

# Is focal LVSI a benign finding in FIGO 2023 stage 1 endometrial cancer? A large cohort analysis

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## ABSTRACT

**Objective:** To evaluate whether focal lymphovascular space invasion (LVSI) affects 5-year disease-free survival (DFS) in patients with stage 1 endometrial cancer according to the 2023 FIGO classification.

**Material and Methods:** This retrospective cohort study included 475 patients with FIGO 2023 stage 1 endometrial cancer treated between 2014 and 2018. Patients were categorized as LVSI-negative (n=444) or focal LVSI (n=31). Those with substantial LVSI were excluded. Clinicopathological variables, recurrence patterns, and survival outcomes were compared between the groups. Kaplan–Meier analysis and Cox regression models were used to identify prognostic factors for DFS.

**Results:** Focal LVSI was present in 6.5% of patients. The focal LVSI and LVSI-negative groups were comparable in terms of age, grade, menopausal status, and depth of myometrial invasion. During a median follow-up of 67 months, 12 recurrences occurred in the LVSI-negative group, whereas no recurrences were observed among patients with focal LVSI. The 5-year DFS rates were 97.3% and 100%, respectively (log-rank p=0.48). In multivariate Cox regression analysis, focal LVSI was not an independent predictor of DFS (p=0.982).

**Conclusion:** Focal LVSI, as defined by FIGO 2023 and WHO criteria, was not associated with an increased risk of recurrence or reduced DFS in stage 1 endometrial cancer. These results suggest that patients with focal LVSI may not require adjuvant therapy, supporting a more individualized and conservative management approach, pending validation in prospective molecularly characterized studies.

**Keywords:** Disease-free survival, endometrial cancer, FIGO 2023, focal LVSI, lymphovascular space invasion, prognosis.

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## INTRODUCTION

Accurate staging of endometrial cancer is essential for guiding treatment and predicting outcomes.<sup>[1,2]</sup> The International Federation of Gynecology and Obstetrics (FIGO) staging system serves as a key framework, influencing both prognosis and therapeutic planning.<sup>[1,2]</sup> The updated FIGO 2023 system refines risk stratification by integrating molecular markers and clarifying pathological definitions.<sup>[3]</sup>

Although stage 1 endometrial cancer generally carries a favorable prognosis, it represents a biologically heterogeneous group with variable recurrence risk.<sup>[4,5]</sup> Identifying reliable prognostic indicators helps prevent both overtreatment and undertreatment. Among these, lymphovascular space invasion (LVSI), defined as the presence of tumor emboli within endothelial-lined spaces, has long been considered one of the strongest predictors of recurrence and nodal spread.<sup>[6–8]</sup> However, recent data suggest that not all LVSI carries the same prognostic weight, prompting the FIGO 2023 update to distinguish between focal (single focus) and substantial (multifocal or  $\geq 5$  spaces) invasion.<sup>[3,9]</sup> This refinement raises a key question: does focal LVSI truly indicate increased recurrence risk, or might it represent a lower-risk finding? This study aims to answer that question in a large cohort of patients with stage 1 disease staged according to the new FIGO 2023 criteria.

Historically, any presence of LVSI was considered a high-risk feature, often prompting adjuvant therapy.<sup>[10]</sup> However, recent evidence suggests that the extent of LVSI matters.<sup>[11]</sup> The 2023 FIGO update, adopting the 2020 WHO definition, now formally stratifies LVSI into focal (a single focus) and substantial (multifocal or  $\geq 5$  involved spaces).<sup>[3,9]</sup> This distinction creates a “gray zone” around focal LVSI, raising a critical clinical question: Does focal LVSI carry the same poor prognosis as substantial LVSI, or does it represent a lower-risk feature? Answering this question is vital for deciding on adjuvant therapy in otherwise low-risk stage 1 patients.<sup>[12,13]</sup> This study aims to evaluate the association of focal LVSI with prognostic factors and disease-free survival (DFS) in a large cohort of patients with FIGO 2023 stage 1 endometrial cancer.

