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Nomogram Based on Immune-Inflammatory Score and Classical Clinicopathological Parameters for Predicting the Recurrence of Endometrial Carcinoma: A Large, Multi-Center Retrospective Study

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Background: Surgery is the best approach to treat endometrial cancer (EC); however, there is currently a deficiency in effective scoring systems for predicting EC recurrence post-surgical resection. This study aims to develop a clinicopathological-inflammatory parameters-based nomogram to accurately predict the postoperative recurrence-free survival (RFS) rate of EC patients.

Methods: A training set containing 1068 patients and an independent validation set consisting of 537 patients were employed in this retrospective study. The prognostic factors for RFS were identified by univariable and multivariable Cox proportional hazards regression analyses, and integrated into nomogram. The C-index, area under the curves (AUC), and calibration curves were employed to determine the predictive discriminability and accuracy of nomogram. Utilizing the nomogram, patients were stratified into low- and high-risk groups, and the Kaplan-Meier survival curve was further employed to assess the clinical efficacy of the model.

Results: Cox regression analyses revealed that age (HR = 1.769, $P = 0.002$), FIGO staging (HR = 1.790, $P = 0.018$), LVSI (HR = 1.654, $P = 0.017$), Ca125 (HR = 1.532, $P = 0.023$), myometrial invasion (HR = 1.865, $P = 0.001$), cervical stromal invasion (HR = 1.655, $P = 0.033$), histology (HR = 2.637, $P < 0.001$), p53 expression (HR = 1.706, $P = 0.002$), PLR (HR = 1.971, $P = 0.003$), SIRI (HR = 2.187, P = 0.003), and adjuvant treatment (HR = 0.521, $P = 0.003$) were independent prognostic factors for RFS in patients with EC. A combined clinicopathologic-inflammatory parameters model was constructed, which outperformed the single-indicator model and other established models in predicting the 1-, 3-, and 5-year RFS rates in patients with EC.

Conclusion: The nomogram demonstrated sufficient accuracy in predicting the RFS probabilities of EC, enabling personalized clinical decision-making for future clinical endeavors.

Keywords: endometrial cancer, recurrence-free survival, nomogram, inflammatory index, risk stratification

Introduction

Endometrial cancer (EC) is one of the most common gynecological malignancies. According to global cancer statistics, there were 417,367 new cases and 97,370 deaths globally in 2021.[1] In China, EC ranks fourth among female neoplasms, with an incidence rate of 12.9–20.1 per 100,000 and a mortality rate of 2.0–2.7 per 100,000, respectively. The mainstay of treatment for EC is total hysterectomy with or without bilateral salpingo-oophorectomy under minimally invasive hysterectomy or open surgery.[2–4] The effective prediction of prognosis in EC patients using postoperative pathological staging has been widely recognized. However, due to the heterogeneous nature of EC, patients at similar stages may still experience

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recurrence, with an overall recurrence rate of 13%.[5] Therefore, there is an urgent need for effective biomarkers to develop an individualized prediction model for treatment outcomes and prognosis in EC.

Numerous studies have demonstrated that cancer is a systemic disease with local manifestations.[6,7] Understanding the complex relationship between the tumor itself and the systemic immune-inflammatory status is crucial for a comprehensive evaluation of tumor recurrence and prognosis. Inflammation-related scoring systems, such as platelet-to-lymphocyte (PLR), neutrophil to lymphocyte ratio (NLR) and systemic inflammation response index (SIRI) have been shown to correlate with prognosis of EC.[8] A meta-analysis involving 5274 patients with EC revealed that pretreatment PLR and NLR are important prognostic markers for adverse outcomes in EC patients. Furthermore, this conclusion remains consistent in subgroup analyses based on different cut-off values, sample sizes, treatment strategies, and ethnics.[9] However, depending solely on individual serum inflammatory indexes is inadequate for accurately predicting the prognosis of EC patients. With the introduction of TCGA molecular classification, molecular markers like P53, known to be unfavorable for prognosis, should also be taken into fully consideration. Therefore, the objective of this study is to investigate the influence of preoperative inflammatory indexes on the prognosis of EC patients and to develop a predictive model by integrating these inflammatory indexes and clinical pathological parameters to effectively predict the recurrence-free survival (RFS) of EC patients.

Materials and Methods

Study Population

This study involved 1605 patients who underwent surgical resection at multiple medical centers in China from September 2014 to December 2021. The study included a training cohort (The First Affiliated Hospital of Chongqing Medical University, FAHCQMU cohort: n = 1068 cases) and an external validation cohort (Women and Children's Hospital of Chongqing Medical University, WCHCQMU cohort: n = 407 cases; Yubei District People's Hospital, YDPH cohort: n = 130 cases).

The exclusion criteria were: (1) without standard surgery; (2) without standard lymph node evaluation; (3) receiving adjuvant therapy prior to surgery; (4) presence of preexisting inflammatory diseases or immune system disorders; (5) with incomplete medical records; (6) presence of other malignancies; (7) lost to follow-up. The flowchart of this study was shown in Figure 1. The study received approved from the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University (Institutional Review Board number, IRB No. 2021-676), Chongqing Maternal and Child Health Hospital (IRB No. 2023-02), Yubei District People's Hospital (IRB No. K2024-03-264). All enrolled patients signed informed consent for data collection during hospitalization.

