Sakarya Tıp Dergisi
Sakarya Medical Journal

e-ISSN : 2146-409X
Publisher : Sakarya University

Vol. 16, No. 1, 147-157, 2026
DOI: http://doi.org/10.31832/smj.1784654

Research Article

Recurrence-Related Factors in Early Stage Endometrial Cancer

Necim Yalcin[1*], Aysun Alci[2], Mustafa Gokkaya[3], Tayfun Toptas[4], Isin Ureyen[4]

[1] Batman Training and Research Hospital, Department of Gynecologic Oncology, Batman, Türkiye, zinaryal@gmail.com

[2] Kahramanmaraş Necip Fazıl City Hospital, Department of Gynecologic Oncology, Kahramanmaraş, Türkiye, aysun_alci@hotmail.com

[3] Gaziantep City Hospital, Department of Gynecologic Oncology, Gaziantep, Türkiye, mugokkaya@gmail.com, ror.org/04ak60v12

[4] University of Health Sciences Antalya Training and Research Hospital, Department of Gynecologic Oncology, Antalya, Türkiye, drttoptas@gmail.com, isin.ureyen@gmail.com

* Corresponding Author

Received: 15.09.2025
Accepted: 18.03.2026
Published Online: 27.03.2026

Abstract

Objective: The main objective of this study is to identify clinical and pathological factors associated with recurrence in patients diagnosed with early-stage (stage I–II) endometrial cancer.

Methods: A total of 98 patients diagnosed with stage I–II endometrial cancer who underwent surgical treatment at a single center between 2017 and 2021 were retrospectively analyzed. The patients' clinical and pathological characteristics, the adjuvant therapies administered, and follow-up outcomes were evaluated. Factors associated with recurrence were assessed using univariate analyses.

Results: The mean age of the patients was 59.8 years, and the mean tumor size was 3.58 cm. The mean follow-up period was 49.1 months. The recurrence rate was 8.2%. Five recurrences were identified as locoregional, and three as distant metastases. In univariate analyses, surgical type (p=0.015), adjuvant therapy (p=0.009), and histotype (endometrioid vs. non-endometrioid, p=0.016) were found to be associated with recurrence.

Conclusions: The recurrence rate in early-stage endometrial cancer was found to be low, consistent with the literature, and it was determined that 5 of the recurrences were locoregional in nature, while the remaining 3 were distant metastases. Although surgical type, histological type, and adjuvant therapy were identified as factors associated with recurrence in univariate analyses, there is a need for a detailed examination of these factors through multicenter studies involving larger patient cohorts.

Keywords: Endometrial cancer, Early stage, Recurrence, Prognostic factors

1. INTRODUCTION

Endometrial cancer (EC) is the most prevalent gynaecological malignancy in developed countries.[1] Approximately 90% of patients present with symptoms such as abnormal uterine bleeding or postmenopausal bleeding, which enables early detection in the majority of cases. Consequently, more than 75% of patients are diagnosed with low-grade, early-stage disease (International Federation of Gynaecology and Obstetrics [FIGO] stages I and II), which is associated with favourable clinical outcomes and high overall survival rates.[2]

Surgical management remains the cornerstone of treatment for early-stage EC.[3] Decisions regarding adjuvant therapy in patients with stage I and II disease are based on several clinicopathological factors, including tumour histological type and grade, the presence of lymphovascular space invasion (LVSI), and patient age.[4,5] Evidence from randomised studies has demonstrated that adjuvant radiotherapy reduces the risk of locoregional recurrence in early-stage disease; however, no improvement in overall survival has been shown.[6,8] In contrast, the role of adjuvant systemic therapy in early-stage patients remains unclear and is therefore not routinely recommended.[9,10]

Despite favourable outcomes, tumour recurrence occurs in approximately 5–15% of patients with early-stage EC following primary treatment.[11,12] Although the majority of recurrences develop within the first two years (60%) and within three years (76%), late recurrences occurring up to 15 years after treatment have also been reported.[13-15] Survival outcomes following recurrence are poor, with five-year survival rates markedly reduced and salvage treatment success rates reported to be as low as 40%.[9,16]

Cite as: Yalcin N, Alci A, Gokkaya M, Toptas T, Ureyen I. Recurrence-related factors in early stage endometrial cancer. Sakarya Med J. 2026;16(1):147-57. doi:10.31832/smj.1784654.

This is an open access paper distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License.