## MATERIAL AND METHODS

This retrospective study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of Gazi Yasargil Training and Research Hospital (Approval Number: 229; Approval date: 11.10.2024). Due to the retrospective nature of the study, the requirement for individual informed consent was waived by the ethics committee.

Inclusion criteria were histological confirmation of FIGO 2023 stage 1 endometrial cancer and complete primary treatment at our institution. Exclusion criteria included synchronous neoplasms, recurrent disease, missing critical data, or a non-endometrioid histology. A key exclusion criterion for this specific analysis was the presence of substantial LVSI on final pathology in order to create a clean comparison between the focal LVSI group and the LVSI-negative group.

### Surgical and Pathological Evaluation

All patients underwent a total hysterectomy with bilateral salpingo-oophorectomy, performed via either minimally invasive surgery or laparotomy. Lymph node assessment was performed with either

sentinel lymph node (SLN) biopsy or systematic pelvic (with or without para-aortic) lymphadenectomy, reflecting the evolving standard of care and surgeon preference during the study period.

Pathological specimens were evaluated by gynecologic pathologists experienced in the field. The LVSI status of each patient was determined by a retrospective review of the original, detailed pathology reports. While the slides were not re-reviewed, the descriptive text of each report was analyzed. Cases described with terms such as “a single focus” or “one focus of LVSI” were retrospectively classified as focal LVSI. Reports describing “extensive,” “multifocal,” “diffuse,” or five or more involved spaces were classified as substantial LVSI. Only cases where a clear distinction between LVSI-negative, focal, or substantial could be made from the report text were included in the final cohort. All patients were retrospectively staged according to the 2023 FIGO staging criteria.<sup>[3]</sup>

### Follow-up and Outcome Assessment

Patients were followed for a median of 67.4 months. The primary endpoint was 5-year disease-free survival (DFS), defined as the time from surgery to the first evidence of recurrence.

### Statistical Analysis

Descriptive statistics were used to summarize the data. The Mann–Whitney U test was used for continuous variables and the chi-square or Fisher’s exact test for categorical variables. Survival curves were generated using the Kaplan–Meier method and compared with the log-rank test. Cox proportional hazards models were used for univariate and multivariate analyses to identify predictors of DFS. A  $p$ -value  $< 0.05$  was considered significant. All analyses were performed using IBM SPSS v25.

## RESULTS

A total of 475 patients with FIGO 2023 stage 1 endometrial cancer met the inclusion criteria. Of these, 444 (93.5%) were LVSI-negative and 31 (6.5%) had focal LVSI. The clinical and pathologic characteristics of the patients are detailed in Table 1. The two groups were well matched, with no statistically significant differences observed in age, menopausal status, preoperative or postoperative grade, myometrial invasion depth, rate of frozen section analysis, or type of adjuvant therapy received ( $p > 0.05$  for all).

At a median follow-up of 67 months, a total of 12 recurrences (2.5% of the total cohort) were recorded. All 12 recurrences occurred in the LVSI-negative group, resulting in a recurrence rate of 2.7% (12/444) in this group. Notably, no recurrences were observed in the 31 patients with focal LVSI (Table 2). The most common sites of recurrence were the vagina ( $n=4$ ) and abdomen ( $n=3$ ).

The 5-year DFS rate for the entire cohort was 97.5%. For the LVSI-negative group, the 5-year DFS was 97.3%, and for the focal LVSI group, it was 100%. A Kaplan–Meier survival analysis demonstrated no statistically significant difference in DFS between the LVSI-negative and focal LVSI groups (log-rank  $p=0.481$ ) (Fig. 1).

In both univariate and multivariate Cox regression analyses performed to identify predictors of DFS, focal LVSI was not found to be a significant factor. The results are summarized in Table 3.

