographics of the remaining patients differed according to histology, myometrial invasion depth, and stage. Lymph node metastasis was less frequent in the SLN group than in the LND group (9.4% vs. 3.8%, $p=0.004$). The recurrence rates within 2 years were lower in the SLN group. The SLN group exhibited significantly superior 2-year and overall PFS than the LND group. Among patients with uterus-confined disease, overall PFS was favorable for SLN biopsy. After matching, differences in PFS were no longer observed, although the lymphocele and lymphedema rates were significantly lower in the SLN group.

Conclusion: In patients with endometrial cancer, SLN biopsy without ultrastaging did not compromise survival outcomes and was associated with significantly reduced lymphatic complication rates compared with LND. Therefore, SLN biopsy can be recommended for patients with endometrial cancer without definitive preoperative evidence of distant metastasis.

Keywords: Endometrial Neoplasms; Sentinel Lymph Node Biopsy; Lymphadenectomy; Survival; Lymphedema/Complications; Lymphocele/Complications

Young Tae Kim 
<https://orcid.org/0000-0002-7347-1052>

Sunghoon Kim 
<https://orcid.org/0000-0002-1645-7473>

Sang Wun Kim 
<https://orcid.org/0000-0002-8342-8701>

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Presentation

Women's Cancer Center, Yonsei Cancer Center, Institute of Women's Life Medical Science, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Yonsei University College of Medicine

Author Contributions

Conceptualization: K.Y.N., K.S.W.; Data curation: L.D., K.Y.N., C.S.H., Y.H.S.; Formal analysis: K.Y.N., C.S.H.; Investigation: L.D.; Methodology: K.Y.N.; Project administration: K.S.W.; Resources: K.Y.T., K.S.; Supervision: K.Y.N., K.S.W.; Validation: K.S.W.; Writing - original draft: L.D., K.Y.N.; Writing - review & editing: K.Y.N.

Synopsis

Survival outcomes of sentinel node (SLN) biopsy without ultrastaging and lymphadenectomy (LND) were retrospectively compared. With propensity score matching, SLN biopsy without ultrastaging demonstrated comparable survival outcomes. SLN biopsy without ultrastaging exhibited a lower rate of lymphatic complications than LND.

INTRODUCTION

Endometrial cancer, with an increasing incidence rate in developing countries, is the most common gynecological cancer [1]. Prognostic studies, such as those on molecular classification [2] and radiological assessment using computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound [3,4] have been conducted to improve survival outcomes. The introduction of sentinel lymph node (SLN) mapping in 1996 was a game-changer in surgical management [5]. Previously, complete lymphadenectomy (LND), which involves removing all pelvic and para-aortic lymph nodes, was the standard surgical staging for endometrial cancer. Lymph node status not only provides prognostic information but also therapeutic and predictive implications that guide the selection of adjuvant therapy [6-8]. Accurately assessing lymph nodes during surgery helps determine whether a patient should receive chemotherapy or radiotherapy [8,9].

Complete LND inadvertently can cause surgical morbidities, such as lymphedema, lymphocele, and nerve injury [10,11]. SLN mapping is an attractive alternative because it can provide equivalent information about lymph node status while sparing patients from unnecessary lymph node dissection and associated morbidities [7,12-14]. Large-scale trials, such as the FIRES and SENTI-ENDO trials [7,12], have demonstrated high diagnostic accuracy, sensitivity, and negative predictive value, leading to a change in the standard of care [15,16]. SLN biopsy is increasingly being used alone, especially for patients with suspected early-stage or histologically low-risk endometrial cancer, based on current guidelines [16,17]. However, evidence is still required for the surgical management of preoperative high-risk endometrial cancer [18,19].

Regarding the oncological outcomes of SLN biopsy, high-quality prospective evidence is lacking. Several retrospective studies suggested that the oncological outcomes of SLN biopsy are comparable to those of complete LND [8,14,20,21], although many of these studies mostly considered patients with early-stage endometrial cancer, and their survival outcomes are immature [14,22]. Retrospective studies also face potential bias due to the time lag between the phase of LND and introduction of SLN biopsy. Large-scale trials such as the PORTEC-3 were introduced during this time span, which could have impacted both the surgical and adjuvant aspects of patient care, potentially changing the trend of adjuvant therapy at the same time [6,23]. Moreover, previous studies on SLN mapping outcomes were based on ultrastaging [16], which varies among centers and incurs extra costs and resources [24]. In practice, many centers have no alternative but to bypass ultrastaging and to assess SLN biopsy samples using conventional hematoxylin and eosin (H&E) staining.

