Article

Discovery Medicine 2026; 38(214): 3600–3609
https://doi.org/10.24976/Discov.Med.202638214.274

Association of Tumor Size and Lymphovascular Space Invasion With Recurrence in Estrogen Receptor-Positive Endometrial Cancer

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Submitted: 26 June 2026 Revised: 20 July 2026 Accepted: 10 August 2026 Published: 25 November 2026

Background: Estrogen receptor (ER) positivity is associated with favorable outcomes in endometrial cancer but recurrence risk remains heterogeneous. This study evaluated clinicopathological factors associated with recurrence in ER-positive endometrial cancer, with particular emphasis on tumor size and lymphovascular space invasion.
Methods: This retrospective cohort study included 139 patients with ER-positive endometrial cancer who underwent primary surgical treatment between 2010 and 2025. Disease-free survival was assessed using Kaplan–Meier analysis and Cox's proportional hazards regression. Time-dependent receiver operating characteristic analysis was used to evaluate the discriminatory ability of tumor size for 3-year and 5-year disease-free survival, while accounting for censoring.
Results: During a median follow-up of 48 months, recurrence occurred in 33 (23.7%) patients. Tumor size was independently associated with recurrence (adjusted hazard ratio [aHR] 1.208 per 1-cm increase, 95% confidence interval [CI] 1.047–1.395, p = 0.010), as was International Federation of Gynecology and Obstetrics (FIGO) stage III or IV disease (aHR 2.454, 95% CI 1.080–5.578, p = 0.032). Lymphovascular space invasion did not reach significance after adjustment (aHR 2.007, 95% CI 0.923–4.363, p = 0.079). The time-dependent areas under the curve were 0.673 for 3-year and 0.696 for 5-year disease-free survival.
Conclusion: Larger tumor size and advanced FIGO stage were independently associated with recurrence in ER-positive endometrial cancer. Tumor size showed modest discriminatory ability and could provide complementary prognostic information, although validation in larger cohorts is required.

Keywords: endometrial cancer; estrogen receptor; tumor size; lymphovascular space invasion; recurrence

Introduction

Endometrial cancer is the most common gynecological malignancy in high-income countries, and although many patients are diagnosed early, recurrence remains a major cause of cancer-related mortality [1,2]. Accurate postoperative risk stratification is therefore essential for guiding adjuvant treatment and surveillance strategies [3]. Estrogen receptor (ER) positivity is associated with favorable clinicopathological characteristics and improved oncological outcomes in endometrial cancer [4,5,6]. However, increasing evidence suggests that ER-positive tumors are not prognostically uniform and that clinically meaningful heterogeneity persists within this subgroup [7,8]. Consequently, ER positivity alone might be insufficient for identifying truly low-risk disease.

Conventional pathological factors, including International Federation of Gynecology and Obstetrics (FIGO) stage, tumor grade, depth of myometrial invasion, lymph node involvement, and lymphovascular space invasion remain important components of prognostic assessment [9,10,11]. Lymphovascular space invasion is an established adverse pathological feature and has been associated with nodal dissemination, recurrence, and unfavorable oncological outcomes in endometrial cancer [10,11]; however, its prognostic contribution specifically within ER-positive disease remains insufficiently characterized.

In contrast, tumor size can reflect overall tumor burden and obscure biological aggressiveness beyond conventional histopathological parameters. Although ER expression has increasingly been incorporated into prognostic stratification in endometrial cancer, the prognostic relevance of conventional clinicopathological variables (in-

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cluding tumor size) within ER-positive tumors remains incompletely characterized [6,12].

In our study, we aimed to evaluate the clinicopathological factors associated with recurrence in surgically treated patients with ER-positive endometrial cancer, with particular emphasis on tumor size and lymphovascular space invasion.

Methods

Study Population and Eligibility Criteria

This retrospective study was conducted at Afyonkarahisar Health Sciences University Health Application and Research Center, a tertiary referral center. The source population consisted of 603 consecutive patients who underwent primary surgical treatment for histopathologically confirmed endometrial carcinoma between January 2010 and December 2025. Patients were eligible for inclusion if they met all the criteria: had histopathologically confirmed endometrial carcinoma, primary surgical treatment was performed at our institution, ER immunohistochemistry results were available, had ER positivity (ie, nuclear staining in at least 10% of tumor cells), clinicopathological variables required for the study were available, and postoperative follow-up and recurrence information were available. Patients were excluded if they had ER-negative disease, ER immunohistochemistry results were unavailable, primary surgery performed at another institution, had incomplete clinicopathological records, were missing follow-up or recurrence data, or had duplicate patient records. In total, 139 patients with ER-positive endometrial cancer were included in the final analysis. The patient selection process is presented in Fig. 1.

