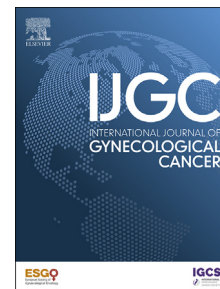


Risk factors for the involvement of sentinel lymph nodes in endometrial cancer (TRSGO-SLN-010)



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ABSTRACT

Objective: This research was undertaken to identify risk factors for the involvement of sentinel lymph nodes (SLNs) in cases of endometrial cancer.

Methods: From February 2016 to April 2021, the cases of 874 women with endometrial cancer treated with the SLN algorithm at 11 institutions were analyzed in this retrospective study. Clinical and pathologic data were reviewed, and logistic regression was applied to identify predictive factors for SLN involvement.

Results: After the exclusion of 81 patients, the remaining cohort of 793 patients was analyzed. The involvement of SLNs occurred in 9.2% of these cases ($n = 73$). In univariate analysis, the risk of SLN involvement was seen to be significantly higher among patients aged >60 years and those with high-grade tumors, non-endometrioid histology, lymphovascular space invasion, deep myometrial invasion, tumor diameters of ≥ 2 cm, and cervical stromal invasion. Multivariate analysis identified the occurrence of deep myometrial invasion (OR 2.42, 95% CI 1.29 to 4.56; $p = .006$), cervical stromal invasion (OR 2.18, 95% CI 1.13 to 4.21; $p = .020$), and lymphovascular space invasion (OR 7.27, 95% CI 3.82 to 13.81; $p < .001$) as risk factors independently predictive of SLN involvement in the treatment of endometrial cancer.

Conclusion: Deep myometrial invasion, cervical stromal invasion, and lymphovascular space invasion were found to be independently predictive of the involvement of SLNs in cases of endometrial cancer. For cases in which SLN dissection was not or could not be performed, the identified independent risk factors are crucial for guiding adjuvant therapy.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Sentinel lymph node (SLN) biopsy is a minimally invasive method used to stage endometrial cancer accurately, reducing the need for extensive lymphadenectomy. When bi-lateral SLN mapping fails or nodal staging is not performed, it is crucial to identify cases with a high likelihood of SLN involvement for appropriate adjuvant treatment selection.

WHAT THIS STUDY ADDS

Our study identified deep myometrial invasion, cervical stromal invasion, and lymphovascular space invasion as independently predictive risk factors for SLN involvement.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

The study's findings could influence the decision-making process for selecting appropriate adjuvant therapy in patients with endometrial cancer who have not undergone proper surgical staging.

Keywords:

Endometrial Neoplasms;
Lymphatic Metastasis;
Sentinel Lymph Node

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INTRODUCTION

Endometrial cancer ranks among the gynecologic malignancies with the highest global rates of prevalence, and its incidence is increasing.¹ A crucial determinant of the patient's prognosis and treatment decisions in endometrial cancer is the occurrence of metastasis to the lymph nodes. Prognosis is significantly worse in cases with lymphatic metastasis than in those limited to the uterus.^{2,3} This underscores the critical importance of determining lymph node status for making appropriate adjuvant treatment decisions. Historically, systematic lymphadenectomy was the standard approach for staging in endometrial cancer, primarily to assess lymph node involvement. However, this procedure was associated with significant morbidity, including lymphedema, neurovascular injuries, and extended recovery times, leading to a re-evaluation of its routine use, particularly in patients with low-to-intermediate risk.⁴ As a result, sentinel lymph node (SLN) mapping emerged as a less invasive alternative, capable of providing accurate staging information with fewer complications.

According to the European guidelines published in 2021, SLN biopsy for staging can be considered for patients at low-to-intermediate risk.⁵ Furthermore, in cases of high-to-intermediate risk to high-risk disease, these guidelines propose the use of SLN biopsy as an acceptable alternative to systematic lymphadenectomy in the staging of lymph nodes. There are also instances in which the bi-lateral mapping of SLNs fails, accounting for 15% to 25% of all applications.⁶⁻⁸ Recent studies focusing on the ways in which obesity affects the outcome of SLN mapping revealed that groups of patients with higher body mass index (BMI) values had less successful SLN mapping results, and the differences reached the level of statistical significance.^{9,10} In addition, according to a survey conducted among Society of Gynecologic Oncology members before the SLN era, it was noted that 88% of survey respondents performed lymphadenectomy in only approximately 50% of cases.¹¹ With contemporary practical applications, situations in which nodal staging is neither implemented nor feasible may emerge.