This study aimed to compare the oncological outcomes of complete LND and SLN biopsy, without ultrastaging. Progression-free survival (PFS) was compared using propensity

score matching (PSM), and lymphatic complications were compared between patients with endometrial cancer who underwent SLN biopsy and a historical cohort of those who underwent LND.

MATERIALS AND METHODS

1. Patient selection

We retrospectively analyzed patients with International Federation of Gynecology and Obstetrics (FIGO) 2009 stage I-III endometrial cancer who underwent surgical staging at Yonsei Cancer Center, Seoul, Republic of Korea, from 2006 to 2021. Patients were classified into an LND and SLN group based on the use of the SLN technique. Patients who did not undergo SLN biopsy or LND were excluded. The LND group underwent surgical staging mostly from 2006 to 2013, while the SLN group underwent surgical staging from 2014 to 2021. For a brief period since the introduction of SLN biopsy in 2014, SLN biopsy was followed by validation LND at the clinician's discretion. Thus, patients in whom more than five non-SLNs removed as a result of undergoing both SLN biopsy and LND were excluded from the SLN group. The exclusion criteria included suspected distant organ metastasis, prior hysterectomy or LND for endometrial cancer, contraindication for indocyanine green (ICG), or history of liver disease for the SLN group. The study was approved by the Institutional Review Board (IRB) of Severance Hospital (IRB No #4-2022-0250), and the requirement for informed consent was waived owing to the retrospective design.

2. Lymph node assessment

All patients in the LND group underwent pelvic LND. The extent and number of removed lymph nodes in para-aortic LND were at the clinician's discretion. Generally, para-aortic LND was performed in the following cases: 1) preoperative histology indicated high-risk, such as endometrioid grade 3, serous type, or clear cell carcinoma, or other non-endometrioid histology of any grade, 2) when preoperative imaging (CT, MRI, or positron emission tomography [PET]) revealed an enlarged lymph node or increased F-18 fluorodeoxyglucose uptake in the lymph node in the para-aortic area beyond normal physiological levels, or 3) when enlarged para-aortic lymph nodes were discovered during the surgery. SLN biopsy was performed using either one-step or two-step SLN mapping, as per the protocol detailed in a previous study [25]. The decision to omit LND in the SLN group was mainly based on the SLN algorithm of the National Comprehensive Cancer Network (NCCN) guidelines and negative findings for enlarged lymph nodes confirmed during surgery [16]. Briefly, two-step SLN detection was performed using laparoscopic or robotic platforms by injecting ICG into each cornu through an injection needle inserted at a depth of 1 cm into the bilateral uterine cornu after tubal ligation. Lymphatics drained from the uterus were identified, and biopsy of the para-aortic SLN was conducted. After completing the para-aortic SLN biopsy, ICG was injected at the 3 and 9 o'clock positions of the ectocervix at the superficial and deep cervix. ICG was injected into the cervix for one-step SLN mapping. Intraoperative SLN detection and localization were guided using the PinPoint endoscopic platform (Novadaq Technologies Inc., Toronto, ON, Canada) or robotic platform (da Vinci platform; Intuitive Surgical, Inc., Sunnyvale, CA, USA) for real-time imaging. Successful SLN mapping observed lymphatic drainage to at least one node at either side of the hemipelvis or at the para-aortic level. The harvested SLN was sent for either frozen section during the operation or permanent pathological examination at the end of surgery. No additional surgical procedures were performed even if the SLNs were positive for metastasis.

3. Pathologic examination of lymph nodes

The SLNs, along with the lymph nodes obtained from LND, were sliced into 2–3-mm thick pieces with longitudinal cross-sections and subjected to conventional H&E staining without ultrastaging or accompanying immunohistochemistry, following institutional protocol. Dedicated pathologists examined all removed nodes.

4. Postoperative adjuvant treatment

The postoperative adjuvant therapy followed the NCCN guidelines. For endometrioid or serous histology, paclitaxel 175 mg/m² and carboplatin with an area under the curve 5 to 6 were administered for six cycles of every 3-week regimen. Adjuvant therapy for a rare histology, such as carcinosarcoma or endometrial stromal sarcoma, varied depending on the clinician's discretion within the NCCN guidelines. The field of radiotherapy was determined according to the FIGO stage and was administered according to the NCCN guidelines, including intracavitary radiation, radiation for the whole pelvis, or for the extended abdominal area [16].

5. Data collection

Electronic medical records were reviewed for age at the time of diagnosis, body mass index (BMI), pathologic findings, FIGO staging, disease status during the follow-up period, date of recurrence, and date of the last follow-up of all patients. High-risk histology included endometrioid grade 3 and all non-endometrioid histologies of any grade such as clear cell carcinoma, serous carcinoma, and carcinosarcoma, and others. Low-risk histology included endometrioid grade 1 or 2.