In 2013, the Cancer Genome Atlas (TCGA) project revolutionised endometrial cancer classification by identifying four molecular subtypes: POLE ultra-mutated, microsatellite instability (MSI)/hypermutated, low-copy number, and high-copy number tumours. Subsequently, the ProMisE and TransPORTEC initiatives independently developed clinically applicable and cost-effective classification tools using focused next-generation sequencing (NGS) and immunohistochemistry (IHC).[17,18] Numerous studies have since demonstrated the prognostic significance and clinical applicability of molecular classification in EC. As a result, molecular classification has been incorporated into risk stratification and adjuvant treatment recommendations in updated guidelines published by the European Society of Gynecologic Oncology (ESGO), the European Society for Radiotherapy and Oncology (ESTRO), and the European Society of Pathology (ESP).[19] These advances have further emphasised the importance of molecular classification in predicting prognosis and more accurately assessing recurrence risk, including in early-stage disease.

Nevertheless, the implementation of molecular classification remains limited, particularly in underdeveloped and developing countries where resources are scarce. In many settings, treatment decisions and staging continue to rely primarily on traditional histopathological factors. Therefore, in a period when molecular classification has not yet been universally adopted into routine clinical practice, it is essential to highlight the importance of classical clinicopathological factors in predicting recurrence among patients with early-stage EC.

Accordingly, a better understanding of the factors associated with disease recurrence in early-stage EC is crucial for optimising treatment strategies, including personalised adjuvant therapy planning and post-treatment surveillance. In the present study, we aimed to identify factors associated with recurrence in patients with early-stage EC.

2. METHOD

Following approval by the Institutional Review Board of the Ethics Committee of Antalya Training and Research Hospital, this single-centre retrospective cohort study was conducted between January 2017 and December 2021. The study included patients diagnosed with stage I–II EC according to the 2009 FIGO staging system based on final pathology reports. All patients underwent at least total hysterectomy with bilateral salpingo-oophorectomy (TH/BSO), with or without nodal staging (pelvic ± para-aortic lymphadenectomy), in accordance with current clinical guidelines. Study data were obtained from patient medical records and the hospital's electronic database. All histological subtypes of stage I–II EC were eligible for inclusion.

Patients were excluded if they had concomitant malignancies, insufficient clinical data, stage III or IV EC, or if they died within 30 days following completion of treatment.

Systematic pelvic and para-aortic lymphadenectomy was performed in patients with grade 3 endometrioid EC, high-grade histological subtypes (serous, clear cell, carcinosarcoma, mixed type, and dedifferentiated/undifferentiated histology), and/or myometrial invasion greater than 50%. In patients with grade 1 or 2 endometrioid EC and myometrial invasion less than 50%, pelvic lymphadenectomy was performed in conjunction with TH/BSO. Decisions regarding adjuvant therapy were made by the operating surgeon or the gynaecological oncology multidisciplinary council in accordance with international guidelines. Adjuvant treatment modalities included vaginal brachytherapy (VBT), external beam radiotherapy (EBRT), and/or chemotherapy, as appropriate.

Patients were followed up at three-month intervals during the first two years, at six-month intervals until the fifth year, and annually thereafter. At each follow-up visit, patient symptoms were evaluated, and routine systemic and gynaecological examinations were performed. Complete blood counts and blood chemistry analyses were also obtained. Although not

routinely recommended by current guidelines, abdominal ultrasonography was generally performed at the discretion of the treating physician. Additional imaging modalities were used when clinically indicated.

Recurrence was defined as the detection of new metastatic lesions confirmed by imaging studies (computed tomography, magnetic resonance imaging, or positron emission tomography-computed tomography) and/or histopathological verification via biopsy, occurring after completion of primary treatment. Recurrences were classified as locoregional (vaginal cuff recurrence or pelvic recurrence) or distant metastasis. The date of recurrence was recorded as the date of the confirmatory imaging study or biopsy, whichever was earlier.

2.1. Statistical analysis

All statistical analyses were performed using SPSS software, version 22.0 (SPSS Inc., Chicago, IL, USA). Continuous variables (age, tumor size, follow-up duration, time to recurrence) were summarized as mean ± standard deviation (SD) or median (minimum–maximum), while categorical variables were presented as frequencies (n) and percentages (%).

Due to the low number of recurrence events (n=8), multivariate analyses (logistic or Cox regression) were deliberately avoided to prevent overfitting and unstable estimates. Univariate associations between recurrence and clinical/pathological variables were assessed using the Pearson chi-square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant.