In this context, it is crucial to identify cases in which SLN involvement is likely to occur. Previous studies identified several predictors of SLN involvement, including BMI, tumor size, lymphovascular space invasion, lower uterine segment involvement, grade, myometrial invasion, and cervical stromal invasion, although small sample sizes have limited the generalizability of these findings.^{12,13} The recent prospective Predicting the risk of nodal disease with histological and molecular features in endometrial cancer (PROME) trial, involving 223 patients, identified lymphovascular space invasion and deep myometrial invasion as predictors of SLN involvement.¹⁴ However, there remains a need for larger and more comprehensive studies to better elucidate these predictive factors across diverse patient populations, particularly in cases in which full nodal staging is not feasible. To address that need, this multi-centric retrospective study was planned with the aim of identifying risk factors predictive of SLN involvement in cases of endometrial cancer.

METHODS

In accordance with the journal's guidelines, we will provide our data for independent analysis by a team selected by the Editorial

Team for the purposes of additional data analysis or for the reproducibility of this study in other centers if such is requested.

This retrospective study began with the data of 874 women with endometrial cancer treated between February 2016 and April 2021 at 11 different institutions that applied the SLN algorithm for their cases. These institutions have centers with experience in sentinel biopsy and gynecologic cancer surgery, and they are involved in Turkish Society of Gynecologic Oncology (TRSGO) SLN studies. They have gynecologic pathologists who have performed sentinel node pathologic examination procedures. Updated data from all centers included in the study are periodically added to the TRSGO SLN study database by study group representatives working in the centers, including pre-operative, surgical, adjuvant treatment, and survival data. The Ondokuz Mayıs University institutional review board confirmed its approval of the study protocol (approval number: 2022/494), and all patients had provided written informed consent for their relevant medical data to be used for scientific purposes.

The inclusion criteria were as follows: (1) patients with histologically confirmed endometrial cancer of any sub-type, including endometrioid, clear cell, serous, carcinosarcoma, de-differentiated, or un-differentiated; (2) clinical evaluation using the Memorial Sloan Kettering SLN algorithm,¹⁵ implemented by all participating centers; and (3) successful unilateral or bi-lateral SLN mapping. Exclusion criteria included (1) incomplete medical records; (2) failure of bi-lateral SLN mapping; (3) evident ovarian disease or bulky metastatic lymph nodes detected during the pre-operative workup or intra-operative evaluation; and (4) presence of synchronous malignancy, defined as any primary malignancy other than endometrial cancer.

Total hysterectomy with or without adnexectomy and SLN biopsies were performed for all patients. The decision to perform adnexectomy was made in accordance with European guidelines that recommend ovarian preservation in specific cases on the basis of patient age, tumor grade, depth of myometrial invasion, and absence of extra-uterine disease.⁵ An infra-colic omentectomy was performed when applicable. SLN mapping was performed with indocyanine green (ICG) or blue dye as the tracer, injected into the cervix at the 3 o'clock or 9 o'clock position, respectively. Near-infra-red/ICG-compatible endoscopic systems were used for surgeries involving ICG. In the TRSGO-SLN-006 study, we provided a more detailed description of the technical aspects of the SLN mapping procedure.¹⁶ Briefly, after the peritoneal evaluations, the retroperitoneum was entered, and all observed SLNs were excised. Only nodes containing dye were deemed SLNs in this analysis. Enlarged or otherwise suspicious non-SLNs were similarly excised during the procedure. Side-specific lymphadenectomy was applied if the mapping procedure was not successful. Subsequently, a total hysterectomy with or without adnexectomy was conducted.