During the first 2 years after surgery, recurrence was assessed every 3 months using CT, MRI, or PET-CT, confirmed by hospital radiologists. Afterward, recurrence was evaluated every 6 months. The incidence of postoperative complications related to LND, such as lymphocele and lymphedema, were calculated for each group. For lymphocele, only those ≥ 1 cm on CT/MRI within a year after surgery were considered. Lymphedema was diagnosed clinically when the patient required rehabilitation and medical treatment. Postoperative adjuvant therapy was administered at the clinician's discretion, based on the NCCN guidelines. Recurrence site was determined via imaging or biopsy, classified as lymph nodes (pelvic, para-aortic, or both), vagina (stump, vault, or wall), peritoneal seeding or metastases (except nodal in the abdominal-pelvic region), distant organ metastases (such as lung or bone, and supraclavicular lymph nodes).

6. Statistical methods

Statistical analyses were performed using R version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria). Baseline characteristics were compared using Student's t-test for continuous variables and the χ^2 test for categorical variables. PSM was performed using the 'MatchIt' package to adjust for differences in cohort size and baseline characteristics. Specifically, 1:1 nearest-neighbor matching was performed using the propensity score, which was estimated based on covariates such as age, histology, and FIGO stage.

Clinical outcomes were evaluated based on PFS, including overall PFS and 2-year-PFS. PFS was compared between the LND and SLN groups before and after the matching. A Cox proportional hazards regression model was used to calculate the hazard ratio (HR) for lymph node evaluation method and other prognostic variables. In the matched cohort, the proportion of patients with nodal metastasis, recurrence rate for uterus-confined stage I or II

disease, anatomical pattern of recurrence location, and postoperative complications such as lymphocele and lymphedema were investigated.

RESULTS

The Yonsei Cancer Center reviewed patients with endometrial cancer who underwent staging operations between 2006 and 2021. Of the 1,115 patients, 645 patients underwent LND, and 470 underwent SLN biopsy. Only 257 patients were included in the SLN group after excluding those who had undergone both SLN biopsy and LND (**Fig. 1**). The LND group had a higher proportion of patients with high-risk histology and deep myometrial invasion. The rate of LN metastasis was significantly higher in the LND group than in the SLN group (9.4% and 3.8%, respectively, $p=0.004$), although the rate of para-aortic LN metastasis was comparable between the two cohorts (4.7% and 1.9% in the LND and SLN groups, respectively). Adjuvant use was similar between the two cohorts; however, chemotherapy was more frequently implemented in the LND group. The median follow-up duration was 2.1 years for patients who underwent SLN biopsy alone and 5.3 years for those belonging to the LND cohort (**Table 1**, **Table S1**).

The SLN group had a significantly lower rate of recurrence within 2 years (3.1% vs. 7.8%, $p=0.006$) and a superior PFS ($p=0.007$; **Fig. 2A**, **Fig. S1**). Based on univariate analysis with respect to overall PFS, patients who underwent SLN biopsy showed a lower HR than those who underwent LND (0.40, $p=0.023$) (**Table S2**). Multivariate analysis showed that the HR for the SLN group was lower than that in the LND group (0.44, $p=0.050$) (**Fig. 3**, **Fig. S2**), even after accounting for other potential factors affecting PFS.