3. RESULTS

A total of 98 patients who underwent surgery for EC during the study period and met the eligibility criteria were included in the final analysis. The mean age of the study population was 59.8 years, and the mean tumour size was 3.58 cm. The overall recurrence rate was 8.2%. Of the 8 recurrence cases, 5 were classified as locoregional recurrences and 3 as distant metastases. All recurrences were initially detected by imaging methods; in most cases, they were confirmed by surgery. The earliest recurrence was detected at 6 months, while the latest recurrence occurred at 79 months. The mean follow-up duration was 49.1 months. Detailed demographic and clinical characteristics of the patients are presented in Table 1.

Table 1.

Characteristics of the cases

Variable			**Distribution†**
	Minimum	**Maximum**	**Mean**
Age (years)	42	85	59.8
Tumour size (cm)	0.2	22	3.58
Time to recurrence (months)	6	79	21.12
Follow up time (months)	7	114	49.1

† Qualitative data is expressed as frequency (N) and percentage (%). Quantitative variables are expressed as mean ± SD or median (minimum – maximum)

The case-specific details regarding recurrences are described in detail in Table 2.

Table 2.

Case-specific details regarding recurrences

Patient	Age (years)	Histotype	FIGO Stage	LVSI	Time to Recurrence (months)	Recurrence Site	Recurrence Type	Diagnosis Method
1	63	Non-endometrioid	IB	Positive	24	Vaginal cuff	Locoregional	PET/CT
2	66	Non-endometrioid	IA	Negative	6	Vaginal cuff	Locoregional	PET/CT
3	64	Non-endometrioid	IA	Negative	7	Colon	Distant metastasis	Colonoscopic biopsy
4	70	Endometrioid	IB	Negative	13	Paraaortic lymph node	Distant metastasis	PET/CT
5	65	Non-endometrioid	IA	Negative	12	Vaginal cuff	Locoregional	MRI
6	54	Non-endometrioid	IA	Positive	6	Vaginal cuff	Locoregional	PET/CT
7	44	Endometrioid	II	Negative	79	Pelvic peritoneum	Locoregional	PET/CT
8	59	Endometrioid	IA	Negative	22	Omentum	Distant metastasis	PET/CT

Abbreviations: PET/CT: Positron Emission Tomography / Computed Tomography, MRI: Magnetic Resonance Imaging, FIGO:International Federation of Gynecology and Obstetrics, LVSI: Lymphovascular Space Invasion

The most frequent histological subtypes were grade 1 endometrioid EC (38.8%) and grade 3 endometrioid EC (22.4%). In addition to TH/BSO, systematic pelvic and para-aortic lymph node dissection was performed in 51% of patients, while pelvic lymph node dissection alone was performed in 42.9%. Deep myometrial invasion was observed in 38.7% of cases, and LVSI was present in 25.5%. No positive peritoneal cytology was detected in any patient. According to the 2009 FIGO staging system, disease stages were distributed as follows: stage IA in 59.2%, stage IB in 37.7%, and stage II in 6.1% of patients. Detailed clinicopathological characteristics are shown in Table 3.

Table 3.

Clinicopathological characteristics of the cases

Histotype	**Endometrioid**	**75(76.5%)**
	Grade 1 Endometrioid	38 (38.8%)
	Grade 2 Endometrioid	15 (15.3%)
	Grade 3 Endometrioid	22 (22.4%)
	Non-Endometrioid	**23 (23.5%)**
	Serous	10 (10.2%)
	Clear cell	0 (0.0%)
	DE/Undifferentiated	2 (2.1%)
	Mixed	6 (6.1%)
	Choriocarcinoma	5 (5.1%)

Table 3. (Continued)

Surgery	TH/BSO alone	6 (6.1%)
	TH/BSO plus pelvic lymphadenectomy	42 (42.9%)
	TH/BSO plus pelvic -paraaortic lymphadenectomy	50 (51%)
Cytology	Negative	98 (100%)
	Positive	0 (0%)
Myometrial invasion	No	13 (13.3%)
	<50	47 (48%)
	≥50	38 (38.7%)
Lymphovascular space involvement	Negative	73 (74.5%)
	Positive	25 (25.5%)
Stage	IA	58 (59.2%)
	IB	34 (37.7%)
	II	6 (6.1%)

Abbreviations: TH/BSO: Total hysterectomy plus bilateral salpingo-oophorectomy

Postoperative treatment outcomes were subsequently evaluated. A total of 37.8% of patients were followed up without receiving any adjuvant treatment. EBRT with or without VBT was administered in 27.6% of cases. After a mean follow-up period of 49.1 months, disease recurrence was observed in 8 patients (8.2%), and 5 patients (5.1%) died due to EC. The majority of patients (79.6%) remained alive without evidence of disease at the last follow-up. Detailed disease outcomes are presented in Table 4.