Treatment

All patients underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, and lymph node staging surgery (sentinel lymph node ± pelvic ± para-aortic lymph node dissection). Based on international guidelines, multidisciplinary discussions, and individual patient preferences, appropriate adjuvant treatment options were selected. Radiotherapy primarily consisted of either vaginal brachytherapy (administered in 5.5–6Gy x 4 fractions, with 2 fractions/week) or pelvic external beam radiotherapy (delivered in 1.8–2Gy x 25 fractions, with 5 fractions/week).[10] The main chemotherapy protocol involved the TP regimen (carboplatin + paclitaxel) administered every three weeks for a total of 6–8 cycles.[11,12]

Variable and Outcomes

In the current study, the endpoint of interest was RFS, defined as the duration from the date of diagnosis to recurrence or to the date of the last follow-up. OS was defined as the duration from diagnosis to death or to the last follow-up.[10] The last follow-up was on April 10, 2024.

Statistical Analysis

Patients enrolled from 2014 to 2021 were randomly assigned into two cohorts, the training and the external validation sets. Univariate and multivariate Cox regression analyses were conducted on all thirteen variables, and variables with $P < 0.05$ were deemed independent risk factors. These selected variables were then incorporated into the nomogram, which

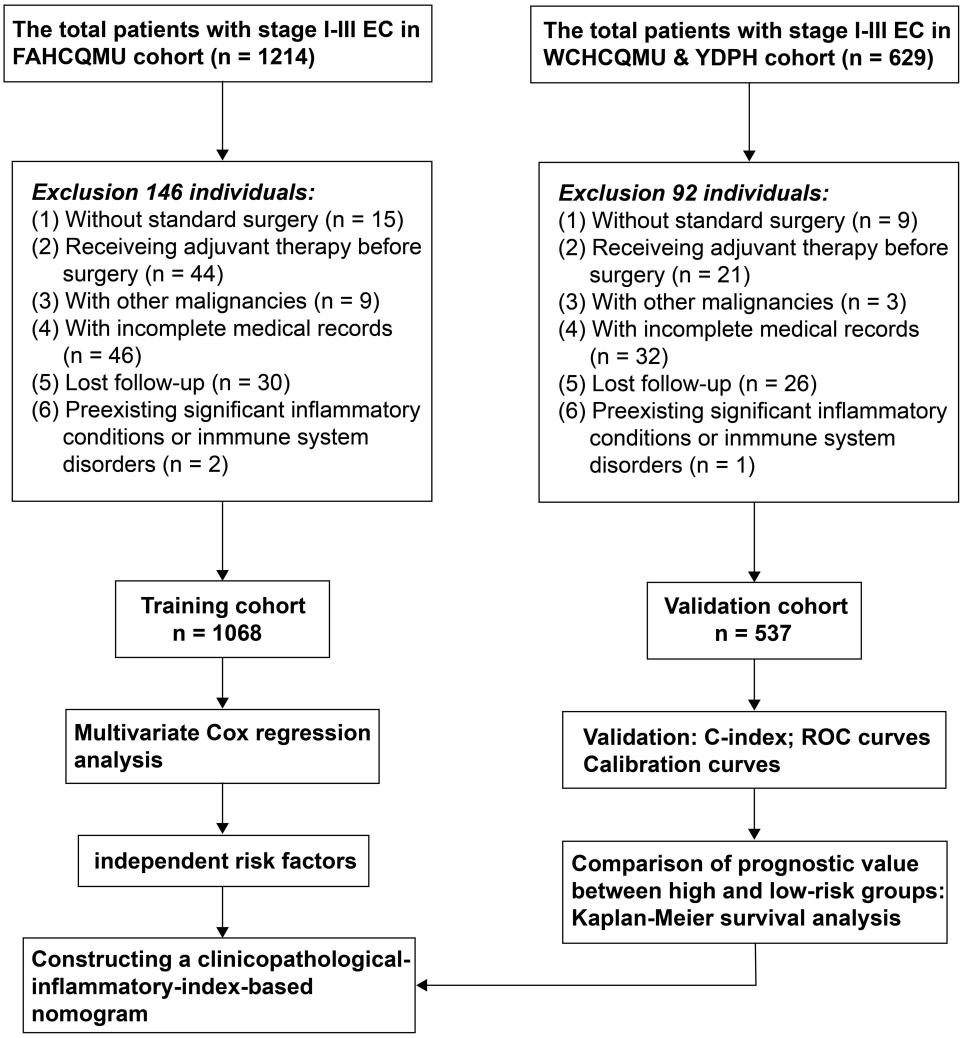

Figure 1 Flow chart of eligible EC patients.

was used to estimate the probabilities of 1-, 3-, and 5-year RFS. All $P < 0.05$ were considered statistically significant using a two-tailed test. All statistical analyses were performed using SPSS (version 24.0) and R software (version 3.6.1; http://www.r-project.org/).[13]

Results

Patient Characteristics

In this study, we analyzed the clinicopathological characteristics and inflammatory parameters of 1605 EC patients: 1068 cases in the training cohort, and 537 cases in the validation cohort (Table 1). Among them, the average age of patients was 53.59 years. The majority of patients had FIGO staging I (69.7%, 1118/1605 cases), superficial myometrial invasion (70.2%, 1126/1605 cases), and serum Ca125 below 35 U/mL (76.1%, 1221/1605 cases). It was found that patients with positive LVSI, histological type II, and p53 abnormal expression accounted for 25.7%, 27.7%, and 37.1%, respectively. In the entire cohort, a total of 992 (61.8%) patients received postoperative adjuvant treatment. Except for a few patients who chose to receive chemotherapy only due to personal preference (2.9%, 47/1605 cases), the majority of patients opted for radiotherapy (32.0%, 514/1605 cases) or chemoradiotherapy (26.9%, 431/1605 cases).