All SLNs were subjected to serial sectioning at intervals of 50 to 200 μm , and histopathologic evaluations were performed. For SLNs found to have positive results by hematoxylin and eosin (H&E) staining, no additional evaluations were pursued. If the H&E staining revealed no metastasis, ultra-staging procedures were conducted. A single unstained slide was prepared for evaluation with pan-keratin immunoperoxidase staining. SLN metastases were categorized in line with the staging definitions of the American Joint Committee on Cancer, with which cases are classified as entailing

macro-metastasis, micro-metastasis, or isolated tumor cells (ITCs).¹⁷ Non-SLNs were evaluated using routine H&E staining. On the basis of final pathology results, all cases were staged using FIGO 2009 endometrial cancer staging system.¹⁸

Statistical Analysis

IBM SPSS Statistics 23 (IBM Corp) was used during all data analysis performed in this retrospective study. In cases of continuous variables, the data are provided as median values with ranges, whereas findings obtained for binary variables are presented in the form of counts and percentages. For the identification of correlations of various tumor characteristics with the presence of SLN involvement, we conducted simple logistic regression analysis. Values of $p < .05$ were acknowledged as reflecting statistical significance, and all variables found to have $p < .05$ were incorporated in subsequent multiple logistic regression analyses. The impact of each considered factor on SLN involvement was evaluated.

Logistic regression for the binary response variable (SLN involvement) and a binary independent variable (eg, cervical stromal invasion) achieved 80% power at the 0.05 significance level for detecting a change in Prob(SLN = 1) from an initial value of 0.092 to 0.181 with a sample size of 793 observations (68% in the group with no cervical stromal invasion and 32% in the group with cervical stromal invasion). This change corresponded to an OR of 2.18. Multiple regression performed for the independent variable of interest on the other independent variables from logistic regression yielded an r^2 value of 0.10, and adjustments were made.

RESULTS

Of the 874 initial patients, 81 were excluded from the analysis for the following reasons: primary synchronous malignancy ($n = 2$), incomplete medical records ($n = 10$), SLN mapping failure ($n = 61$), contra-lateral lymph node metastasis in cases of unilateral SLN mapping ($n = 5$), and evident ovarian disease ($n = 3$). Accordingly, the final data analysis was performed with the records of a cohort of 793 patients (Fig.); 583 of the patients (73.5%) had bi-lateral SLN mapping, whereas 210 (26.5%) had unilateral SLN mapping. The number of SLNs removed per patient ranged from 1 to 16, with a mean value of 3 nodes. SLN metastases were

observed in 73 cases (9.2%), with macro-metastasis, micro-metastasis, and ITC accounting for 36 (4.5%), 17 (2.2%), and 20 (2.5%), respectively. In Table 1, we provide an overview of the clinicopathologic features of the patients analyzed.

In the course of multivariate analysis, we identified deep myometrial invasion (OR 2.42, 95% CI 1.29 to 4.56; $p = .006$) and the presence of lymphovascular space invasion (OR 7.27, 95% CI 3.82 to 13.81; $p < .001$) or cervical stromal invasion (OR 2.18, 95% CI 1.13 to 4.21; $p = .020$) as independent risk factors predicting the occurrence of SLN involvement in cases of endometrial cancer (Table 2). When only the cases with successful bi-lateral mapping were analyzed ($n = 583$), the multivariate analysis once again revealed that deep myometrial invasion (OR 3.05, 95% CI 1.52 to 6.11; $p = .002$) and the presence of lymphovascular space invasion (OR 8.51, 95% CI 4.19 to 17.27; $p < .001$) or cervical stromal invasion (OR 2.53, 95% CI 1.17 to 5.46; $p = .017$) were independent risk factors predictive of the occurrence of SLN involvement (Table S1).