Table 4.

Disease outcome of cases

		Distribution †
Adjuvant therapy	No	37 (37.8%)
	Brachytherapy alone	11 (11.2%)
	EBRT +/- Brachytherapy	27(27.6%)
	Chemotherapy alone	6 (6.1%)
	Chemotherapy + EBRT	17(17.3%)
Recurrence	Yes	8 (8.2%)
	No	90 (91.8%)
Survival	Alive with no evidence of disease	78 (79.6%)
	Alive with disease	3 (3.1%)
	Dead of disease	5 (5.1%)
	Dead of other reasons	12 (12.2%)

† Qualitative data is expressed as frequency (N) and percentage (%). Quantitative variables are expressed as mean ± SD or median (minimum – maximum).
Abbreviations: EBRT: External Beam Radiation Therapy

Univariate analysis demonstrated that type of surgery (p=0.015), adjuvant therapy (p=0.009), and histological type (endometrioid vs non-endometrioid, p=0.016) were significantly associated with disease recurrence. Detailed results of the univariate analysis of factors associated with recurrence are presented in Table 5.

Table 5.

Factors associated with disease recurrence

Variable		Recurrence		P-value
		No	Yes	
Histotype	Endometrioid	72(80%)	3 (37.5%)	**0.016**
	Non-Endometrioid	18 (20%)	5 (62.5%)	
Surgery	TH/BSO alone	6 (6.6%)	0 (0%)	**0.015**
	TH/BSO plus pelvic LA	42 (46.7%)	0 (0%)	
	TH/BSO plus pelvic + paraaortic LA	42 (46.7%)	8 (100%)	
Myometrial invasion	No	12 (13.3%)	1 (12.5%)	0.99
	<50	43 (47.7%)	4 (50%)	
	≥50	35 (39%)	3 (37.5%)	
Lymphovascular space involvement	Negative	67 (74.5%)	6 (75%)	0.97
	Positive	23 (%25.5)	2 (25%)	
Stage	IA	53 (59%)	5 (62.5%)	0.66
	IB	32 (35.5%)	2 (25%)	
	II	5 (5.5%)	1 (12.5%)	
Adjuvant therapy	No	36 (40%)	1 (12.5%)	**0.009**
	Brachytherapy alone	11 (12.2%)	0 (0%)	
	EBRT +/- Brachytherapy†	26 (28.8%)	1 (12.5%)	
	Chemotherapy alone	4 (4.5%)	2 (25%)	
	Chemotherapy + EBRT	13 (14.5%)	4 (50%)	

Variables are expressed as frequency (N) and percentages (%).
Abbreviations: TH/BSO: Total hysterectomy plus bilateral salpingo-oophorectomy, EBRT: External Beam Radiation Therapy, LA: Lymphadenectomy

4. DISCUSSION

Current treatment guidelines recommend adjuvant radiotherapy, chemotherapy, or observation following surgery in patients with early-stage EC, based on risk stratification systems incorporating FIGO stage, histological grade, LVSI, and patient age.[3,6,7] Despite these recommendations, the optimal selection of adjuvant treatment remains controversial. A comprehensive understanding of the factors associated with disease recurrence is therefore essential, as recurrence is directly related to survival outcomes in this patient population. In the present study, univariate analysis revealed significant associations between recurrence and type of surgery (p=0.015), adjuvant therapy (p=0.009), and histological subtype (endometrioid vs non-endometrioid, p=0.016).

The recurrence rate of early-stage EC has been reported to range between 5% and 15%.[11,12] In our cohort, the recurrence rate was 8.2%, which is consistent with previously published data. Variations in recurrence rates across studies are likely related to differences in sample size, follow-up duration, and the proportion of high-grade and non-endometrioid histologies included. In studies comparable to the present that evaluated both endometrioid and non-endometrioid subtypes, Takahashi et al., Dou et al., and Sasada et al. reported recurrence rates of 6.4%, 5.1%, and 5.6%, respectively, closely aligning with our findings.[11,12,20]

Several clinicopathological factors have been associated with recurrence in EC, including advanced age, high tumour grade, deep myometrial invasion, LVSI, cervical stromal involvement, FIGO stage, and molecular

alterations such as TP53 mutation.[21-24] However, when analyses are restricted to early-stage disease, the prognostic significance of these factors becomes less consistent across studies.