ER immunohistochemistry was not routinely performed throughout the study. Testing became more frequently incorporated into pathological practice over time as its clinical and prognostic relevance became more established. In some earlier cases, retrospective assessment was not feasible because of incomplete historical pathology records, limited availability or inadequate quality of archived tissue specimens, and institutional resource limitations.

Clinicopathological Assessment

Clinicopathological variables were extracted from the final surgical pathology reports, prepared according to institutional pathological practice. The recorded variables included histological subtype, tumor grade, depth of myometrial invasion, tumor size, cervical stromal involvement, lymphovascular space invasion, lymph node status, and peritoneal cytology.

Tumor stage was assigned according to the 2009 FIGO staging system, which was used during most of the study period [13]. The 2023 FIGO staging system incorporates additional histopathological and molecular variables [14]. Because several variables required for reliable reclassification were not consistently available throughout the study period, the 2023 staging system was not retrospectively applied.

Tumor size was determined macroscopically from the surgical specimen and was recorded as the greatest tumor diameter. In multifocal tumors, the maximum diameter of the largest tumor mass was used for analysis.

Lymphovascular space invasion was evaluated on routine hematoxylin and eosin-stained sections and was defined as the presence of tumor cells or clusters within endothelial-lined lymphatic or vascular spaces. Before implementation of the 2023 FIGO staging system at our institution, lymphovascular space invasion was recorded in pathology reports as either present or absent. Following implementation of the 2023 FIGO staging system, lymphovascular space invasion was classified as either negative, focal, or substantial [14]. Focal lymphovascular space invasion was defined as the involvement of fewer than five lymphovascular spaces, whereas substantial lymphovascular space invasion was the involvement of five or more lymphovascular spaces. Because information regarding the extent of lymphovascular space invasion was not consistently available throughout the entire study period, focal and substantial involvement were combined and analyzed as being lymphovascular space invasion positive.

ER Immunohistochemistry

ER immunohistochemical staining was performed on formalin-fixed, paraffin-embedded tissue sections using a Patholab anti-ER monoclonal antibody (clone SP1) on the Leica Bond-Max fully automated immunostaining platform. Antigen retrieval was performed using a pH 9 solution and 3,3′-diaminobenzidine was used as the chromogen. Samples showing unequivocal nuclear staining in at least 10% of tumor cells were classified as ER-positive [4].

Surgical and Adjuvant Treatment

All patients underwent primary surgical treatment consisting of total hysterectomy and bilateral Salpingo-oophorectomy. Additional surgical staging procedures were performed according to preoperative and intraoperative risk assessment, institutional practice, and the guideline recommendations applicable at the time of treatment.

When indicated, pelvic lymphadenectomy was performed from the distal common iliac vessels to the circumflex iliac vein and included the obturator regions. Paraaortic lymphadenectomy was selectively performed in patients with suspicious imaging findings, enlarged lymph nodes that were identified intraoperatively, or high-risk clinicopathological features. Omental sampling or omentectomy was performed when clinically indicated, particularly in patients with non-endometrioid histology or suspected extrauterine disease. Sentinel lymph node mapping was not routinely available during the study period because of institutional technical limitations.