**Table 1: Comparison of maternal age and gestational week at diagnosis according to normal and abnormal karyotype results**

Characteristic	LVSI Negative (n=444)	Focal LVSI (n=31)	p
Age (years), Median (IQR)	62 (55-69)	61 (54-68)	0.812
Menopausal status, n (%)			0.245*
Premenopausal	120 (27.0)	6 (19.4)	
Postmenopausal	324 (73.0)	25 (80.6)	
Postoperative grade, n (%)			0.654*
Grade 1	234 (52.7)	15 (48.4)	
Grade 2	199 (44.8)	16 (51.6)	
Grade 3	11 (2.5)	0 (0.0)	
Myometrial invasion, n (%)			0.176*
<50%	381 (85.8)	25 (80.6)	
≥50%	63 (14.2)	6 (19.4)	
Adjuvant therapy, n (%)			0.138*
None	269 (60.6)	12 (38.7)	
Radiotherapy (Any)	158 (35.6)	18 (58.1)	
Chemotherapy	17 (3.8)	1 (3.2)	

\*Fisher's exact test. LVSI: Lymphovascular space invasion; IQR: Interquartile range.

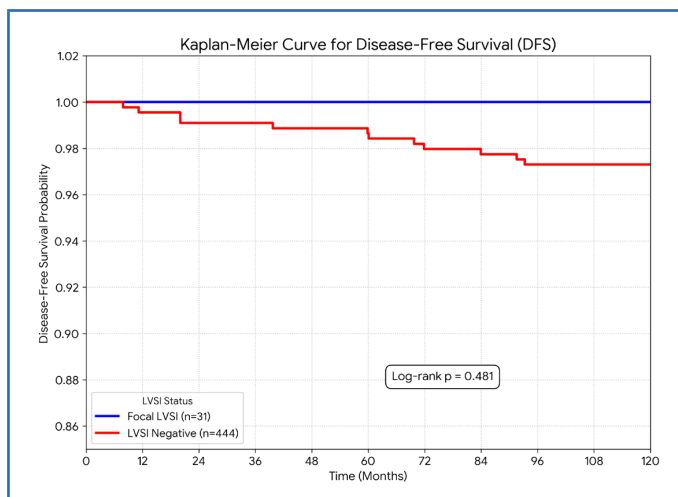
**Table 2: Recurrence status and site according to LVSI status**

Recurrence Details	LVSI Negative (n=444)	Focal LVSI (n=31)	p
Recurrence, n (%)	12 (2.7)	0 (0.0)	1.000*
Recurrence site, n (%)			-
Vagina	4 (33.3)	0	
Pelvis	2 (16.7)	0	
Abdomen	3 (25.0)	0	
Lung	1 (8.3)	0	
Multiple sites	2 (16.7)	0	

\*Fisher's exact test. LVSI: Lymphovascular space invasion; IQR: Interquartile range.

**Subgroup Analysis**

To investigate whether the prognostic value of focal LVSI was consistent across different risk strata, a subgroup analysis based on postoperative grade and depth of myometrial invasion was



**Figure 1: Kaplan-meier curve for disease-free survival by LVSI status.**

**Table 3: Cox regression analysis for predictors of disease-free survival**

Variable	Univariate Analysis	Multivariate Analysis
	HR (95% CI)	p
Focal LVSI (vs. Negative)	Not Applicable <sup>1</sup>	0.481 <sup>2</sup>
Age (per year)	1.02 (0.98-1.06)	0.280
Postop grade (G2-3 vs. G1)	2.95 (1.01-8.62)	0.048
Myometrial invasion (≥50%)	4.18 (1.43-12.2)	0.009

<sup>1</sup>Hazard ratio cannot be calculated as there were no events (recurrences) in the focal LVSI group. <sup>2</sup>p-value from log-rank test. HR: Hazard ratio; CI: Confidence interval; LVSI: Lymphovascular space invasion.