Non-endometrioid histological subtypes account for approximately 15–20% of EC but are characterised by a substantially higher risk of recurrence and mortality.[25,26] Previous studies have demonstrated histological subtype as an important prognostic factor. Han et al. identified myometrial invasion and tumour grade as independent predictors of recurrence in patients with stage I disease,[27] while Jeppesen et al. reported non-endometrioid histology as a significant risk factor in a large cohort of stage I–II patients.[28] Similarly, Dou et al. demonstrated grade 3 histology as an independent predictor of early recurrence.[12] In the present study, In our cohort, grouping histologies as endometrioid versus non-endometrioid yielded a statistically significant association with recurrence in univariate analysis (p=0.016). This finding is consistent with the literature and supports the prognostic relevance of histological subtype even in early-stage disease.

LVSI is widely recognised as a predictor of nodal metastasis and an independent prognostic factor for recurrence in EC, and it plays a central role in adjuvant treatment decision-making.[2,3] Several studies, including those by Dou et al., Misirlioglu et al., and Tortorella et al., have reported LVSI as an independent risk factor for recurrence in early-stage disease.[2,12,29] In contrast, studies by Takahashi et al. and Ureyen et al. did not identify LVSI as an independent predictor of recurrence in early-stage cohorts.[11,23] Similarly, LVSI was not significantly associated with recurrence in our univariate analysis. This inconsistency may be explained by the relatively low number of recurrence events in our study, which likely limited the statistical power to detect an independent effect of LVSI.

Depth of myometrial invasion has also been established as a key prognostic factor in EC, with deeper invasion associated with increased lymph node metastasis and poorer survival outcomes.[30,31] While several studies have reported a significant association between deep myometrial invasion and recurrence in early-stage disease,[12,27,32] others have failed to confirm this relationship.[11,28] In line with the latter findings, no independent association between myometrial invasion and recurrence was observed in the present study, which may again be related to limited event numbers.

In our univariate analysis, type of surgery was significantly associated with recurrence. However, this finding should be interpreted with caution. Patients who underwent more extensive surgical staging, including pelvic and para-aortic lymph node dissection, likely represented a higher-risk subgroup based on tumour grade, histology, or depth of invasion. Therefore, the observed association between surgical extent and recurrence is more likely reflective of confounding by indication rather than a causal relationship between surgical approach and recurrence risk.

Similarly, adjuvant therapy was significantly associated with recurrence in univariate analysis. This association should not be interpreted as adjuvant treatment being a risk factor for recurrence. Rather, this finding likely reflects reverse causality, as adjuvant therapy is preferentially administered to patients with higher-risk disease characteristics. Consequently, adjuvant treatment in this context serves as a marker of underlying recurrence risk rather than a direct contributor to disease recurrence.

A number of studies have investigated the effect of age on the risk of recurrence, particularly in early-stage disease. However, only three of these studies reported statistically significant findings.[33-35] This difference may be attributed to age-related changes in tumour biology, the presence of comorbidities, and a decline in immune function. In the present study, consistent with the findings of many previous reports, no significant relationship between age and recurrence was observed.

In the FIGO 2009 staging system, peritoneal cytology is no longer considered a variable for determining stage, and the FIGO staging system was revised in 2023, but peritoneal cytology continues to be excluded from the staging criteria.[36-38] Although some studies have reported

an association between positive peritoneal cytology and poorer outcomes in early-stage disease,[11,39,40] no patients in the present study had positive cytology, precluding analysis of its prognostic significance. This finding is most likely related to the limited sample size.

The main limitations of the present study include its retrospective design, single-center nature, and limited statistical power due to the low number of recurrences (n=8). Furthermore, the absence of molecular classification limits the evaluation of its prognostic importance in terms of recurrence. Despite these limitations, the strengths of the study include a homogeneous cohort of early-stage patients, a medium-to-long follow-up period, standardized surgical and follow-up protocols, and recurrence rates consistent with the literature. Overall, these findings provide valuable insights into recurrence patterns in early-stage EC in settings where molecular classification is not yet routinely used.