In terms of inflammatory index, the ROC curves and the maximum of Youden index (Youden index = sensitivity + specificity – 1)[14,15] indicated that the optimal thresholds for MLR, NLR, PLR and SIRI in predicting the recurrence of EC were 0.315, 3.135, 148.23, and 1.24, respectively (Figure 2). The demographic and clinicopathological characteristics

Table 1 Demographic and Clinical Characteristics of Patients with EC

Characteristic	Whole Population [Cases (%)]	Training Cohort [Cases (%)]	Validation Cohort [Cases (%)]	*P* value
Total	1605	1068	537	
Age (years)	53.59 ± 9.28	53.77 ± 9.48	53.40 ± 9.07	0.359
BMI (kg/m^2)	24.55 ± 3.71	24.56 ± 3.71	24.55 ± 3.72	0.972
FIGO staging				0.513
I	1118 (69.7)	750 (70.2)	368 (68.5)	
II	157 (9.8)	107 (10.0)	50 (9.3)	
III	330 (20.5)	211 (19.8)	119 (22.2)	
LVSI				0.644
Negative	1192 (74.3)	797 (74.6)	395 (73.6)	
Positive	413 (25.7)	271 (25.4)	142 (26.4)	
Serum CA125				0.194
≤ 35U/mL	1221 (76.1)	802 (75.1)	419 (78.0)	
> 35U/mL	384 (23.9)	266 (24.9)	118 (22.0)	
Myometrial invasion				0.752
< 1/2	1126 (70.2)	752 (70.4)	374 (69.6)	
≥ 1/2	479 (29.8)	316 (29.6)	163 (30.4)	
Cervical stromal invasion				0.857
No	1316 (82.0)	877 (82.1)	439 (81.8)	
Yes	289 (18.0)	191 (17.9)	98 (18.2)	
Histological type				0.864
Type I	1161 (72.3)	774 (72.5)	387 (72.1)	
Type II	444 (27.7)	294 (27.5)	150 (27.9)	
P53 expression				0.948
Normal	1009 (62.9)	672 (62.9)	337 (62.8)	
Abnormal	596 (37.1)	396 (37.1)	200 (37.2)	
MLR				0.499
< 0.315	1209 (75.3)	810 (75.8)	399 (74.3)	
≥ 0.315	396 (24.7)	258 (24.2)	138 (25.7)	
NLR				0.185
< 3.135	1040 (64.8)	704 (65.9)	336 (62.6)	
≥ 3.135	565 (35.2)	364 (34.1)	201 (37.4)	
PLR				0.724
< 148.23	996 (62.1)	666 (62.4)	330 (61.5)	
≥ 148.23	609 (37.9)	402 (37.6)	207 (38.5)	
SIRI				0.411
< 1.24	985 (61.4)	663 (62.1)	322 (60.0)	
≥ 1.24	620 (38.6)	405 (37.9)	215 (40.0)	
Adjuvant treatment				0.953
Follow-up	613 (38.2)	406 (38.0)	207 (38.5)	
Radiotherapy only	514 (32.0)	341 (31.9)	173 (32.2)	
Chemotherapy only	47 (2.9)	33 (3.1)	14 (2.7)	
Chemoradiotherapy	431 (26.9)	288 (27.0)	143 (26.6)	
Recurrence				0.788
No	1389 (86.5)	926 (86.7)	463 (86.2)	
Yes	216 (13.5)	142 (13.3)	74 (13.8)	
RFS time (months)				0.883
Mean (±SD)	49.76 ± 19.24	49.82 ± 18.98	49.70 ± 19.50	
Median (range)	47.0 (6–91)	47.0 (6–91)	46.0 (6–91)	

Abbreviations: BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; LVSI, lymphatic vessel space invasion; MLR, monocyte/lymphocyte ratio; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; SIRI, systemic inflammation response index; RFS, recurrence-free survival.

of EC patients in both cohorts exhibited a high degree of consistency, as all parameters had *P* values greater than 0.05 in the comparison.

Independent Risk Factors for RFS in EC Patients

As shown in Table 2, univariate and multivariate Cox regression analysis indicated that age (Hazard ratio [HR] = 1.769, $P = 0.002$), FIGO stage (HR = 1.790, $P = 0.018$), LVSI (HR = 1.654, $P = 0.017$), Ca125 (HR = 1.532, $P = 0.023$), myometrial invasion (HR = 1.865, $P = 0.001$), cervical stromal invasion (HR = 1.655, $P = 0.033$), histology (HR = 2.637, $P < 0.001$), p53 expression (HR = 1.706, $P = 0.002$), PLR (HR = 1.971, $P = 0.003$), SIRI (HR = 2.187, $P = 0.003$), and adjuvant treatment (HR = 0.521, $P = 0.003$) were the independence factors for RFS in EC patients.

Nomogram Construction and Validation

Based on the multivariate Cox regression analysis, a risk predictive nomogram for predicting RFS integrating eleven independent predictors was constructed (Figure 3). In the nomogram, the length of each line segment corresponding to a predictor indicates the predictor's contribution to EC recurrence.

In both the training and external validation sets, the AUC values of the established model for predicting 1-, 3-, and 5-year RFS were above 0.83, demonstrating a satisfactory level of predictive accuracy (Figure 4). In addition, the calibration curves in both the training and validation sets indicated that the nomogram-based predictions were consistent with the actual prognosis results (Figure 5).