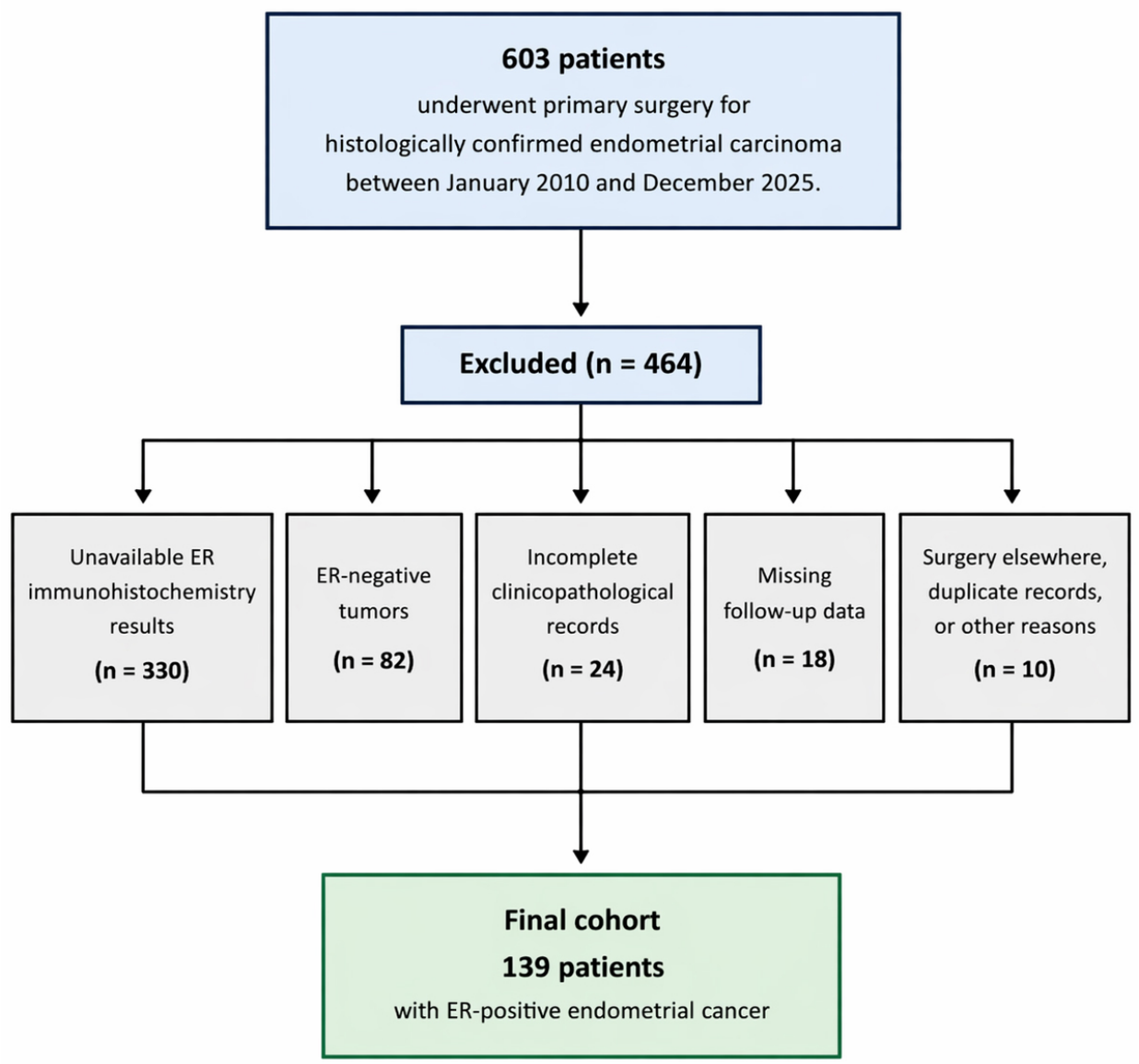

Fig. 1. Flow diagram of patient selection. ER, estrogen receptor.

Adjuvant treatment decisions were based on each patient's clinicopathological risk profile and the national and international guideline recommendations applicable during the corresponding treatment period. Because the study covered a prolonged interval, adjuvant chemotherapy and radiotherapy strategies have evolved over time. Patients received contemporary standard treatment available at the time of their diagnosis. Detailed patient-level adjuvant treatment data were not consistently available and therefore could not be included in the survival analyses.

Outcomes and Follow-up

The primary endpoint was disease-free survival, defined as the interval from primary surgery to the first objectively documented recurrence. Patients without recurrence were censored at the date of their last documented follow-up.

Postoperative surveillance consisted of clinical evaluation every 3 months during the first 2 years, every 6 months between years 3 and 5, and annually thereafter. Follow-up visits included symptom assessment, physical examination, and gynecological examination when clinically appropriate. Routine imaging was not performed at every follow-up visit. Computed tomography, magnetic resonance imaging, or positron emission tomography with computed tomography was requested when new symptoms, suspicious examination findings, or other clinical findings raised concern for recurrence.

Recurrence was defined as radiological, histopathological, or clinically documented evidence of disease after the completion of primary treatment. Histopathological confirmation was obtained whenever feasible. In patients without tissue confirmation, recurrence was established based on compatible imaging findings together with

clinical assessment. The date of recurrence was defined as the date on which recurrent disease was first objectively documented.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA), and Python, version 3.13.5 (Python Software Foundation, Wilmington, DE, USA; https://www.python.org/). The distributions of continuous variables were assessed using the Shapiro–Wilk test. Because body mass index (BMI) and tumor size did not follow a normal distribution, continuous variables were summarized as median and range and compared between patients with and without recurrence using the Mann–Whitney U test. Categorical variables were presented as number and percentage and compared using Pearson's Chi-squared test or Fisher's exact test. Fisher's exact testing was used when expected cell counts were less than 5.