Table 3 presents a separate analysis of the factors influencing both macro- and micro-metastasis. Multivariate analysis identified high tumor grade (OR 2.36, 95% CI 1.05 to 5.29; $p = .037$) and the presence of lymphovascular space invasion (OR 9.43, 95% CI 4.15 to 21.41; $p < .001$) or cervical stromal invasion (OR 2.37, 95% CI 1.15 to 4.88; $p = .019$) as independent risk factors predictive of macro- and micro-metastasis in women with endometrial cancer. Additional analyses were performed for only the cases with successful bi-lateral mapping ($n = 583$), and the multivariate analysis similarly revealed that age >60 years (OR 2.10, 95% CI 1.00 to 4.38; $p = .048$) and the presence of lymphovascular space invasion (OR 13.61, 95% CI 5.42 to 34.17; $p < .001$) or cervical stromal invasion (OR 2.51, 95% CI 1.09 to 5.74; $p = .029$) were independent risk factors predicting the occurrence of macro- and micro-metastasis among these cases (Table S2).

Table 4 lists the rates of macro- and micro-metastasis of SLNs categorized according to the presence or absence of specific factors including lymphovascular space invasion, tumor grade, and cervical stromal invasion. The co-existence of all 3 factors—lymphovascular space invasion, high-grade tumors, and cervical stromal invasion—was associated with a metastasis rate of 51.7%.

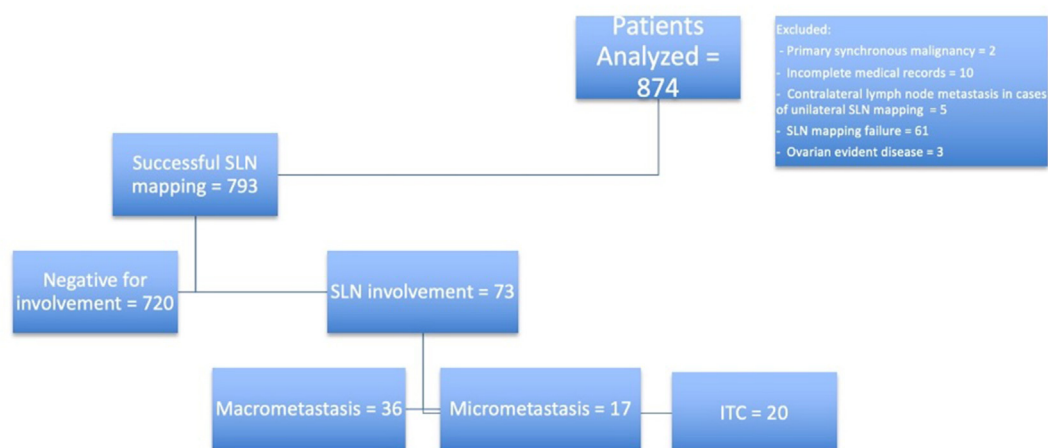


Figure Summary of the study population. ITC, isolated tumor cell; SLN, sentinel lymph node.

Table 1 Clinicopathologic Characteristics

Characteristics (N = 793)	Values
Age at surgery, median, y	59 (29-87)
Menopausal status, n (%)	
Pre-menopause	164 (20.7)
Post-menopause	629 (79.3)
Dye, n (%)	
Indocyanine green	486 (61.3)
Blue dye	307 (38.7)
Surgical route, n (%)	
Laparotomy	211 (26.4)
Laparoscopy	539 (68.0)
Robotic	43 (5.4)
Lymphadenectomy, n (%)	
SLND	182 (23.0)
SLND + BPLND	377 (47.5)
SLND + BPPALND	234 (29.5)
Stage, n (%)	
I	680 (85.7)
II	49 (6.2)
III	56 (7.1)
IV	8 (1.0)
Histopathology, n (%)	
Endometrioid	719 (90.7)
Non-endometrioid	60 (7.5)
Mixed	14 (1.8)
Endometrioid tumor grade, n (%)	
Grade 1	367 (51.0)
Grade 2	281 (39.0)
Grade 3	71 (10.0)
Depth of myometrial invasion, n (%)	
None	114 (14.4)
<1/2	461 (58.1)
≥1/2	218 (27.5)
LVSI, n (%)	
Absent	611 (77.0)
Present	182 (23.0)
Tumor size, n (%)	
<2 cm	207 (26.1)
2-3.9 cm	328 (41.4)
≥4 cm	258 (32.5)
CSI, n (%)	
Absent	714 (90.0)
Present	79 (10.0)
Detection rate ^a	
Bi-lateral	583 (73.5)
Unilateral	210 (26.5)
No. of SLNs removed/patient	3 (1-16)
Para-aortic SLN	