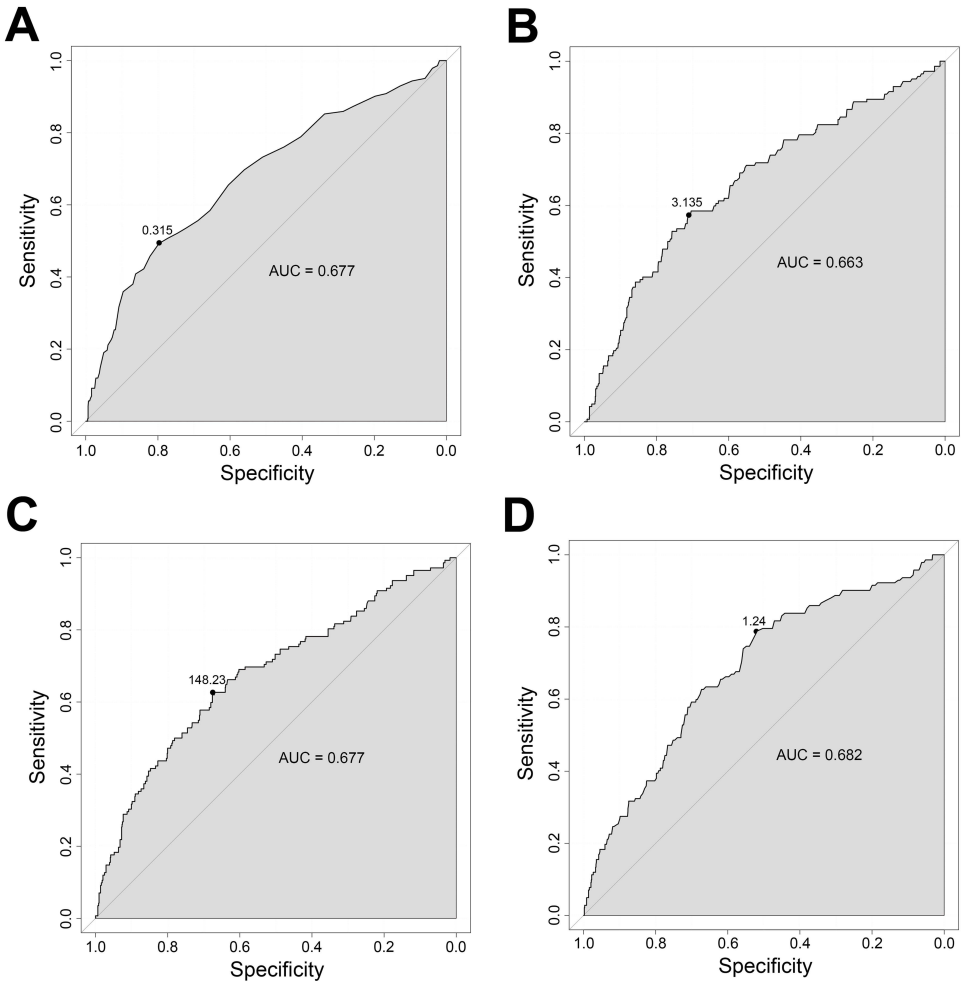

Figure 2 The ROC curves of (**A**) MLR; (**B**) NLR; (**C**) PLR; and (**D**) SIRI for predicting the recurrence of EC. The black dot represents the optimal cutoff value of the corresponding inflammation index for predicting EC recurrence (MLR: 0.315; NLR: 3.135; PLR: 148.23; SIRI: 1.24).

Table 2 Univariate and Multivariate Cox Analyses on Variables for the Prediction of RFS of Patients with EC

Variable	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	*P* value	HR	95% CI	*P* value
Age						
≥ 60 years vs < 60 years	2.017	1.439–2.827	<0.001	1.769	1.235–2.531	0.002
FIGO staging						
I	Ref		<0.001	Ref		0.005
II	2.219	1.244–3.957	0.007	0.781	0.371–1.645	0.515
III	6.950	4.859–9.940	<0.001	1.790	1.107–2.895	0.018
LVSI						
Positive vs Negative	4.655	3.335–6.497	<0.001	1.654	1.094–2.501	0.017
Serum CA125						
> 35U/mL vs ≤ 35U/mL	2.700	1.940–3.757	<0.001	1.532	1.061–2.212	0.023
Myometrial invasion						
≥1/2 vs < 1/2	3.561	2.554–4.966	<0.001	1.865	1.270–2.739	0.001
Cervical stromal invasion						
Yes vs No	2.880	2.043–4.058	<0.001	1.655	1.040–2.633	0.033
Histological type						
Type II vs Type I	6.018	4.249–8.523	<0.001	2.637	1.709–4.068	<0.001
P53 expression						
Abnormal vs Normal	1.997	1.436–2.776	<0.001	1.706	1.212–2.402	0.002
MLR						
≥ 0.315 vs < 0.315	3.444	2.478–4.787	<0.001	1.135	0.739–1.742	0.564
NLR						
≥ 3.135 vs < 3.135	2.971	2.128–4.149	<0.001	1.207	0.759–1.922	0.427
PLR						
≥ 148.23 vs < 148.23	3.761	2.646–5.345	<0.001	1.971	1.266–3.069	0.003
SIRI						
≥ 1.24 vs < 1.24	4.658	3.231–6.715	<0.001	2.187	1.305–3.664	0.003
Adjuvant treatment						
Yes vs No	1.669	1.155–2.413	0.006	0.521	0.339–0.801	0.003

Abbreviations: Ref, reference; FIGO, International Federation of Gynecology and Obstetrics; LVSI, lymphatic vessel space invasion; MLR, monocyte/lymphocyte ratio; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; SIRI, systemic inflammation response index.