Disease-free survival was estimated using the Kaplan–Meier method, and survival distributions were compared using the log-rank test. Univariable Cox proportional hazards regression analyses were performed to evaluate associations between clinicopathological variables and disease-free survival. Since only 33 recurrence events occurred, the primary multivariable Cox model was restricted to four clinically selected variables: tumor size, FIGO stage, lymphovascular space invasion, and histological subtype. Variables closely related to or incorporated within FIGO stage were not simultaneously included to reduce collinearity and model overfitting. The proportional hazards assumption was evaluated using Schoenfeld residuals. The linearity of the association between tumor size and the log hazard was assessed by comparing the linear Cox model with a natural cubic spline model using a likelihood ratio test. A ridge-penalized Cox regression model was also fitted as a sensitivity analysis. The penalty parameter was selected using five-fold cross-validation based on the mean Harrell concordance index. An additional sensitivity analysis was performed by adding BMI to the primary multivariable model to evaluate its potential confounding effect.

Cumulative and dynamic time-dependent receiver operating characteristic (ROC) analysis was performed to assess the discriminatory ability of tumor size for recurrence at 3 and 5 years while accounting for censored observations and differences in follow-up duration. Censoring was handled using marginal inverse probability of censoring weighting. The corresponding 95% confidence intervals for the time-dependent areas under the curve were estimated using 5000 bootstrap resamples.

All statistical tests were two-sided, and a p value of less than 0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 139 patients with ER-positive endometrial cancer were included in the final analysis. The median age was 62 years (range 37–91 years) and the median BMI was 33 kg/m^2 (range 25–45 kg/m^2). The median tumor size was 4 cm (range 1–13 cm). The median follow-up duration was 48 months (range 5–156 months).

During follow-up, recurrence occurred in 33 (23.7%) patients, whereas 106 (76.3%) patients remained recurrence-free. 76.3% of patients had FIGO stage I or II disease and endometrioid adenocarcinoma was the predominant histological subtype, accounting for 87.1%. Lymphovascular space invasion was present in 27.3% of patients, and lymph node metastasis was identified in 7.2%. The clinicopathological characteristics of the study cohort are summarized in Table 1.

Table 1. Clinicopathological characteristics.

	n (%) or median (range)
Age (years)	62 (37–91)
Body mass index (kg/m^2)	33 (25–45)
Tumor size (cm)	4 (1–13)
Surgical stage	
I–II	106 (76.3%)
III–IV	33 (23.7%)
Histopathology	
Endometrioid adenocarcinoma	121 (87.1%)
Malignant mixed Müllerian tumor	7 (5.0%)
Serous carcinoma	11 (7.9%)
Grade	
I–II	103 (74.1%)
III	36 (25.9%)
Myometrial invasion	
<1/2	63 (45.3%)
≥1/2	76 (54.7%)
Positive peritoneal cytology	10 (7.2%)
Lymphovascular space invasion	38 (27.3%)
Cervical involvement	23 (16.5%)
Lymph node metastasis	10 (7.2%)

Continuous variables are presented as median and range. Categorical variables are presented as number and percentage. FIGO, International Federation of Gynecology and Obstetrics.

Comparison of Clinicopathological Characteristics by Recurrence Status

Patients who developed recurrence had significantly larger tumors than those who remained recurrence-free, with median tumor sizes of 5 cm and 3 cm, respectively ($p < 0.001$). FIGO stage III or IV disease was more frequent among patients with recurrence than among those

Table 2. Comparison of clinicopathological characteristics by recurrence status.

Variable	No recurrence (n = 106)	Recurrence (n = 33)	Test statistic	*p* value
Age, years, median (range)	62 (37–91)	64 (49–88)	z = −1.481	0.139
Body mass index, kg/m^2, median (range)	33 (25–45)	34 (27–45)	z = −1.319	0.187
Tumor size, cm, median (range)	3 (1–11)	5 (3–13)	z = −4.127	<0.001*
FIGO stage			χ^2 = 11.269	0.001*
Stage I or II, n	88 (83.0%)	18 (54.5%)		
Stage III or IV, n	18 (17.0%)	15 (45.5%)		
Tumor grade			χ^2 = 1.246	0.264
Grade I or II, n	81 (76.4%)	22 (66.7%)		
Grade III, n	25 (23.6%)	11 (33.3%)		
Histopathology			Fisher's exact test	0.038*
Endometrioid adenocarcinoma, n	96 (90.6%)	25 (75.8%)		
Non-endometrioid histology, n	10 (9.4%)	8 (24.2%)		
Myometrial invasion			χ^2 = 5.690	0.017*
<1/2, n	54 (50.9%)	9 (27.3%)		
≥1/2, n	52 (49.1%)	24 (72.7%)		
Lymphovascular space invasion			χ^2 = 0.783	0.376
Negative, n	79 (74.5%)	22 (66.7%)		
Positive, n	27 (25.5%)	11 (33.3%)		
Cervical stromal involvement			Fisher's exact test	0.006*
Absent, n	94 (88.7%)	22 (66.7%)		
Present, n	12 (11.3%)	11 (33.3%)		
Peritoneal cytology			Fisher's exact test	0.012*
Negative, n	102 (96.2%)	27 (81.8%)		
Positive, n	4 (3.8%)	6 (18.2%)		
Lymph node involvement			Fisher's exact test	0.248
Absent, n	100 (94.3%)	29 (87.9%)		
Present, n	6 (5.7%)	4 (12.1%)		