**Table 4: Subgroup analysis of recurrence rates by LVSI status**

Subgroup	LVSI Negative	Focal LVSI	p
	Recurrence / Total (Rate %)	Recurrence / Total (Rate %)	
Postoperative grade			
Grade 1	3 / 234 (1.3)	0 / 15 (0.0)	1.000
Grade 2-3	9 / 210 (4.3)	0 / 16 (0.0)	1.000
Myometrial invasion			
< 50%	4 / 381 (1.0)	0 / 25 (0.0)	1.000
≥ 50%	8 / 63 (12.7)	0 / 6 (0.0)	1.000

<sup>1</sup>Hazard ratio cannot be calculated as there were no events (recurrences) in the focal LVSI group. <sup>2</sup>p-value from log-rank test. HR: Hazard ratio; CI: Confidence interval; LVSI: Lymphovascular space invasion.

performed. As shown in Table 4, no recurrences were observed in the focal LVSI group, regardless of tumor grade or invasion status. Among LVSI-negative patients, recurrences were, as expected, more frequent in the high-grade (4.3%) and deep-invasion (12.7%) subgroups. However, in all subgroup comparisons, there was no statistically significant difference in recurrence rates between the focal LVSI and LVSI-negative groups ( $p > 0.05$  for all).

## DISCUSSION

This study, conducted on one of the largest cohorts to date evaluating the new FIGO 2023 staging, investigated the prognostic significance of focal LVSI in stage 1 endometrial cancer. Our principal finding is that the presence of focal LVSI, as defined by the restrictive 2020 WHO criteria, was not associated with a worse 5-year disease-free survival compared to LVSI-negative patients. This significant negative finding challenges the historical paradigm that any LVSI is a harbinger of poor prognosis and has profound implications for the management of early-stage endometrial cancer.<sup>[14,15]</sup>

The absence of recurrences in our focal LVSI group is striking and suggests that the new staging system's distinction between "focal" and "substantial" LVSI is clinically meaningful. It appears to successfully isolate a subgroup of patients whose risk profile is not significantly altered by the presence of a single microscopic tumor embolus.<sup>[16]</sup> This aligns with emerging evidence from studies like Li et al.<sup>[10]</sup> and the SLYMEC II study, which have also begun to stratify LVSI by extent and have found that limited LVSI has a different prognostic impact than extensive invasion.<sup>[10,17]</sup> Historically, studies reporting LVSI as a major risk factor often did not quantify its extent, potentially grouping truly low-risk focal cases with high-risk substantial cases, thus inflating the perceived risk of all LVSI.<sup>[18,19]</sup>

This finding gains further importance when considering the interplay between LVSI and nodal status. Several contemporary studies have demonstrated that even focal LVSI, when accompanied by positive sentinel lymph nodes, is a powerful predictor of poor survival and recurrence risk in early-stage cervical cancer.<sup>[20–23]</sup> These studies establish that in the presence of nodal metastasis, LVSI signals a more aggressive tumor biology. Our study provides a critical counterpoint: in a largely node-negative, early-stage population, the presence of focal LVSI alone may not confer the same high risk. This suggests that the prognostic weight of LVSI is not absolute but is heavily modified by the nodal status, reinforcing the need for accurate nodal staging, such as with SLN mapping, to truly contextualize the risk associated with LVSI.

Furthermore, our subgroup analyses lend additional support to the benign nature of focal LVSI in this cohort. Our data indicate that the prognostic insignificance of focal LVSI holds true even in patients with other traditionally high-risk features, such as grade 2–3 tumors or deep myometrial invasion. While recurrences were more common in the LVSI-negative group when these risk factors were present, the addition of focal LVSI did not appear to confer any extra risk, as the recurrence rate remained zero across all subgroups. This finding robustly suggests that focal LVSI, when present in isolation or alongside other low- to intermediate-risk features in stage 1 disease, may not be a powerful enough driver to alter prognosis, further

strengthening the argument for a more conservative approach to adjuvant therapy.