The C-index was calculated to compare the predictive accuracy between the nomogram developed in this study and other risk stratification systems. These results indicated that our model can more accurately predict the RFS of EC patients (Table 3).

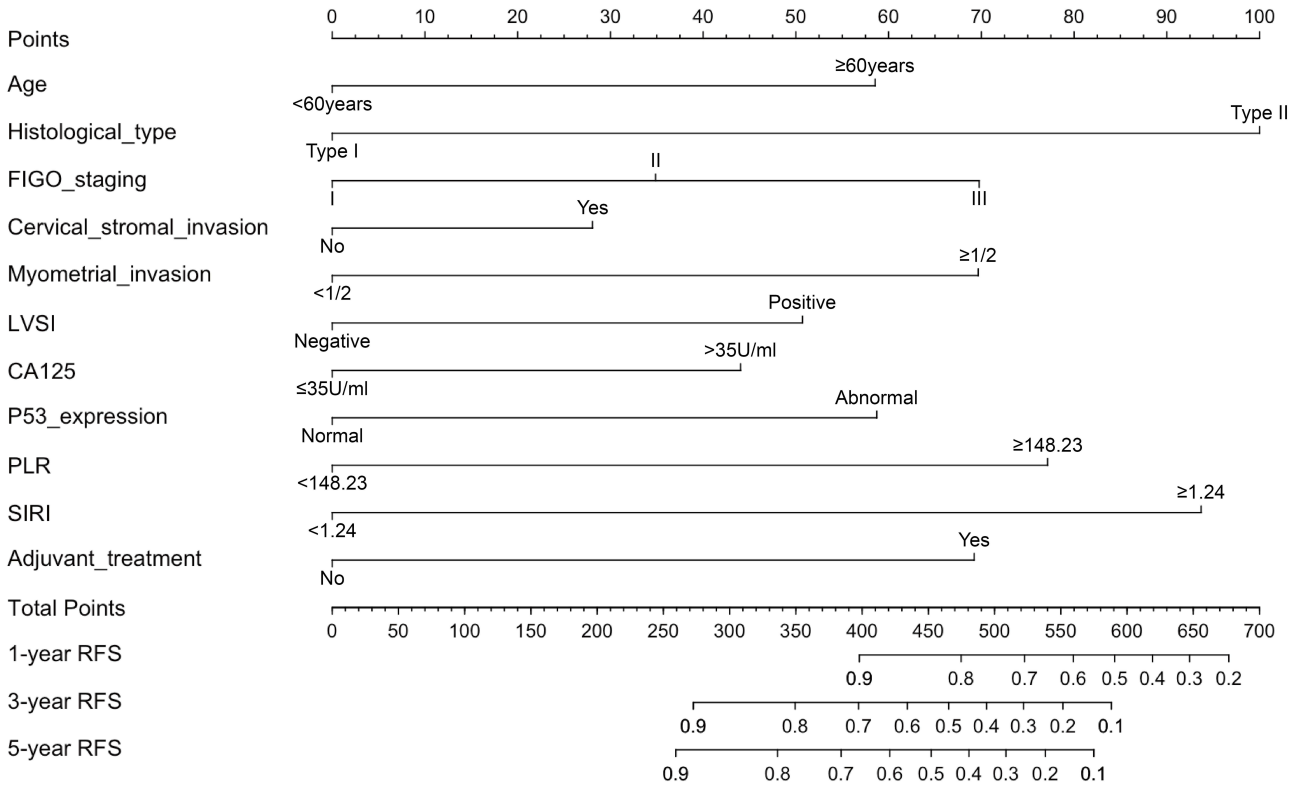

Figure 3 The nomogram for 1-, 3-, and 5-year RFS in patients with EC.