Continuous variables are presented as median (range) and were compared using the Mann–Whitney U test. Categorical variables are presented as number (percentage) and were compared using Pearson's Chi-squared test or Fisher's exact test. Fisher's exact testing was used when an expected cell count was less than 5. All tests were two-sided. FIGO, International Federation of Gynecology and Obstetrics. *Statistically significant at $p < 0.05$.

without recurrence (45.5% versus 17.0%; $p = 0.001$). Non-endometrioid histology, myometrial invasion of 50% or greater, cervical stromal involvement, and positive peritoneal cytology were also significantly more frequent in the recurrence group. Tumor grade, lymphovascular space invasion, and lymph node involvement did not differ significantly according to recurrence status. Detailed comparisons are presented in Table 2.

Survival Analysis

Kaplan–Meier analysis showed numerically lower disease-free survival among patients with lymphovascular space invasion than among those without lymphovascular space invasion. However, the difference was not significant (log-rank $\chi^2 = 2.154$, $p = 0.142$; Fig. 2).

In a separate Kaplan–Meier analysis, patients with lymph node involvement also showed numerically lower disease-free survival than patients without lymph node involvement. This difference did not reach significance (log-rank $\chi^2 = 3.389$; $p = 0.066$).

Cox Regression Analysis

According to univariable Cox regression analysis, larger tumor size, FIGO stage III or IV disease, non-endometrioid histology, myometrial invasion of 50% or greater, cervical stromal involvement, and positive peritoneal cytology were associated with worse disease-free survival.

In the primary multivariable Cox model, tumor size remained independently associated with recurrence, with an adjusted hazard ratio (aHR) of 1.208 per 1 cm increase (95% confidence interval [CI] 1.047–1.395, $p = 0.010$). FIGO stage III or IV disease was also independently associated with recurrence (aHR 2.454 95% CI 1.080–5.578, $p = 0.032$). Lymphovascular space invasion did not reach significance after adjustment (aHR 2.007, 95% CI 0.923–