This finding has direct implications for clinical decision-making regarding adjuvant therapy. According to major international guidelines, including ESGO/ESTRO/ESP, LVSI is a key factor that upstages patients and often triggers recommendations for adjuvant radiation or chemotherapy to reduce recurrence risk.<sup>[6,24]</sup> Our data suggest that for patients with stage 1 disease and no other high-risk features (high grade, deep myometrial invasion), the presence of focal LVSI alone may not be a sufficient indication for adjuvant treatment. This supports a growing movement toward de-escalation of therapy in low-risk endometrial cancer, aiming to spare patients from treatment-related morbidity without compromising oncologic outcomes.<sup>[25,26]</sup>

The overall 5-year DFS of 97.5% in our stage 1 cohort is excellent and consistent with survival rates reported in other large series of early-stage endometrial cancer.<sup>[27,28]</sup> This confirms that our study population is representative of a typical low-risk cohort and strengthens the validity of our findings regarding focal LVSI within this context. It is crucial, however, to contextualize our findings. We deliberately excluded patients with substantial LVSI, a group known to have a significantly worse prognosis and a higher risk of lymph node metastasis.<sup>[8,29]</sup> Our results should therefore not be extrapolated to all LVSI-positive patients but should be interpreted as specific to the "focal" subgroup.

A critical dimension that our study could not address is the integration of the FIGO 2023 molecular classifications (POLEmut, MMRd, p53abn, NSMP). It is highly plausible that the prognostic impact of focal LVSI is not uniform across these distinct biological entities. For instance, in the prognostically favorable POLEmut and NSMP subgroups, the presence of focal LVSI may indeed be an entirely benign finding. Conversely, in a p53-abnormal tumor, which is known for its aggressive behavior and high recurrence rates, even a single focus of LVSI could signal a significantly worse prognosis. The true value of focal LVSI as a biomarker will likely be defined by its interaction with the underlying molecular profile of the tumor. Therefore, future research incorporating both extensive pathological review and molecular subtyping is essential to create more refined risk-stratification models for stage 1 endometrial cancer.

## Limitations

The primary strength of our study is its large sample size and the specific application of the new, globally accepted FIGO 2023 and WHO criteria. Furthermore, all surgeries were performed by experienced gynecologic oncologists and pathological assessments by dedicated gynecopathologists, ensuring high data quality and consistency.

However, the study has several limitations. Its retrospective nature is the most significant. This design inherently carries a risk of selection bias, as patient inclusion depended on the availability and completeness of clinicopathologic and follow-up data. Information bias may also exist, since LVSI extent was abstracted from narrative pathology reports rather than through centralized slide re-review, and misclassification bias cannot be entirely excluded.

Second, while the prevalence of focal LVSI in our cohort (6.5%) is consistent with rates reported in the literature, the absolute number of patients in this group (n=31) is relatively small. This is not a limitation of patient selection, but rather one of statistical power. The complete absence of recurrence events in the focal LVSI group, while a clinically powerful observation, makes it statistically impossible to calculate a hazard ratio and limits the ability to detect a very small, but potentially real, difference in risk between the groups.

Third, this is a single-center study, and its findings require validation in larger, multi-center cohorts. Finally, our analysis did not include the new molecular classifications (POLEmut, MMRd, p53abn, NSMP) from the FIGO 2023 system, which are now recognized as the most powerful prognostic drivers and could further stratify risk within the focal LVSI group.<sup>[3,30,31]</sup>

Finally, although our groups were well matched for major prognostic factors, the retrospective design cannot eliminate all potential confounders. Future validation studies could employ methods such as propensity score matching to create perfectly balanced cohorts and further strengthen these findings.

Nevertheless, from a clinical perspective, our findings have potential implications for current treatment strategies. According to international guidelines such as ESGO, ESTRO, and ESP, the presence of LVSI often prompts recommendations for adjuvant therapy. However, our results indicate that when LVSI is focal, as defined by the FIGO 2023 and WHO criteria, it may not independently justify adjuvant treatment in otherwise low-risk stage 1 patients. This supports a more individualized approach that avoids overtreatment while maintaining excellent oncologic outcomes, in line with the global trend toward therapeutic de-escalation in endometrial cancer management.

## CONCLUSION

In conclusion, our study demonstrates that in a large, well-characterized cohort of FIGO 2023 stage 1 endometrial cancer patients, the presence of focal LVSI was not associated with an increased risk of recurrence or a lower 5-year DFS. These findings support the new risk stratification that distinguishes between focal and substantial LVSI and suggest that adjuvant therapy may be safely omitted in patients whose only risk factor is focal LVSI. Further validation through large, prospective, and molecularly classified studies is essential to confirm these findings and solidify their role in clinical guidelines.