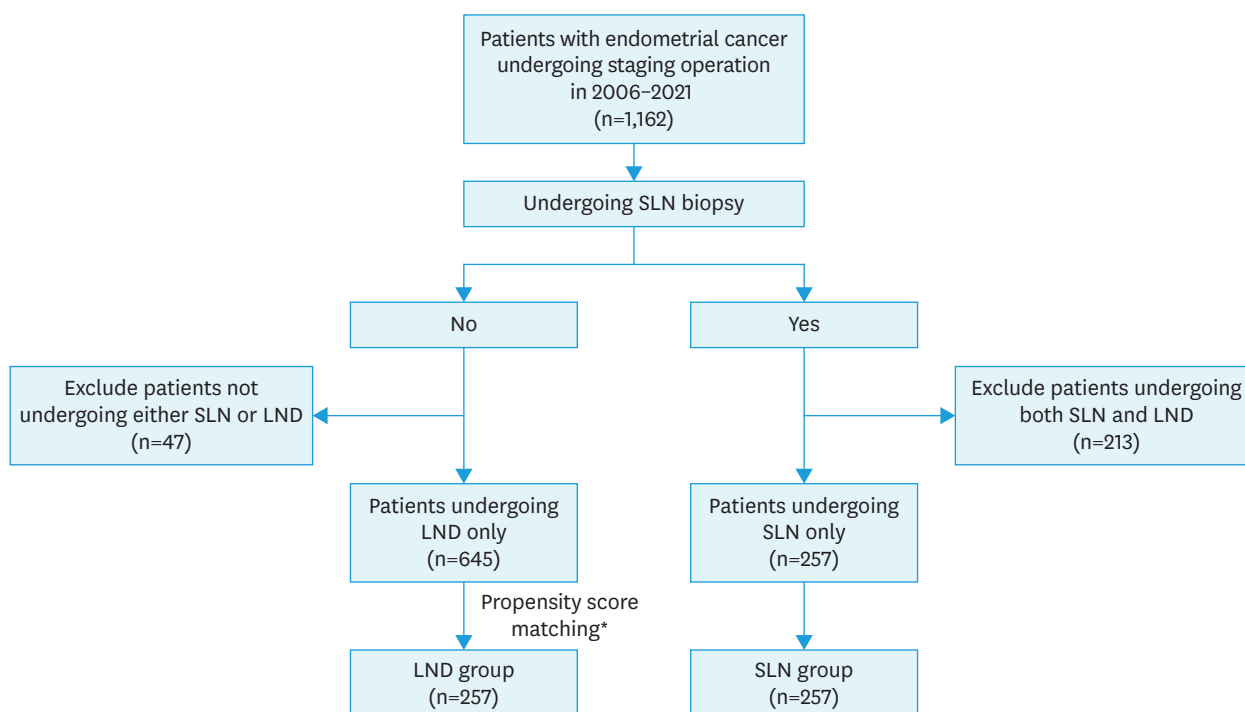


Fig. 1. Patient flow chart. Matching age, histology, and stage.
LND, lymphadenectomy; SLN, sentinel lymph node.

Table 1. Patient demographics before matching

| Variables | SLN group (n=257) | LND group (n=645) | p-value |
|----------------------|-------------------|-------------------|---------|
| Age | 53.5±10.6 | 54.1±10.0 | 0.433 |
| BMI | 25.2±4.6 | 25.2±4.2 | 0.108 |
| Histology | | | 0.003 |
| Endometrioid G1 | 123 (47.9) | 294 (45.6) | |
| Endometrioid G2 | 88 (34.2) | 175 (27.1) | |
| Endometrioid G3 | 26 (10.1) | 69 (10.7) | |
| Serous | 9 (3.5) | 24 (3.7) | |
| Carcinosarcoma | 6 (2.3) | 25 (3.9) | |
| Other* | 5 (2.0) | 58 (9.0) | |
| Myometrial invasion | | | 0.001 |
| Less than half | 220 (85.6) | 484 (85.6) | |
| More than half | 37 (14.4) | 161 (14.4) | |
| LVSI | | | 0.423 |
| No | 221 (86.0) | 539 (83.6) | |
| Yes | 36 (14.0) | 106 (16.4) | |
| FIGO stage | | | 0.004 |
| 1A | 204 (79.4) | 433 (67.1) | |
| 1B | 26 (10.1) | 85 (13.2) | |
| 2 | 11 (4.3) | 46 (7.0) | |
| 3A or 3B | 6 (2.3) | 21 (2.3) | |
| 3C1 | 5 (1.9) | 30 (4.7) | |
| 3C2 | 5 (1.9) | 30 (4.7) | |
| Any adjuvant therapy | 89 (34.6) | 254 (39.4) | 0.211 |
| Chemotherapy | 28 (10.9) | 130 (20.2) | 0.001 |
| Radiotherapy | 76 (29.6) | 155 (24.0) | 0.102 |

Values are presented as mean ± standard deviation or number (%).

BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; G, grade; LND, lymphadenectomy; LVSI, lymphovascular space invasion; SLN, sentinel lymph node.

*Adenocarcinoma and clear cell carcinoma were classified as other.

In the unmatched cohort, patients with FIGO stage I or II disease were investigated, and a trend of better overall PFS in the SLN group was observed. Among these patients, 32 had recurrences within 2 years. The 2-year recurrence rates were 2.1% (5/241) in the SLN and 4.8% (27/564) in the LND group ($p=0.048$). A trend of better overall PFS in the SLN group was observed, despite the lack of statistical significance ($p=0.073$; **Fig. 2B**).

PSM was performed (**Table 2, Table S3**), and after matching, the 2-year recurrence rates did not differ between the SLN and LND groups (3.1% vs. 4.3%, $p=0.101$). There was no difference in 2-year and overall PFS (**Fig. 2C, Fig. S1**). No significant difference was observed between the low-risk and high-risk groups in terms of the 2-year and overall PFS rates (**Figs. S3 and S4**). Recurrence sites for those who experienced recurrences within 2 years are shown in **Table 3**. LND was associated with higher recurrence rates at the peritoneum than SLN biopsy (3.11% vs. 0.39%, $p=0.019$). While no significant difference in the nodal recurrence rates was observed between the two groups, LND was associated with a trend toward higher rates. Lymphatic complications were significantly lower in the SLN group than in the LND group (lymphocele: 2.3% vs. 8.9%, $p=0.002$; lymphedema: 0.8% vs. 4.3%, $p=0.025$) (**Table S4**).