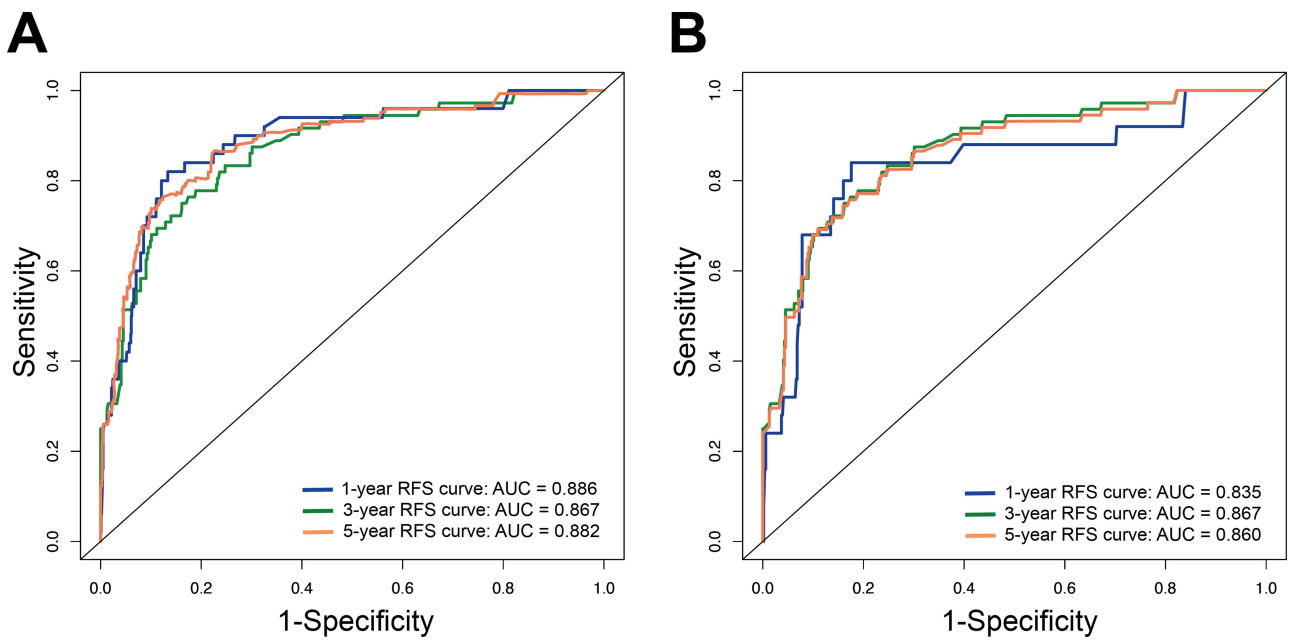

Figure 4 The ROC curves of the nomogram. The ROC curves of the model were used to predict 1-, 3-, 5-year RFS probability in the training cohort (**A**) and validation cohort (**B**).

Risk Stratification Based on the Nomogram

We determined the optimal cut-off value for risk stratification in the nomogram (cut-off value = 0.874, Supplementary Figure 1) through ROC curve analysis, which was categorized into two risk groups: high-risk group (3-year RFS rates <

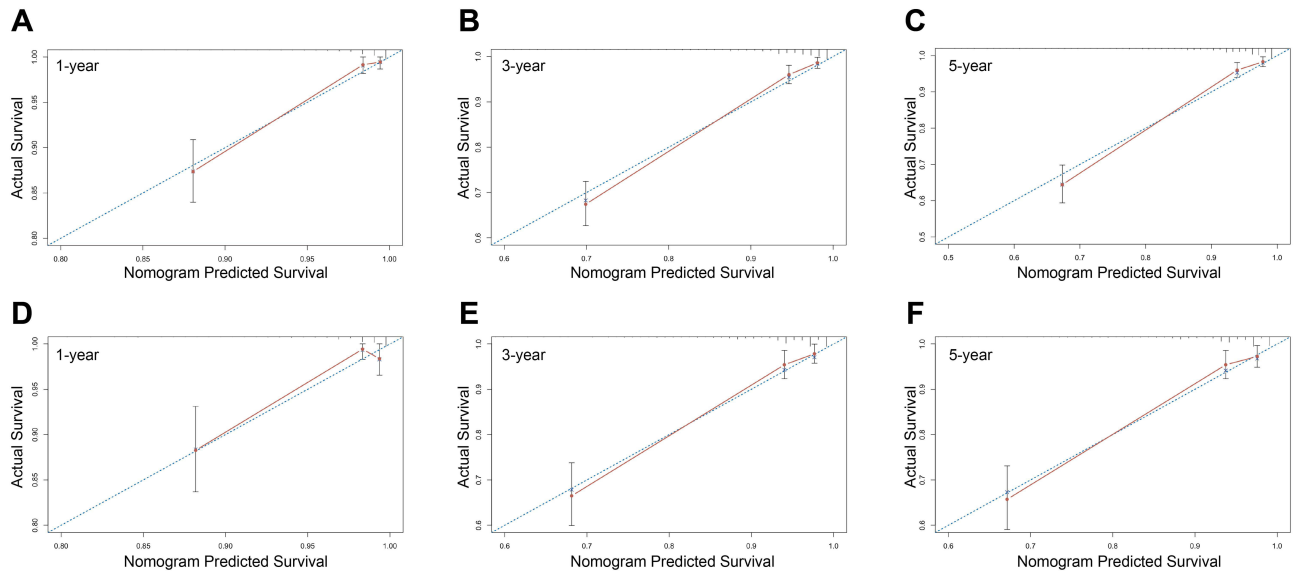

Figure 5 The calibration curves of the nomogram. Calibration curves of 1-, 3-, 5-year RFS in the training set (**A**–**C**); and the validation set (**D**–**F**).

0.874) and low-risk group (3-year RFS rates ≥ 0.874). Survival analysis indicated that patients in the high-risk group have significantly worse survival outcomes compared to those in the low-risk group (Figure 6 and Table 4).

The Kaplan-Meier curves indicated that the prediction model could effectively distinguish either RFS or OS in high-risk patients, with high-risk patients benefiting significantly from adjuvant therapy; while no significant difference in survival rates was observed among low-risk patients who received adjuvant therapy and those who did not receive adjuvant therapy (Figure 7 and Supplementary Figure 2).