## Disclosures

**Ethics Committee Approval:** The study was approved by University of Health Sciences, Gazi Yasargil Training and Research Hospital Ethics Committee (No: 229, Date: 11.10.2024).

**Informed Consent:** Due to the retrospective nature of the study, the requirement for individual informed consent was waived by the ethics committee.

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## REFERENCES

- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209–49.
- Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, et al. FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet* 2023;162:383–94.
- Abu-Rustum NR, Yashar CM, Bradley K, Campos SM, Chino J, Chon HS, et al. NCCN guidelines® insights: uterine neoplasms, version 3.2021. *J Natl Compr Canc Netw* 2021;19:888–95.
- Morice P, Leary A, Creutzberg C, Abu-Rustum N, Darai E. Endometrial cancer. *Lancet* 2016;387:1094–108.
- Creasman WT, Odicino F, Maisonneuve P, Quinn MA, Beller U, Benedet JL, et al. Carcinoma of the corpus uteri. FIGO 26th annual report on the results of treatment in gynecological cancer. *Int J Gynaecol Obstet* 2006;95(Suppl 1):S105–43.
- Bosse T, Nout RA, McAlpine JN, McConechy MK, Britton H, Hussein YR, et al. Molecular classification of grade 3 endometrioid endometrial cancers identifies distinct prognostic subgroups. *Am J Surg Pathol* 2018;42:561–8.
- Guntupalli SR, Zigelboim I, Kizer NT, Zhang Q, Powell MA, Thaker PH, et al. Lymphovascular space invasion is an independent risk factor for nodal disease and poor outcomes in endometrioid endometrial cancer. *Gynecol Oncol* 2012;124:31–5.
- Koskas M, Bassot K, Graesslin O, Aristizabal P, Barranger E, Clavel-Chapelon F, et al. Impact of lymphovascular space invasion on a nomogram for predicting lymph node metastasis in endometrial cancer. *Gynecol Oncol* 2013;129:292–7.
- WHO Classification of Tumours Editorial Board. Female Genital Tumours. WHO Classification of Tumours, 5th ed. IARC Press; 2020.
- Li Z, Peng J, Zhang B, Zhao C, Chen Z, Xiao H, et al. The prognostic and clinical significance of substantial lymphovascular space invasion in early-stage endometrial carcinoma. *Eur J Cancer* 2025;218:115258.
- Stelloo E, Nout RA, Osse EM, Jürgenliemk-Schulz IJ, Jobsen JJ, Lutgens LC, et al. Improved risk assessment by integrating molecular and clinicopathological factors in early-stage endometrial cancer-combined analysis of the PORTEC cohorts. *Clin Cancer Res* 2016;22:4215–24.
- Pifer PM, Jaishankar S, Bhargava R, Schad MD, Keller A, Musunuru HB, et al. Is substantial lymphovascular space invasion prognostic in patients with pathologically lymph node-negative endometrial cancer? *Int J Radiat Oncol Biol Phys* 2023;117:148–53.
- Oliver-Perez MR, Padilla-Iserte P, Arencibia-Sanchez O, Martin-Arriscado C, Muruzabal JC, Diaz-Feijóo B, et al. Lymphovascular Space Invasion in Early-Stage Endometrial Cancer (LySEC): Patterns of recurrence and predictors. a multicentre retrospective cohort study of the Spain gynecologic oncology group. *Cancers (Basel)* 2023;15:2612.