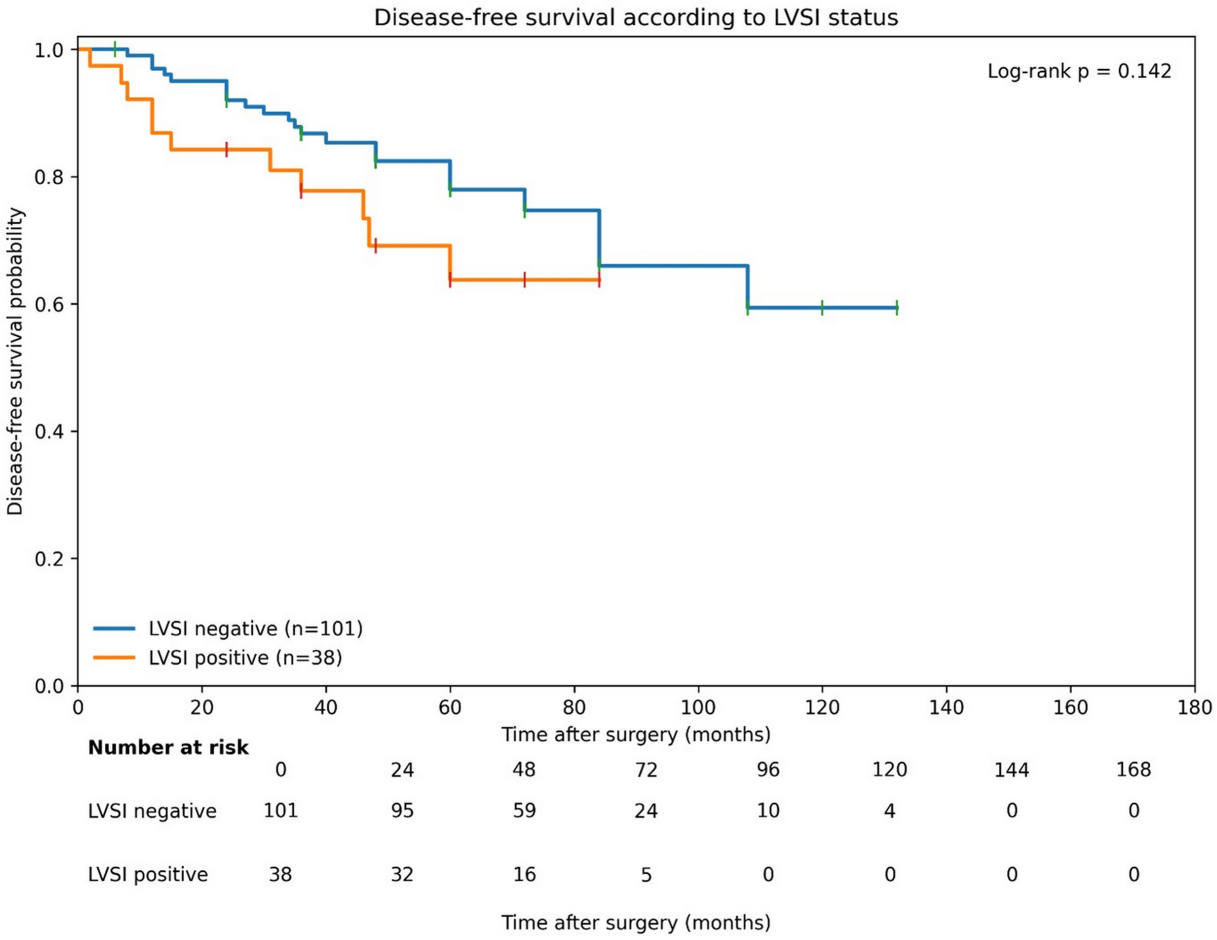

Fig. 2. Kaplan–Meier curves for disease-free survival according to lymphovascular space invasion status in patients with ER-positive endometrial cancer. Numbers at risk are presented below the curves. Disease-free survival was numerically lower in the LVSI-positive group, but the difference was not significant (log-rank $\chi^2 = 2.154$, $p = 0.142$). Vertical marks indicate censored observations. ER, estrogen receptor; LVSI, lymphovascular space invasion.

4.363, $p = 0.079$). Also, non-endometrioid histology was not independently associated with recurrence in the adjusted model (aHR 1.169, 95% CI 0.457–2.994, $p = 0.744$). The complete results of the univariable and multivariable Cox regression analyses are presented in Table 3.

No significant violation of the proportional hazards assumption was identified for tumor size ($p = 0.072$), FIGO stage ($p = 0.151$), lymphovascular space invasion ($p = 0.572$), or histological subtype ($p = 0.082$). Comparison of the linear tumor size model with a three-degree-of-freedom natural cubic spline model showed no evidence of a nonlinear association between tumor size and recurrence (likelihood ratio $p = 0.359$).

Ridge-penalized Cox regression yielded attenuated but directionally consistent estimates for tumor size (HR 1.062), FIGO stage III or IV disease (HR 1.297), lymphovascular space invasion (HR 1.104), and non-endometrioid histology (HR 1.231). Although these penalized estimates did not reach statistical significance, their directions were consistent with those of the primary multivariable model.

In an additional sensitivity analysis, BMI was not independently associated with recurrence (aHR 1.045 per 1 kg/m^2 increase, 95% CI 0.975–1.119, $p = 0.214$). The inclusion of BMI did not materially alter the primary findings. Tumor size remained independently associated with recurrence (aHR 1.186, 95% CI 1.023–1.375, $p = 0.024$), as did FIGO stage III or IV disease (aHR 2.417, 95% CI 1.038–5.629, $p = 0.041$).

Time-dependent ROC Analysis

Time-dependent ROC analysis showed that tumor size had an area under the curve of 0.673 for 3-year disease-free survival (95% CI 0.540–0.798) and 0.696 for 5-year disease-free survival (95% CI 0.559–0.824). These findings indicated modest discriminatory ability of tumor size for recurrence at both timepoints. The corresponding time-dependent ROC curves are presented in Fig. 3.

Table 3. Univariable and multivariable Cox proportional hazards regression analyses for disease-free survival.

Variable	Univariable HR (95% CI)	*p* value	Multivariable HR (95% CI)	*p* value
Age, per year	1.024 (0.988–1.061)	0.189	Not included	
Body mass index, per kg/m^2	1.060 (0.994–1.129)	0.075	Not included	
Tumor size, per 1-cm increase	1.301 (1.164–1.453)	<0.001*	1.208 (1.047–1.395)	0.010*
FIGO stage III or IV versus I or II	3.828 (1.916–7.645)	<0.001*	2.454 (1.080–5.578)	0.032*
Grade III versus I or II	1.522 (0.738–3.143)	0.256	Not included	
Non-endometrioid versus endometrioid histology	3.081 (1.379–6.883)	0.006*	1.169 (0.457–2.994)	0.744
Myometrial invasion of ≥50%	2.404 (1.115–5.182)	0.025*	Not included	
Lymphovascular space invasion	1.717 (0.824–3.576)	0.149	2.007 (0.923–4.363)	0.079
Cervical stromal involvement	3.221 (1.557–6.666)	0.002*	Not included	
Lymph node involvement	2.594 (0.909–7.401)	0.075	Not included	
Positive peritoneal cytology	3.040 (1.242–7.440)	0.015*	Not included	

Variables included in the primary multivariable model were tumor size, FIGO stage, lymphovascular space invasion, and histological subtype. Variables closely related to or incorporated within FIGO stage were not simultaneously included to reduce collinearity and model overfitting. HR, hazard ratio; CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics. *Statistically significant ($p < 0.05$).