5. CONCLUSION

A comprehensive understanding of factors associated with recurrence in patients with early-stage EC is crucial for optimally directing adjuvant treatment strategies. In this retrospective analysis, the recurrence rate in early-stage EC was determined to be 8.2%, which is consistent with previous literature. Univariate analysis identified type of surgery, adjuvant therapy, and histotype (endometrioid vs non-endometrioid) as factors associated with recurrence. These associations should be interpreted cautiously due to potential confounding by indication and the low number of recurrence events. Larger, multicenter studies with higher event numbers are needed to confirm prognostic factors and guide personalized treatment in early-stage endometrial cancer.

Article Information Form

Author Contributions

Conceptualization: N.Y., T.T., I.U.; Methodology: N.Y., T.T., I.U.; Software: N.Y, A.A, M.G.; Validation: N.Y, A.A, M.G.; Formal analysis: N.Y, T.T, I.U.; Investigation: N.Y, A.A, M.G.; Resources: N.Y, A.A, M.G.; Data curation: N.Y, A.A, M.G.; Writing – original draft: N.Y,T.T, I.U.; Writing – review & editing: N.Y,T.T, I.U.; Visualization: N.Y, A.A, M.G.; Supervision: N.Y,T.T, I.U.; Project administration: N.Y.

The Declaration of Conflict of Interest/ Common Interest

No conflict of interest or common interest has been declared by authors.

The Declaration of Ethics Committee Approval

The study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki and approved by the Ethics Committee of Antalya Training and Research Hospital (approval date: 13 Jun 2024, approval number: 2024-171). As this was a retrospective study, the participants were not asked to provide informed consent prior to their involvement.

Artificial Intelligence Statement

No artificial intelligence tools were used while writing this article.

Copyright Statement

Authors own the copyright of their work published in the journal and their work is published under the CC BY-NC 4.0 license.

REFERENCES

1. Makker V, MacKay H, Ray-Coquard I, Levine DA, Westin SN, Aoki D, et al. Endometrial cancer. Nat Rev Dis Primers. 2021;7(1):88. doi:10.1038/s41572-021-00324-8.
2. Misirlioglu S, Guzel A, Gulec U, Gumurdulu D, Vardar M. Prognostic factors determining recurrence in early-stage endometrial cancer. Eur J Gynaecol Oncol. 2012;33(6):2012. doi:10.12892/ejgo201206610.
3. Abu-Rustum NR, Campos SM, Amarnath S, Arend R, Barber E, Bradley K, et al. NCCN Guidelines® Insights: Uterine Neoplasms, Version 3.2025: Featured Updates to the NCCN Guidelines®. J Natl Compr Canc Netw. 2025;23(8):284-91. doi:10.6004/jnccn.2025.0038.
4. Creutzberg CL, Van Stiphout RG, Nout RA, Lutgens LC, Jürgenliemk-Schulz IM, Jobsen JJ, et al. Nomograms for prediction of outcome with or without adjuvant radiation therapy for patients with endometrial cancer: a pooled analysis of PORTEC-1 and PORTEC-2 trials. Int J Radiat Oncol Biol Phys.