DISCUSSION

The replacement of complete LND, with SLN biopsy has become increasingly common, from low-risk to high-risk disease and suspected advanced-stage disease [14,19-21]. In our study, we analyzed a sizable cohort of patients with endometrial cancer undergoing SLN

SLN without ultrastaging vs. LND in uterine cancer

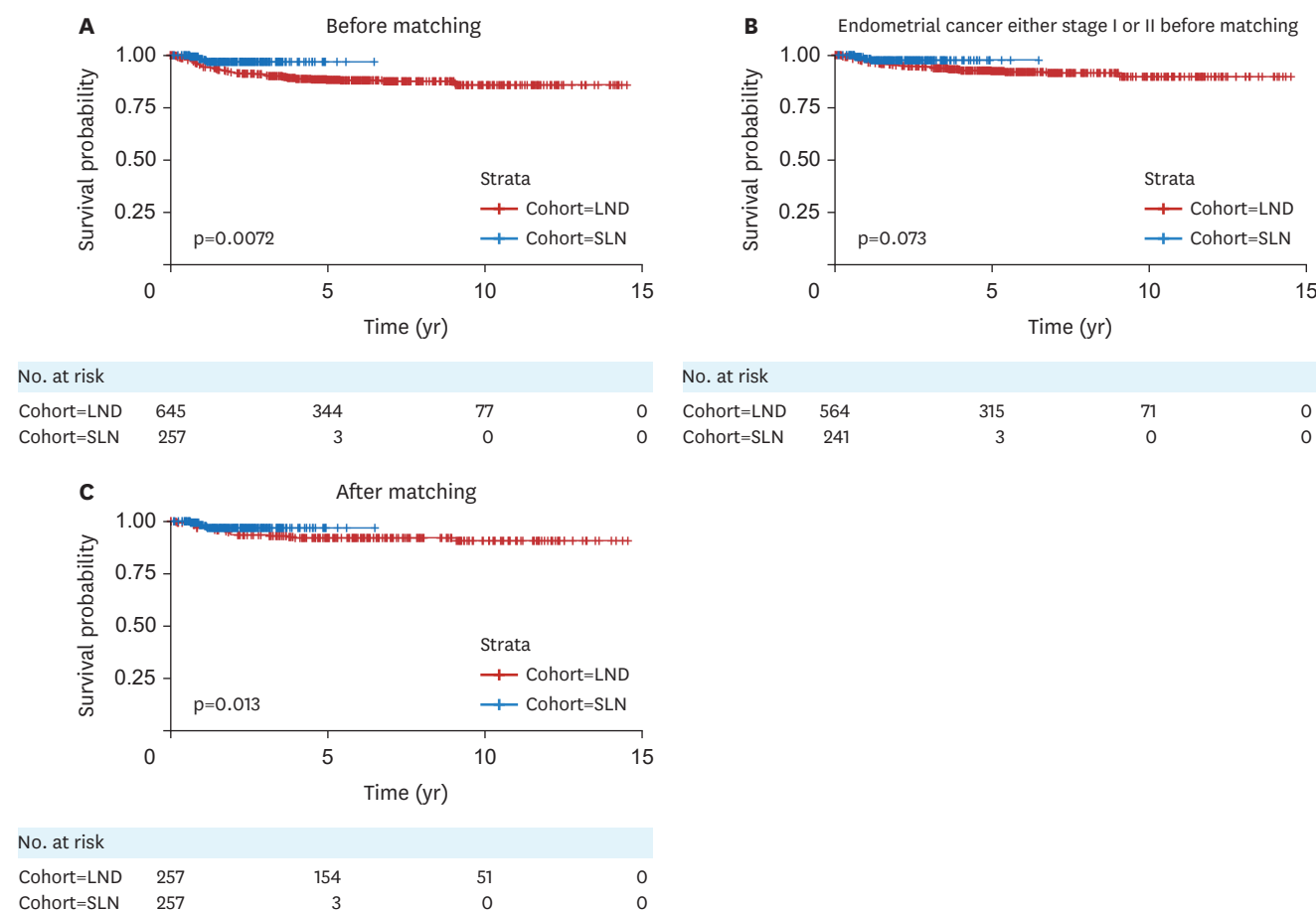


Fig. 2. Overall progression-free survival of patients. (A) Before matching (B) Endometrial cancer either stage I or II before matching (C) After matching. LND, lymphadenectomy; SLN, sentinel lymph node.

mapping without ultrastaging and a historical cohort of patients who underwent LND. PSM was utilized to address potential biases. Our study showed a clinical trend toward improved PFS in patients who underwent SLN mapping compared with those who underwent LND. Differences in survival outcomes were no longer observed after PSM, although the rate of lymphatic complications was lower in patients who underwent SLN mapping.