Table 1 (continued)

Characteristics (N = 793)	Values
Absent	767 (96.7)
Present	26 (3.3)
SLN involvement, n (%)	73 (9.2)
Macro-metastasis	36 (4.5)
Micro-metastasis	17 (2.2)
Isolated tumor cells	20 (2.5)

Abbreviations: BPLND, bi-lateral pelvic lymph node dissection; BPPLND, bi-lateral pelvic and para-sentinel lymph node aortic lymph node dissection; CSI, cervical stromal invasion; LVSI, lymphovascular space invasion; SLN, sentinel lymph node; SLND, sentinel lymph node dissection.

^a Side-specific lymphadenectomy was applied if the mapping procedure was not successful.

DISCUSSION

Summary of Main Results

The present study has shown that lymphovascular space invasion or cervical stromal invasion and deep myometrial invasion were independently predictive of SLN involvement. Furthermore, the presence of lymphovascular space invasion or cervical stromal invasion and high-grade tumors was established as independent predictors for both macro- and micro-metastasis in SLNs. Our findings indicated that patients who experienced lymphovascular space invasion were 7 times more likely to experience SLN involvement. Moreover, in cases with lymphovascular space invasion, the risk of macro-metastasis and micro-metastasis was found to be 9 times higher.

Results in the Context of the Literature

Studies have shown that higher BMI values are linked to lower rates of success in bi-lateral SLN mapping. Vargiu and colleagues⁹ reported that patients with obesity had lower rates of overall SLN detection and higher rates of failure in bi-lateral mapping, and these differences reached the level of statistical significance. Furthermore, patients with obesity experienced an 8.2% incidence of empty packet dissection. Fennimore and colleagues¹⁰ showed that individuals with BMI values of ≥45 had a lower success rate in SLN mapping than did those with BMI values <45; again, this difference was statistically significant. A recent study by the FRANCOGYN group evaluated the adherence of surgeons to the relevant guidelines during surgeries for patients with morbid obesity.¹⁹ The study included 2375 patients, and the adherence rate to the guidelines in surgical management was found to be 30% in cases of patients with morbid obesity, 44% in patients with obesity, and 48% in patients with normal weight or overweight. Pelvic lymphadenectomy was performed less often for patients with morbid obesity at low risk and intermediate risk. Canlorbe and colleagues²⁰ reported that in their high-risk group, only 70% of patients with obesity underwent nodal staging compared with 90% of patients without obesity ($p < .0001$). Ultimately, considering the low adherence to surgical management (especially due to the absence of lymph node staging) across these studies, the significance of our study in identifying risk factors for SLN metastasis becomes evident.

Table 2 Univariate and Multivariate Analysis in Women With SLN Involvement

Characteristics	Cases	Univariate analyses <i>p</i>	Multivariate analyses OR 95% CI <i>p</i>
Age (y)			
≤60	27/428 (6.3)	.002	
>60	46/365 (12.6)		
Menopausal status, <i>n</i> (%)			
Pre-menopause	10/164 (6.1)	.12	
Post-menopause	63/629 (10.0)		
Dye, <i>n</i> (%)			
Indocyanine green	36/486 (7.8)	.08	
Blue dye	35/307 (11.4)		
Histopathology, <i>n</i> (%)			
Endometrioid	59/719 (8.2)	.006	
Others	14/74 (18.9)		
Grade, ^a <i>n</i> (%)			
Low grade	40/648 (6.2)	< .001	
High grade	33/145 (22.8)		
Depth of MI, <i>n</i> (%)			
<1/2	21/575 (3.7)	< .001	2.42 1.29-4.56 .006
≥1/2	52/218 (23.9)		
LVSI, <i>n</i> (%)			
Absent	17/611 (2.8)	< .001	7.27 3.82-13.81 < .001
Present	56/182 (30.8)		
Tumor size, <i>n</i> (%)			
<2 cm	5/207 (2.4)	< .001	
≥2 cm	68/586 (11.6)		
CSI, <i>n</i> (%)			
Absent	48/714 (6.7)	< .001	2.18 1.13-4.21 .020
Present	25/79 (31.6)		

Abbreviations: CSI, cervical stromal invasion; LVSI, lymphovascular space invasion; MI, myometrial invasion.