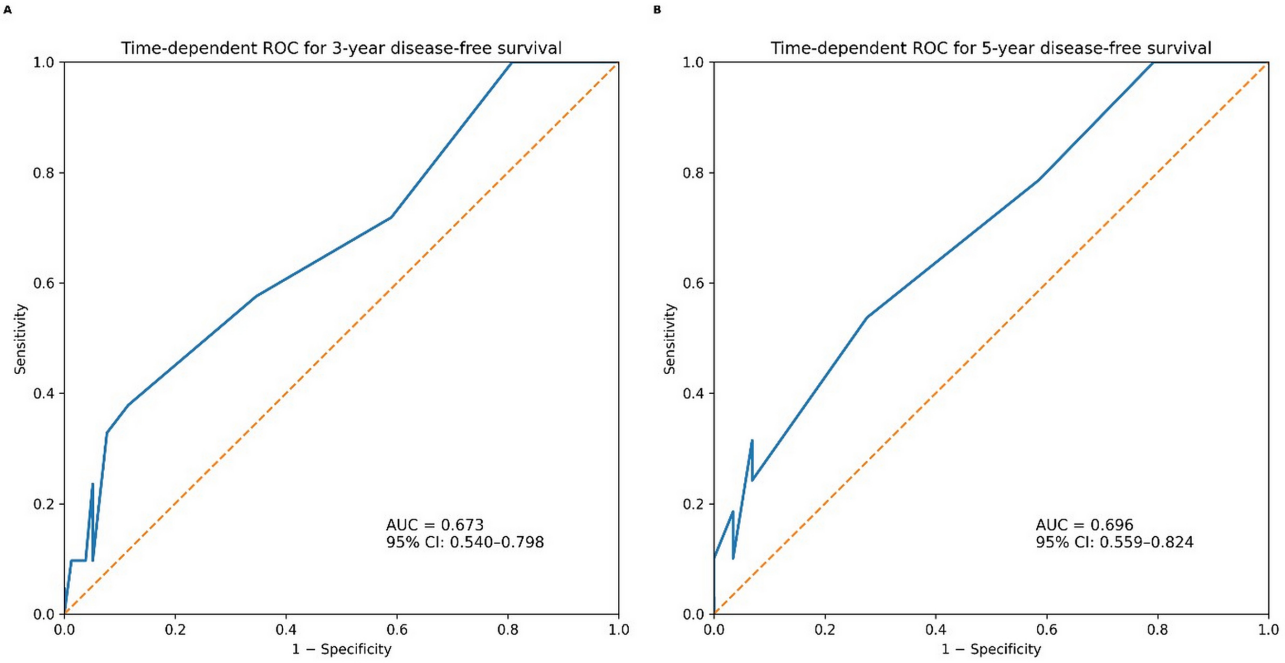

Fig. 3. Time-dependent ROC curves evaluating the discriminatory ability of tumor size for recurrence in patients with ER-positive endometrial cancer. (A) 3-year disease-free survival: AUC 0.673, 95% CI 0.540–0.798. (B) 5-year disease-free survival: AUC 0.696, 95% CI 0.559–0.824. AUC, area under the curve; CI, confidence interval; ER, estrogen receptor; ROC, receiver operating characteristic.

Discussion

In this retrospective cohort of patients with ER-positive endometrial cancer, tumor size and advanced FIGO stage were independently associated with recurrence. Although lymphovascular space invasion was associated with an approximately twofold increase in the adjusted hazard of recurrence, this association did not reach statistical significance. Tumor size also showed modest discriminatory ability for recurrence at 3 and 5 years in time-dependent ROC analyses. These findings highlight the prognostic heterogeneity that persists within ER-positive endometrial cancer and suggest that conventional clinicopathological characteristics remain clinically relevant in this apparently favorable subgroup.