Our study examined the SLN alone with H&E staining, without ultrastaging, which is unique. Previous research has shown that ultrastaging of SLNs improves the detection of lymph node involvement in low-volume metastasis [14,26,27]. However, there is controversy over the oncological outcomes of detecting metastatic SLNs with ultrastaging [8,20,21] and necessity for adjuvant therapy in cases of isolated tumor cells found in SLNs [22,28]. Despite these controversies, SLN biopsy with ultrastaging is recommended based on the NCCN guidelines [16]. Most previous studies on the oncologic outcomes of SLN mapping involved patients receiving ultrastaging [8,14,20]. In contrast, our study assessed SLNs alone with H&E staining, according to our institution's convention. Our findings demonstrate that patients who received treatment based on SLN biopsy without ultrastaging showed a trend of low nodal recurrence and overall recurrence rates compared with those who underwent conventional LND.

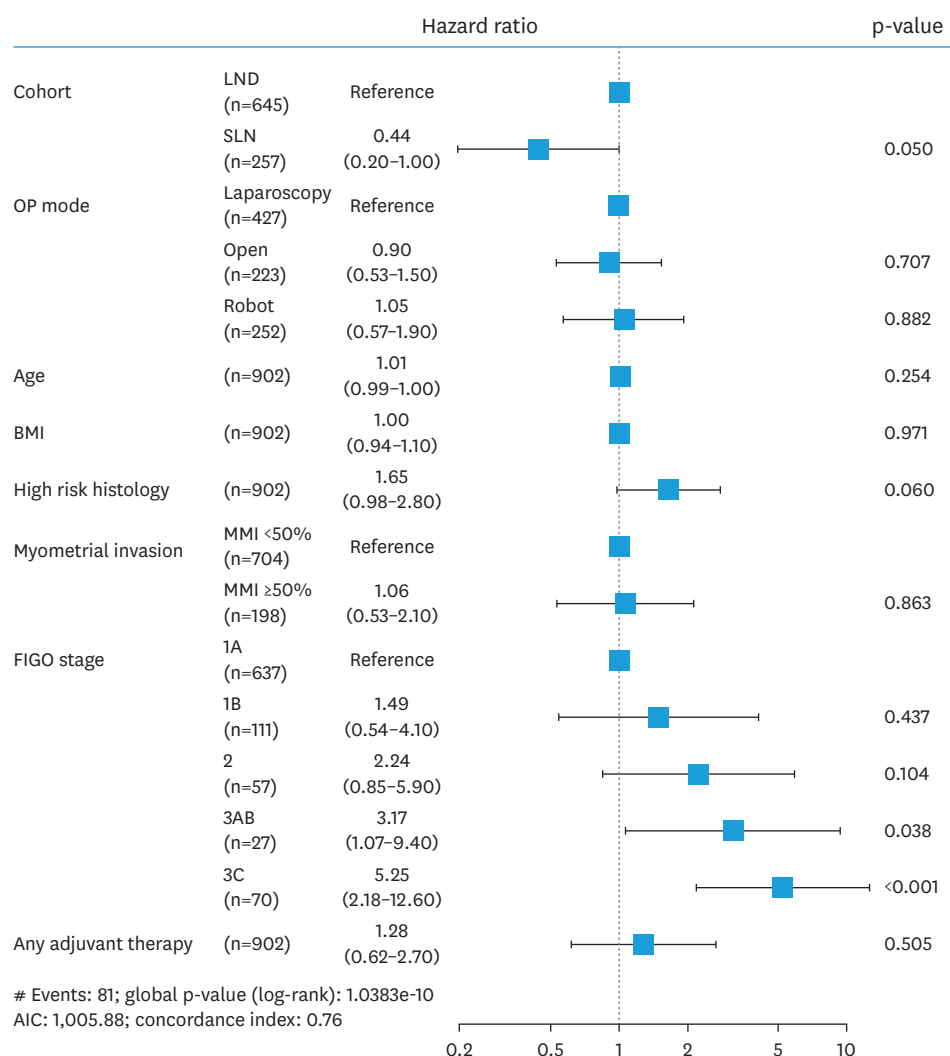


Fig. 3. Multivariate Cox regression analysis with respect to overall progression-free survival before matching. BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; MMI, myometrial invasion; LND, lymphadenectomy; OP, operation; SLN, sentinel lymph node.