2015;91(3):530-9. doi:10.1016/j.ijrobp.2014.11.022.
5. SGO Clinical Practice Endometrial Cancer Working Group, Burke WM, Orr J, Leitao M, Salom E, Gehrig P, et al. Endometrial cancer: a review and current management strategies: part II. Gynecol Oncol. 2014;134(2):393-402. doi:10.1016/j.ygyno.2014.06.003.
6. 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. Lancet. 2000;355(9213):1404-11. doi:10.1016/s0140-6736(00)02139-5.
7. 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(3):744-51. doi:10.1016/j.ygyno.2003.11.048.
8. Sorbe BG, Horvath G, Andersson H, Boman K, Lundgren C, Pettersson B. External pelvic and vaginal irradiation versus vaginal irradiation alone as postoperative therapy in medium-risk endometrial carcinoma: a prospective, randomized study—quality-of-life analysis. Int J Radiat Oncol Biol Phys. 2012;22(7):1281-8. doi:10.1016/j.ijrobp.2011.04.014.
9. Francis SR, Ager BJ, Do OA, Huang Y-HJ, Soisson AP, Dodson MK, et al. Recurrent early stage endometrial cancer: Patterns of recurrence and results of salvage therapy. Gynecol Oncol. 2019;154(1):38-44. doi:10.1016/j.ygyno.2019.04.676.
10. 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(3):295-309. doi:10.1016/S1470-2045(18)30079-2.
11. Takahashi K, Yunokawa M, Sasada S, Takehara Y, Miyasaka N, Kato T, et al. A novel prediction score for predicting the baseline risk of recurrence of stage I–II endometrial carcinoma. J Gynecol Oncol. 2018;30(1):e8. doi:10.3802/jgo.2019.30.e8.
12. Dou Y, Song K, Fu Y, Shen Y, Zhang C, Yao S, et al. Risk factors and prognosis of early recurrence in stage I–II endometrial cancer: a large-scale, multi-center, and retrospective study. Front Med (Lausanne). 2022;9:808037. doi:10.3389/fmed.2022.808037.
13. Creutzberg CL, van Putten WL, Koper PC, Lybeert ML, Jobsen JJ, Wárlám-Rodenhuis CC, et al. Survival after relapse in patients with endometrial cancer: results from a randomized trial☆. Gynecol Oncol. 2003;89(2):201-9. doi:10.1016/s0090-8258(03)00126-4.
14. Creutzberg CL, Nout RA, Lybeert ML, Wárlám-Rodenhuis CC, Jobsen JJ, Mens J-WM, et al. Fifteen-year radiotherapy outcomes of the randomized PORTEC-1 trial for endometrial carcinoma. Int J Radiat Oncol Biol Phys. 2011;81(4):e631-e8. doi:10.1016/j.ijrobp.2011.04.013.
15. Yechieli R, Robbins JR, Schultz D, Munkarah A, Elshaikh MA. Vaginal recurrence more than 17 years after hysterectomy and adjuvant treatment for uterine carcinoma with successful salvage brachytherapy: a case report. Case Rep Oncol. 2011;4(1):242-5. doi:10.1159/000328076.
16. Bendifallah S, Ouldamer L, Lavoue V, Canlorbe G, Raimond E, Coutant C, et al. Patterns of recurrence and outcomes in surgically treated women with endometrial cancer according to ESMO-ESGO-ESTRO Consensus Conference risk groups: results from the FRANCOGYN study Group. Gynecol Oncol. 2017;144(1):107-12. doi:10.1016/j.ygyno.2016.10.025.
17. 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(16):4215-24. doi:10.1158/1078-0432.ccr-15-2878.
18. Stelloo E, Bosse T, Nout RA, MacKay HJ, Church DN, Nijman HW, et al. Refining prognosis and identifying targetable pathways for high-risk endometrial cancer; a TransPORTEC initiative. Mod Pathol. 2015;28(6):836-44. doi:10.1038/modpathol.2015.43.
19. Concin N, Matias-Guiu X, Cibula D, Colombo N, Creutzberg CL, Ledermann J, et al. ESGO–ESTRO–ESP guidelines for the management of patients with endometrial carcinoma: update 2025. Lancet Oncol. 2025;26(8):e423-e35. doi:10.1016/s1470-2045(25)00167-6.
20. Sasada S, Yunokawa M, Takehara Y, Ishikawa M, Ikeda S, Kato T, et al. Baseline risk of recurrence in stage I–II endometrial carcinoma. J Gynecol Oncol. 2017;29(1):e9. doi:10.3802/jgo.2018.29.e9.
21. Dunn EF, Geye H, Platta CS, Gondi V, Rose S, Bradley KA, et al. Predictive factors of recurrence following adjuvant vaginal cuff brachytherapy alone for stage I endometrial cancer. Gynecol Oncol. 2014;133(3):494-8. doi:10.1016/j.ygyno.2014.03.554.
22. Capozzi VA, Sozzi G, Rosati A, Restaino S, Gambino G, Cianciolo A, et al. Predictive score of nodal involvement in endometrial cancer patients: a large multicentre series. Ann Surg Oncol. 2022;29(4):2594-9. doi:10.1245/s10434-021-11083-x.
23. Ureyen I, Karalok A, Turkmen O, Kimyon G, Akdas YR, Akyol A, et al. Factors predicting recurrence in patients with stage IA endometrioid endometrial cancer: what is the importance of LVSI?. Arch Gynecol Obstet. 2020;301(3):737-44. doi:10.1007/s00404-019-05418-z.
24. Nout RA, Bosse T, Creutzberg CL, Jürgenliemk-Schulz IM, Jobsen JJ, Lutgens LC, et al. Improved risk assessment of endometrial cancer by combined analysis of MSI, PI3K–AKT, Wnt/β-catenin and P53 pathway activation. Gynecol Oncol. 2012;126(3):466-73. doi:10.1016/j.ygyno.2012.05.012.
25. Barretina-Ginesta MP, Quindós M, Alarcón JD, Esteban C, Gaba L, Gómez C, et al. SEOM-GEICO clinical guidelines on endometrial cancer (2021). Clin Transl Oncol. 2022;24(4):625-34. doi:10.1007/s12094-022-02799-7.
26. Lu KH, Broaddus RR. Endometrial cancer. N Engl J Med. 2020;383(21):2053-64. doi:10.1056/nejmra1514010.
27. Han KH, Kim HS, Lee M, Chung HH, Song YS. Prognostic factors for tumor recurrence in endometrioid endometrial cancer stages IA and IB. Medicine (Baltimore). 2017;96(21):e6976. doi:10.1097/md.0000000000006976.
28. Jeppesen MM, Jensen PT, Hansen DG, Iachina M, Mogensen O. The nature of early-stage endometrial cancer recurrence—A national cohort study. Eur J Cancer. 2016;69:51-60. doi:10.1016/j.ejca.2016.09.033.
29. Tortorella L, Restaino S, Zannoni GF, Vizzielli G, Chiantera V, Cappuccio S, et al. Substantial lymph-vascular space invasion (LVSI) as predictor of distant relapse and poor prognosis in low-risk early-stage endometrial cancer. J Gynecol Oncol. 2021;32(2):e11. doi:10.3802/jgo.2021.32.e11.
30. Dane C, Bakir S. The effect of myometrial invasion on prognostic factors and survival analysis in endometrial carcinoma. Afr Health Sci. 2019;19(4):3235-41. doi:10.4314/ahs.v19i4.47.
31. Pasternak M, Kessous R, Samueli B, Dreiher J, Meirovitz M, Davidesko S, et al. The prognostic importance of features of myometrial invasion in endometrial endometrioid carcinoma. Arch Gynecol Obstet. 2025;312(4):1215-24. doi:10.1007/s00404-025-08103-6.
32. Nwachukwu C, Baskovic M, Von Eyben R, Fujimoto D, Giaretta S, English D, et al. Recurrence risk factors in stage IA grade 1 endometrial cancer. J Gynecol Oncol. 2021;32(2):e22. doi:10.3802/jgo.2021.32.e22.
33. Stasenko M, Feit N, Lee SS, Shepherd C, Soslow RA, Cadoo KA, et al. Clinical patterns and genomic profiling of recurrent 'ultra-low risk'endometrial cancer. Int J Gynecol Cancer. 2020;30(6):717-23. doi:10.1136/ijgc-2020-001241.