^a Low grade: grade 1 to 2 endometrioid type, High grade: grade 3 endometrioid type and non-endometrioid types.

Zhang and colleagues¹³ retrospectively investigated risk factors for SLN involvement in 79 patients with endometrial carcinoma. The authors identified BMI of ≥ 24 kg/m², tumor diameter of ≥ 2 cm, low differentiation, and cervical stromal involvement as significant risk factors for SLN involvement. Although our study also had a retrospective design, it differed significantly from the previously mentioned study in its analysis of a larger cohort, allowing a more comprehensive evaluation of risk factors for SLN involvement in endometrial cancer. We identified lymphovascular space invasion and deep myometrial invasion as independent risk factors; these factors were not evaluated by Zhang and colleagues.¹³ Another retrospective study by Kang and colleagues¹² explored the pathologic features associated with SLN involvement in 60 patients with endometrial cancer, identifying lower uterine segment involvement, tumor size of ≥ 5 cm, lymphovascular space invasion, cervical stromal involvement, and deep myometrial invasion as key factors. Although Kang and colleagues¹² used univariate analyses without reporting risk measures, our study, based on a larger sample size and multivariate analysis, confirmed the importance of those

factors and also provided more accurate estimates of the strength of their associations with SLN involvement. Our findings reinforce the significance of lymphovascular space invasion, deep myometrial invasion, and cervical stromal involvement as independent risk factors for SLN metastasis, offering a more detailed understanding than that provided by Kang and colleagues.¹² In addition, in the recent PROME trial involving 223 patients, lymphovascular space invasion and deep myometrial invasion were identified as predictors of SLN involvement.¹⁴ The PROME trial was prospectively designed to test the role of molecular features in predicting node positivity in early-stage endometrial cancer but concluded that those features did not significantly contribute to predictions of SLN involvement. Our retrospective study, with a larger sample size, similarly identified lymphovascular space invasion and deep myometrial invasion as significant predictors. We also found cervical stromal invasion to be a key risk factor.

In the 2023 FIGO endometrial cancer staging system, regarding lymph node metastasis, only macro- and micro-metastases are classified as stage 3. Therefore, in the present study, such cases were

Table 3 Univariate and Multivariate Analysis in Women With Macro- and Micro-Metastasis

Characteristics	Cases	Univariate analyses <i>p</i>	Multivariate analyses OR 95% CI <i>p</i>
Age (y)			
≤60	17/428 (4.0)	.001	
>60	36/365 (9.9)		
Menopausal status, <i>n</i> (%)			
Pre-menopause	7/164 (4.3)	.16	
Post-menopause	46/629 (7.3)		
Dye, <i>n</i> (%)			
Indocyanine green	31/486 (6.4)	.66	
Blue dye	22/307 (7.2)		
Histopathology, <i>n</i> (%)			
Endometrioid	41/719 (5.7)	.001	
Others	12/74 (16.2)		
Grade, ^a <i>n</i> (%)			
Low grade	24/648 (3.7)	< .001	2.36 1.05-5.29 .037
High grade	29/145 (20.0)		
Depth of MI, <i>n</i> (%)			
<1/2	15/575 (2.6)	< .001	
≥1/2	38/218 (23.9)		
LVSI, <i>n</i> (%)			
Absent	9/611 (1.5)	< .001	9.43 4.15-21.41 < .001
Present	44/182 (24.2)		
Tumor size, <i>n</i> (%)			
<2 cm	3/207 (1.4)	< .001	
≥2 cm	50/586 (8.5)		
CSI, <i>n</i> (%)			
Absent	32/714 (4.5)	< .001	2.37 1.15-4.88 .019
Present	21/79 (26.6)		

Abbreviations: CSI, cervical stromal invasion; LVSI, lymphovascular space invasion; MI, myometrial invasion.