14. Mauro J, Mueller M, Perrone E, Fanfani F, Scambia G, Buda A et al. SLYMEC II study: Overall survival analysis of the impact of LVSI in apparent early stage endometrioid endometrial cancer. *Eur J Surg Oncol* 2024;50:107570.
15. Cohn DE, Horowitz NS, Mutch DG, Kim SM, Manolitsas T, Fowler JM. Should the presence of lymphovascular space involvement be used to assign patients to adjuvant therapy following hysterectomy for unstaged endometrial cancer? *Gynecol Oncol* 2002;87:243–6.
16. Neal SA, Graybill WS, Garrett-Mayer E, McDowell ML, McLean VE, Watson CH, et al. Lymphovascular space invasion in uterine corpus cancer: What is its prognostic significance in the absence of lymph node metastases? *Gynecol Oncol* 2016;142:278–82.
17. Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marnitz S, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *Int J Gynecol Cancer* 2021;31:12–39.
18. de Boer SM, Powell ME, Mileshkin L, Katsaros D, Bessette P, Haie-Meder C, et al. Adjuvant chemoradiotherapy versus radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): final results of an international, open-label, multicentre, randomised, phase 3 trial. *Lancet Oncol* 2018;19:295–309.
19. Creutzberg CL, van Putten WL, Koper PC, Lybeert ML, Jobsen JJ, Wárlám-Rodenhuis CC, et al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. PORTEC Study Group. *Post Operative Radiation Therapy in Endometrial Carcinoma*. *Lancet* 2000;355:1404–11.
20. Margolis B, Cagle-Colon K, Chen L, Tergas AI, Boyd L, Wright JD. Prognostic significance of lymphovascular space invasion for stage IA1 and IA2 cervical cancer. *Int J Gynecol Cancer* 2020;30:735–43.
21. Weyl A, Illac C, Lusque A, Leray H, Vaysse C, Martinez A, et al. Prognostic value of lymphovascular space invasion in early-stage cervical cancer. *Int J Gynecol Cancer* 2020;30:1493–9.
22. Pache B, Tantari M, Guani B, Mathevet P, Magaud L, Lecuru F, et al. Predictors of non-sentinel lymph node metastasis in patients with positive sentinel lymph node in early-stage cervical cancer: a senticoll group study. *Cancers (Basel)* 2023;15:4737.
23. Bhatla N, Berek JS, Cuello Fredes M, Denny LA, Grenman S, Karunaratne K, et al. Revised FIGO staging for carcinoma of the cervix uteri. *Int J Gynaecol Obstet* 2019;145:129–35.
24. Keys HM, Roberts JA, Brunetto VL, Zaino RJ, Spirtos NM, Bloss JD, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol*. 2004;92:744–51.
25. Cisek P, Kieszko D, Kordzińska-Cisek I, Kutarska E, Grzybowska-Szatkowska L. Retrospective analysis of intravaginal brachytherapy in adjuvant treatment of early endometrial cancer. *Biomed Res Int* 2018;21:7924153.
26. van den Heerik ASVM, Horeweg N, de Boer SM, Bosse T, Creutzberg CL. Adjuvant therapy for endometrial cancer in the era of molecular classification: radiotherapy, chemoradiation and novel targets for therapy. *Int J Gynecol Cancer* 2021;31:594–604.
27. Bassetty KC, Begum D, Barmon D, Baruah U, Gupta S, Kumar M, et al. FIGO 2023 endometrial staging: a leap of faith into the new “prognostic based” rather than “anatomical based” staging—too fast too furious?? *J Cancer Res Clin Oncol* 2024;150:251.
28. León-Castillo A, de Boer SM, Powell ME, Mileshkin LR, Mackay HJ, Leary A, et al. Molecular classification of the portec-3 trial for high-risk endometrial cancer: impact on prognosis and benefit from adjuvant therapy. *J Clin Oncol* 2020;38:3388–97.
29. Höhn AK, Brambs CE, Hiller GGR, May D, Schmoeckel E, Horn LC. 2020 WHO classification of female genital tumors. *Geburtshilfe Frauenheilkd* 2021;81:1145–53.
30. Talhouk A, McAlpine JN. New classification of endometrial cancers: the development and potential applications of genomic-based classification in research and clinical care. *Gynecol Oncol Res Pract* 2016;13:14.
31. Murali R, Soslow RA, Weigelt B. Classification of endometrial carcinoma: more than two types. *Lancet Oncol*. 2014;15:268–78.