Comparing survival outcomes between SLN mapping and LND is more complex than just sample selection bias in retrospective designs. The NCCN guideline evolved from recommending full LND to SLN mapping with a transition period of validation LND before omitting LND. The transition period could span months to years, with variations in surgical techniques employed among different surgeons [29,30]. Additionally, the trend in adjuvant therapy use has changed over the years, with increasing popularity of intracavitary radiotherapy [31,32] and wider use of chemotherapy for stage III based on the PORTEC-3 [6].

Previous studies have utilized statistical methods such as PSM to compare outcomes of SLN mapping and LND. One study by Bogani et al. [20] compared 3-year PFS and OS across the SLN only, SLN plus LND, and LND alone groups using SLN biopsy with ultrastaging and found no difference in outcomes. Schlappe et al. [21] also compared the outcomes of SLN biopsy with ultrastaging with those of LND using PSM and found no difference in the 3-year PFS (69% vs. 80%, $p=0.320$) and OS rates (88% vs. 77%, $p=0.060$). Differences in baseline demographics and adjuvant patterns could explain the discrepancy in PFS between Schlappe

Table 2. Patient demographics after matching

| Variables | SLN group (n=257) | LND group (n=257) | p-value |
|----------------------|-------------------|-------------------|---------|
| Age | 53.5±10.6 | 53.1±10.9 | 0.666 |
| BMI | 25.2±4.6 | 25.1±4.6 | 0.713 |
| Histology | | | 0.120 |
| Endometrioid G1 | 123 (47.9) | 131 (51.0) | |
| Endometrioid G2 | 88 (34.2) | 82 (31.9) | |
| Endometrioid G3 | 26 (10.1) | 15 (5.8) | |
| Serous | 9 (3.5) | 7 (2.7) | |
| Carcinosarcoma | 6 (2.3) | 7 (2.7) | |
| Other* | 5 (2.0) | 15 (5.8) | |
| Myometrial invasion | | | 0.712 |
| Less than half | 220 (85.6) | 216 (84.0) | |
| More than half | 37 (14.4) | 41 (16.0) | |
| LVI | | | 0.282 |
| No | 221 (86.0) | 230 (89.5) | |
| Yes | 36 (14.0) | 27 (10.5) | |
| FIGO stage | | | 0.999 |
| 1A | 204 (79.4) | 202 (78.6) | |
| 1B | 26 (10.1) | 28 (10.9) | |
| 2 | 11 (4.3) | 11 (4.3) | |
| 3A or 3B | 6 (2.3) | 6 (2.3) | |
| 3C1 | 5 (1.9) | 6 (2.3) | |
| 3C2 | 5 (1.9) | 4 (1.6) | |
| Any adjuvant therapy | 89 (34.6) | 69 (26.8) | 0.069 |
| Chemotherapy | 28 (10.9) | 29 (11.3) | 1.000 |
| Radiotherapy | 76 (29.6) | 47 (18.3) | 0.004 |

Values are presented as mean ± standard deviation or number (%).

BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; G, grade; LND, lymphadenectomy; LVI, lymphovascular space invasion; SLN, sentinel lymph node.

*Adenocarcinoma and clear cell carcinoma were classified as other.

Table 3. Recurrence site analysis after matching

| Recurrence location* | SLN group (n=257) | LND group (n=257) | p-value |
|----------------------|-------------------|-------------------|---------|
| Vault | 2 (0.78) | 3 (1.17) | 0.500 |
| Peritoneum | 1 (0.39) | 8 (3.11) | 0.019* |
| Lymph node | 4 (1.56) | 9 (3.50) | 0.130 |
| Distant organ | 3 (1.17) | 6 (2.33) | 0.252 |

Values are presented as number (%).

LND, lymphadenectomy; SLN, sentinel lymph node.

*Each anatomical location was counted for patients with recurrence at multiple sites.

et al.'s study [21] and the current study. As practice patterns (i.e., surgical technique, injection dye and technique, and adjuvant therapy) can differ across institutions and nations, more data on SLN mapping's survival outcome may be necessary.