Discussion

EC is the most common gynecological malignancy in developed countries. Despite the utilization of traditional prognostic factors, the risks of recurrence and mortality remain ambiguously defined. New predictive markers are needed to comprehensively assess EC prognosis and facilitate treatment choices. In recent years, there has been significant focus on the intricate interplay between the tumor immune microenvironment (TME) and tumor cells, with immune cells and inflammatory mediators playing crucial roles.[19–21] By evaluating peripheral blood neutrophils, lymphocytes, platelets,

Table 3 The Predictive Performance of Different Risk Stratification for Predicting EC Recurrence

Risk Stratification	Key Predictors of the Prediction Model	C-index (95% CI)	
		Training Set	Validation Set
Model A[16]	A nomogram including age, surgical staging, histological grade, LVSI, FIGO staging.	0.766 (0.735–0.797)	0.743 (0.700–0.786)
Model B[17]	An inflammation scoring system based on HALP scores.	0.683 (0.640–0.726)	0.674 (0.617–0.731)
Model C[18]	A nomogram model including FIGO staging, myometrial invasion, LVSI, pathological type, ER expression, Ki67 expression, P53 expression, and IINS.	0.815 (0.784–0.846)	0.803 (0.760–0.846)
Our model	A nomogram including age, histological type, FIGO, myometrial invasion, cervical stromal invasion, LVSI, serum Ca125, P53 expression, systemic inflammation score (PLR + SIRI), adjuvant treatment.	0.853 (0.822–0.884)	0.841 (0.796–0.886)

Note: Comparing predictive performance among different models using the C-index.
Abbreviations: FIGO, International Federation of Gynecology and Obstetrics; LVSI, lymphatic vessel space invasion; PLR, platelet/lymphocyte ratio; SIRI, systemic inflammation response index; HALP, hemoglobin, albumin, lymphocyte, and platelet; IINS, inflammation-immunity-nutrition score.

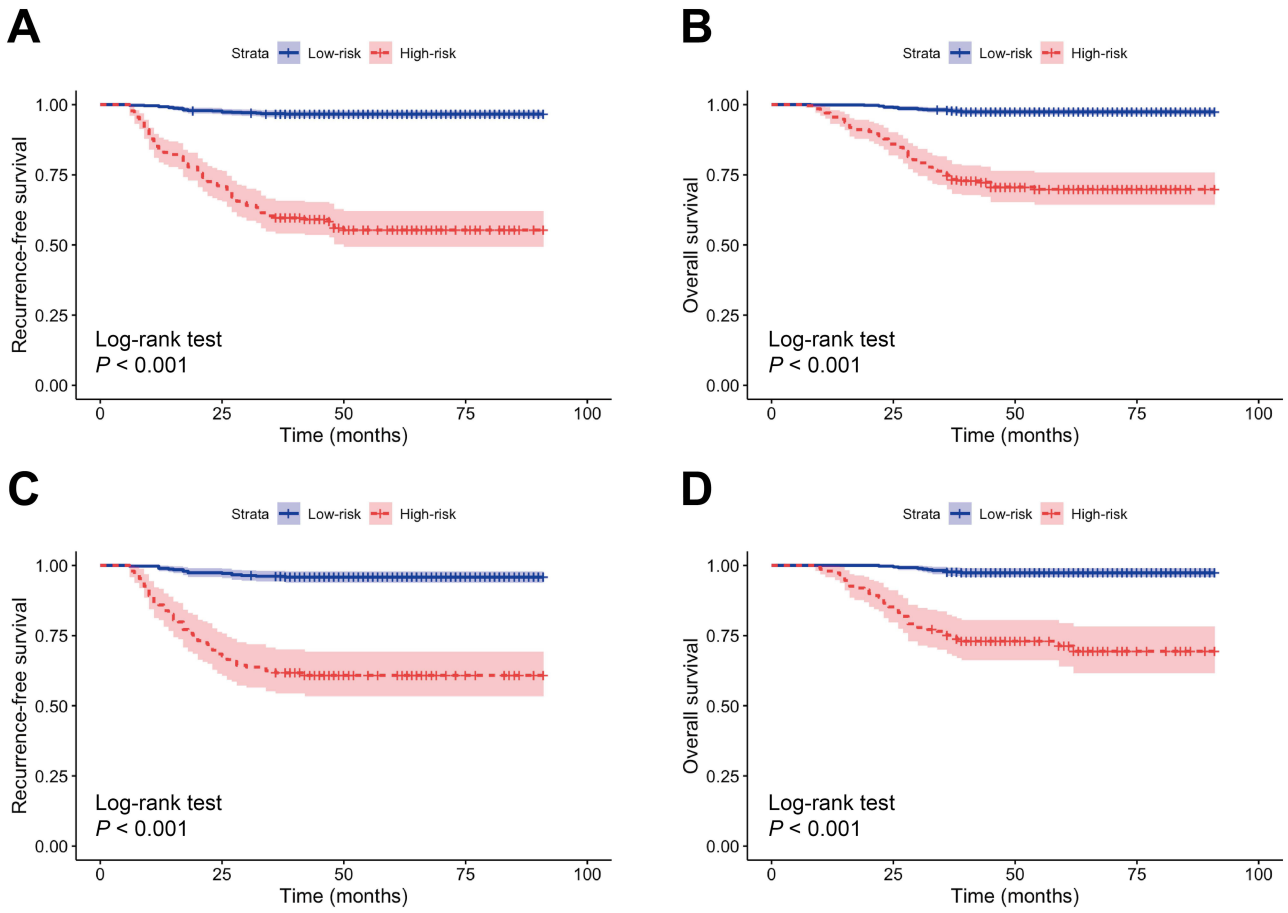

Figure 6 Kaplan-Meier survival curves of patients with EC in different risks stratified by the nomogram. (**A** and **B**) RFS of EC patients in the training and validation sets at high- and low-risk groups stratified by the established model. (**C** and **D**) OS of EC patients in the training and validation sets at high- and low-risk groups stratified by the established model.

and other factors, the systemic inflammatory response can be effectively assessed, providing valuable insights into the TME.