ER positivity is generally associated with endometrioid histology, lower tumor grade, and more favorable oncological outcomes in endometrial cancer [4,5,6,7,8]. In recent years, the clinical relevance of hormonal biomarkers has further increased, and current National Comprehensive Cancer Network guidelines recommend routine assessment

of ER and progesterone receptor status in endometrial carcinoma as part of pathological evaluation and therapeutic decision making [15]. Nevertheless, increasing evidence indicates that ER-positive tumors are not biologically or prognostically uniform, and that bclinically relevant differences in recurrence risk can persist within this subgroup [6,7,8]. The recurrence rate observed in our cohort further supports this heterogeneity. Tumor size remained independently associated with recurrence after adjustment for FIGO stage, lymphovascular space invasion, and histological subtype. The adjusted hazard of recurrence increased by approximately 21% for each 1-cm increase in tumor size. Furthermore, the absence of evidence of nonlinearity supported the evaluation of tumor size as a continuous variable rather than the use of an arbitrary threshold. Tumor size might reflect overall tumor burden, duration of obscure tumor growth, and biological aggressiveness that are not completely captured by other conventional pathological variables [16]. However, the modest time-dependent areas under the curve indicate that tumor size should not be considered a stand-alone prognostic marker. Instead, tumor size could provide complementary information when interpreted together with established clinicopathological and molecular characteristics.

Lymphovascular space invasion is a well-established adverse pathological feature in endometrial cancer and is associated with lymphatic dissemination, recurrence, and unfavorable survival outcomes [17,18,19]. In this study, lymphovascular space invasion was associated with an approximately twofold increase in the adjusted hazard of recurrence; however, the association did not reach statistical significance. The wide CI surrounding this estimate indicates limited precision, and the absence of statistical significance should not be interpreted as evidence of no prognostic association. The relatively small number of recurrence events might have limited the statistical power to detect an independent effect of lymphovascular space invasion after adjustment for FIGO stage, tumor size, and histological subtype.

Advanced FIGO stage remained independently associated with recurrence, confirming that the extent of disease continues to be a major prognostic determinant even within ER-positive endometrial cancer [12,19]. Lymph node involvement was also associated with an unfavorable direction of effect, although the difference in disease-free survival did not reach statistical significance. This finding should be interpreted cautiously because lymph node metastasis was present in only ten patients, resulting in limited statistical power and imprecise risk estimation. Therefore, the absence of statistical significance should not be interpreted as evidence that lymph node involvement lacks prognostic relevance in this population.

As endocrine-based systemic treatment strategies continue to evolve in recurrent or advanced ER-positive endometrial cancer, accurate risk stratification within this subgroup could become increasingly important. ER positivity alone does not identify a prognostically uniform population, and conventional clinicopathological factors, such as tumor size, FIGO stage, lymphovascular space invasion, and lymph node status could provide complementary information regarding recurrence risk. Integration of these factors with molecular classification and other validated biomarkers could ultimately support more individualized surveillance and treatment strategies [20].

The strengths of this study include its focused evaluation of ER-positive endometrial cancer, the use of time-to-event analyses accounting for censoring, and the assessment of tumor size as a continuous variable. Proportional hazards diagnostics and sensitivity analyses were also performed to evaluate the robustness of the findings.

Several limitations should be acknowledged. The retrospective, single-center design and the lack of routine ER testing throughout the study period might have introduced selection bias and limited the generalizability of the findings. Detailed information regarding adjuvant treatment was not consistently available and could not be incorporated into the survival analyses, resulting in potential residual confounding. Comprehensive molecular classification and data on the extent of lymphovascular space invasion were also unavailable. Lastly, the limited number of recurrence events restricted the complexity of the multivariable model, and the findings have not been externally validated.

Conclusion

In ER-positive endometrial cancer, larger tumor size and advanced FIGO stage were independently associated with recurrence. Lymphovascular space invasion showed an unfavorable direction of association but did not reach statistical significance after adjustment. Tumor size showed modest discriminatory ability for recurrence at 3 and 5 years and could provide complementary prognostic information when interpreted together with established clinicopathological and molecular factors. These findings require validation in larger, multicenter cohorts.

Availability of Data and Materials

The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request and subject to institutional approval.

Author Contributions

CYO: Conceptualization, methodology, formal analysis, writing original draft. DCO: Data curation, investigation, resources. NC: Methodology, supervision, data acquisition. DA: Pathological evaluation, data acquisition. CK: Analysis and interpretation of data, writing original draft. SG: Data acquisition. DTA: Conception and design of the study and supervision. All authors have been involved in

revising it critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study protocol was approved by the Afyonkarahisar Health Sciences University Non-Interventional Scientific Research Ethics Committee (meeting no. 2025/15; decision no. 789). Owing to the retrospective and non-interventional nature of the study, the Ethics Committee granted a waiver of individual informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki, and patient data were analyzed anonymously.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

Declaration of Generative AI and AI-Assisted Technologies in Manuscript Preparation

This manuscript was prepared with the assistance of ChatGPT (OpenAI) for language refinement and structural editing. After its use, the authors thoroughly reviewed, verified, and revised all content to ensure accuracy and originality.

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