34. Wang C-J, Chao A, Yang L-Y, Hsueh S, Huang Y-T, Chou H-H, et al. Fertility-preserving treatment in young women with endometrial adenocarcinoma: a long-term cohort study. Int J Gynecol Cancer. 2014;24(4):718-28. doi:10.1097/igc.0000000000000098.
35. Yoney A, Yildirim C, Bati Y, Unsal M. Low risk stage I endometrial carcinoma: prognostic factors and outcomes. Indian J Cancer. 2011;48(2):204-10. doi:10.4103/0019-509x.82895.
36. Pecorelli S, Zigliani L, Odicino F. Revised FIGO staging for carcinoma of the cervix. Int J Gynecol Obstet. 2009;105(2):107-8. doi:10.1016/j.ijgo.2009.02.009.
37. Cibas ES, Cytology D. Diagnostic principles and clinical correlates. Philadelphia; 2019.
38. Kasamatsu T, Onda T, Katsumata N, Sawada M, Yamada T, Tsunematsu R, et al. Prognostic significance of positive peritoneal cytology in endometrial carcinoma confined to the uterus. Br J Cancer. 2003;88(2):245-50. doi:10.1038/sj.bjc.6600698.
39. Garg G, Gao F, Wright JD, Hagemann AR, Mutch DG, Powell MA. Positive peritoneal cytology is an independent risk-factor in early stage endometrial cancer. Gynecol Oncol. 2013;128(1):77-82. doi:10.1016/j.ygyno.2012.09.026.
40. Lee B, Suh DH, Kim K, No JH, Kim YB. Influence of positive peritoneal cytology on prognostic factors and survival in early-stage endometrial cancer: a systematic review and meta-analysis. Jpn J Clin Oncol. 2016;46(8):711-7. doi:10.1093/jjco/hyw063.