^a Low grade: grade 1 to 2 endometrioid type, High grade: grade 3 endometrioid type and non-endometrioid types.

also considered separately from SLN involvement. In cases with positive findings for lymphovascular space invasion, high-grade tumors, and cervical stromal invasion positivity, the rate of macro- and micro-metastasis was 51.7%. According to the current guidelines for

Table 4 The Rate of Macro- and Micro-Metastasis According to the Presence of LVSI, Grade, and CSI

LVSI	Grade	CSI	Rate (%)
No	Low	No	6/516 (1.2)
No	Low	Yes	1/24 (4.2)
No	High	No	2/62 (3.2)
No	High	Yes	0/9
Yes	Low	No	12/91 (13.2)
Yes	Low	Yes	5/17 (29.4)
Yes	High	No	12/45 (26.7)
Yes	High	Yes	15/29 (51.7)

Abbreviations: CSI, cervical stromal invasion; LVSI, lymphovascular space invasion.

endometrial cancer, external beam radiation therapy is advisable in cases of high-to-intermediate risk with or without lymph node staging.²¹ Furthermore, it is noted that in cases in which grade 3 tumors co-exist with lymphovascular space invasion, chemotherapy could be considered as an additional treatment approach.

Detecting ITCs is crucial given they might indicate early stages of cancer spread that might not be visible through routine pathologic assessments. Although the 2023 FIGO staging guidelines for endometrial cancer state that the prognostic significance of ITCs [pNO(i+)] is unclear and adjuvant treatment is not recommended, longer-term follow-up of these patients is important in understanding the impact of ITCs on survival.^{2,22,23} A more recent report by Mueller and colleagues²³ noted that the incidence of ITC-positive disease increased with the increasing depth of myometrial invasion across all grades and histologic subtypes. Moreover, ITCs were detected at a rate of 25% in cases of low-grade tumors and 18% in cases of high-grade tumors among patients with deep myometrial invasion. These factors may explain the diverse findings obtained in the 2 different multivariate analyses conducted in our study.

Strengths and Weakness

One major strength of this study is its large sample size, enhancing the robustness of our findings. However, limitations include the retrospective nature of the research, lack of centralized pathology reviews, and lack of molecular profiling. Without central pathology reviews, we were unable to use the 3-tiered scoring system for lymphovascular space invasion. In addition, the diverse surgical methods and dyes used by the participating centers and the inclusion of cases with unilateral SLN mapping may have influenced the consistency of our results. Furthermore, the lack of BMI data precluded detailed analysis of the impact of obesity on SLN mapping success. Caution is necessary when applying our findings to populations with obesity, and further research is needed to validate the risk factors in this patient sub-group.

Implications for Practice and Future Research

This study highlights the need for future research aimed at identifying risk factors for SLN involvement in endometrial cancer when complete surgical staging cannot be performed or is not performed. Research endeavors including molecular classification and the inclusion of BMI data are necessary to support our findings and enhance their translational impact in the management of endometrial cancer. Understanding the role of obesity in SLN mapping success will be particularly important for treatment strategies tailored to individual patient profiles.

CONCLUSIONS

The study has identified lymphovascular space invasion, deep myometrial invasion, and cervical stromal invasion as risk factors capable of independently predicting SLN involvement in cases of endometrial cancer. For patients in whom SLN dissection was not performed or could not be performed, such as those in the patient group with morbid obesity, the identified independent risk factors are crucial for guiding adjuvant therapy.

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Author contributions IY and ST had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: IY, FD, MA, FO, CT. Acquisition, analysis, or interpretation of data: IY, OT, NT, EK, DA, HT, IK, DV, CC, FK, HS. Drafting of the manuscript: IY. Critical revision of the manuscript for important intellectual content: ST, FO. Statistical analysis: OT, DA, IK, DV, CC, HS. Administrative, technical, or material support: MG, NT, EK, TB, FK, HS. Supervision: TB, FK, ST, MA, FO, CT. Visualization: HT, FK. Software: EK, TB, CT. Project administration: ST. Methodology: MG.

Declaration of Competing Interests None declared.

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