Our study not only compared outcomes in matched cohorts but also investigated survival outcomes in a subset of patients initially diagnosed with uterine-confined disease (stages I and II) to ultimately base the outcome of SLN mapping on patient outcomes. The rationale was that the diagnostic accuracy of pre- and postoperative imaging was far less than 100% [33,34]. Furthermore, because tumors can spread to unusual lymph node locations [8,12,19], validation LND may lead to failed detection of nodal metastasis, and our study showed a trend toward improved outcomes in the SLN cohort compared with the unmatched cohort. This might be related to the higher rate of nodal recurrence observed in LND group. SLN mapping technique traces the lymphatic channels originating from the uterus, whereas LND non-specifically removes lymph nodes. SLN biopsy allows more accurate removal of the lymph nodes that are likely to serve as channels of lymphatic metastasis. This approach offers

a more precise identification and removal of lymph nodes, potentially reducing the risk of nodal recurrence. However, the follow-up duration was shorter in the SLN group, and further follow-up is necessary to verify our findings.

The study found that the rate of lymphatic complications was significantly lower in the SLN group than in the LND group. Previous studies on lymphatic complications reported the rate of lymphocele to be 2.6%–17.3% and that of lymphedema to be 1.3%–49.4%, regardless of the mode of surgery [11,13,35,36]. In our study, the rate of lymphocele was 2.3% in the SLN group and 8.9% in the LND group and that of lymphedema was 0.8% in the SLN group and 4.3% in the LND group. Our lower complication rate compared with that of previous reports may be attributed to factors, such as patient demographics, BMI, number of lymph nodes removed, and Eastern Cooperative Oncology Group (ECOG) performance status. The median number of SLNs removed was similar to that in previous studies [13,36]; while the median number of lymph nodes from LND removed was lower [13,36]. Additionally, our method of counting the lymphoceles and lymphedemas may have overlooked lower-grade complications. However, despite the possibility of underestimating the incidence of lymphatic complications in both groups, our findings are consistent with those of previous studies showing lower complication rates in the SLN group [13,35,36].

To expand our research on the survival and quality of life (QOL) outcomes of SLN mapping, we can focus on specific subgroups such as older patients and those with high fragility scores, which may have an impact on treatment, complications, and survival outcomes [37]. Our study primarily focused on comparing the surgical modality of SLN biopsy with that of LND, with age being the only patient fragility factor taken into account. However, further investigation into other patient factors such as ECOG performance status and personal medical history may be useful in exploring survival and QOL-related outcomes in the aging population setting. Additionally, incorporating the cancer genome atlas (TCGA) molecular classification profiles into outcome analysis, specifically in the context of SLN mapping, could be another avenue worth exploring. Previous studies have suggested that the molecular classification of endometrial cancer is associated with lymph node metastasis [38] and can influence tumor characteristics, such as mismatch repair deficiency tumors frequently found in the low segment of the uterus [39]. These molecular characteristics may also affect patient screening, radiologic or ultrasonographic imaging findings [3,4], surgical treatment options, including whether to perform SLN biopsy or not and which specific SLN biopsy technique to utilize, as well as adjuvant therapy options [40]. Exploring these factors may lead to interesting research avenues regarding outcome and QOL studies in SLN mapping. The limitations of our study include the limited sample size and the selection bias due to its retrospective nature. Although we attempted to correct the imbalance between the two cohorts using statistical methods, it is possible that potential confounders were incompletely addressed. Because we did not have a prospective institutional protocol for the specific details of SLN mapping, the surgical techniques could have varied among different surgeons. Moreover, our assessment of lymphocele and lymphedema was based on CT images and chart reviews.

In conclusion, our study is one of the largest retrospective analyses of SLN mapping and the first to report on outcomes for patients who underwent SLN mapping without ultrastaging. Initially, there was a clinical trend that suggested improved PFS in patients who underwent SLN biopsy without ultrastaging compared with those who underwent LND, although this did not reach statistical significance. However, after addressing the intergroup baseline

characteristic imbalance, the oncologic outcome of SLN biopsy without ultrastaging was comparable to that of LND, and patients receiving SLN mapping showed a significantly lower rate of lymphatic complications, such as lymphocele and lymphedema. Although there were differences in adjuvant treatments between the LND and SLN groups, further prospective studies are needed to confirm the survival outcomes of SLN biopsy without ultrastaging. Nevertheless, SLN biopsy without ultrastaging can be considered for every patient with endometrial cancer who does not have definitive evidence of distant metastasis on preoperative evaluation.

SUPPLEMENTARY MATERIALS

Table S1

Patients with LNs harvested or metastatic at specific anatomic level before matching

[Click here to view](#)

Table S2

Univariate analysis before matching

[Click here to view](#)

Table S3

Patients with LNs harvested or metastatic at specific anatomic level after matching

[Click here to view](#)

Table S4

Lymphatic complication after matching

[Click here to view](#)

Fig. S1

Two-year progression-free survival.

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Fig. S2

Multivariate with respect to 2-year progression-free survival before matching.

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Fig. S3

Two-year progression-free survival in subgroup analysis after matching.

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Fig. S4

Overall progression-free survival in subgroup analysis after matching.

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