Multiple studies have highlighted a strong correlation between the systemic inflammatory response and the recurrence and prognosis of cancer patients.[22,23] In this study, comprehensive haematological indexes of inflammation, including PLR and SIRI, were regarded as independent prognostic factors for EC. By integrating haematological inflammatory markers and clinical pathological parameters, we have created a novel nomogram to precisely predict the 1-, 3-, and

Table 4 Analysis of Survival Differences Between High- and Low-Risk Groups in Training and External Validation Cohorts

Cohort	Group	3-Year RFS Rate (95% CI)	5-Year RFS Rate (95% CI)	P value	3-Year OS Rate (95% CI)	5-Year OS Rate (95% CI)	P value
Training cohort (n = 1068)	High-risk group (n = 270)	59.6% (53.7–65.5%)	55.3% (48.8–61.8%)	< 0.001	74.8% (69.7–79.9%)	69.8% (64.1–75.5)	< 0.001
	Low-risk group (n = 798)	96.7% (95.5–97.9%)	96.6% (95.4–97.8%)		98.0% (97.0–99.0%)	97.4% (96.2–98.6%)	
Validation cohort (n = 537)	High-risk group (n = 149)	61.7% (53.9–69.5%)	60.8% (53.0–68.6%)	< 0.001	75.2% (68.3–82.1%)	71.3% (63.7–78.9%)	< 0.001
	Low-risk group (n = 388)	96.1% (94.1–98.1%)	95.9% (93.9–97.9%)		97.7% (96.1–99.3%)	97.4% (95.8–99.0%)	

Abbreviations: RFS, recurrence-free survival; OS, overall survival; CI, confidence interval.

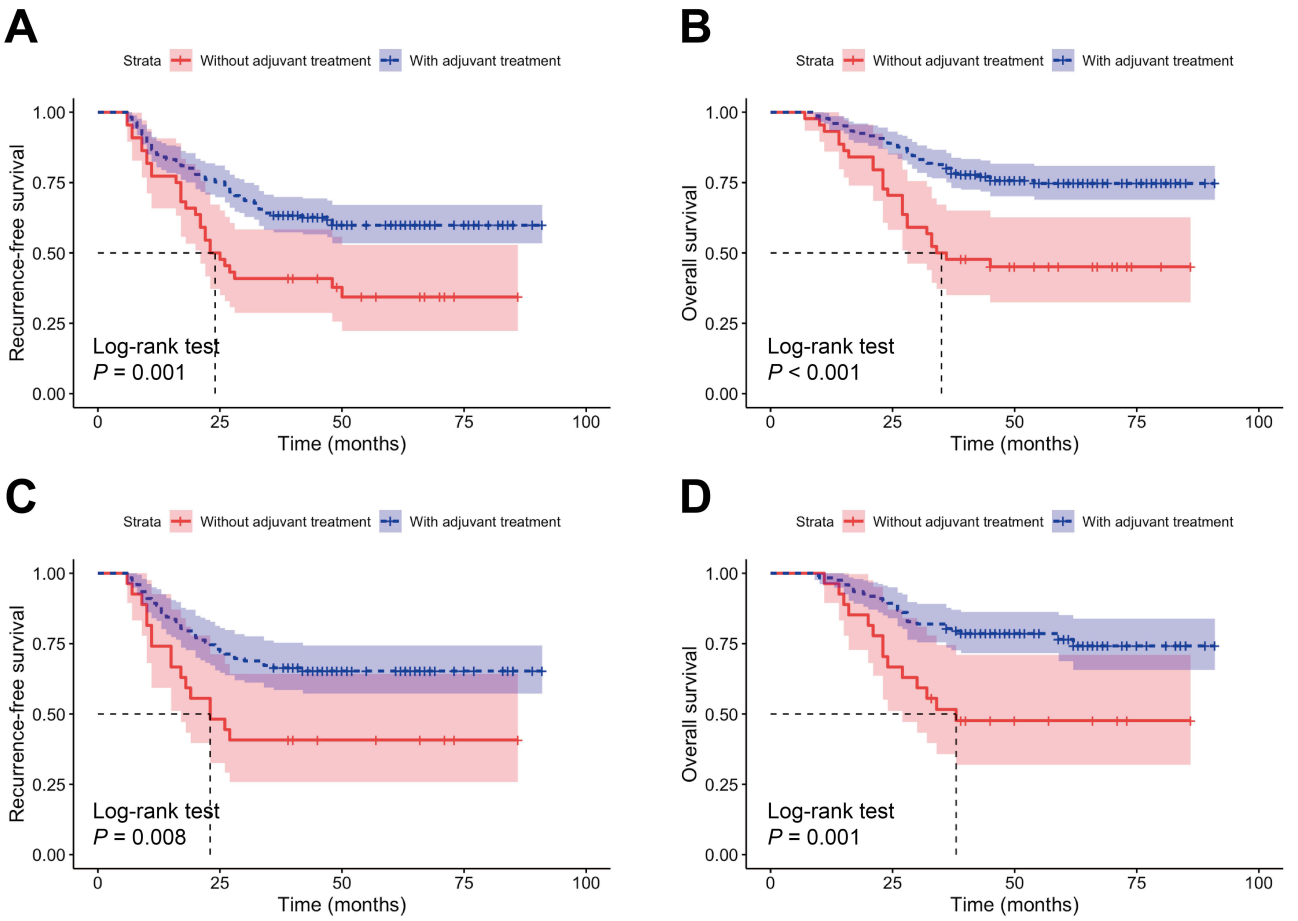

Figure 7 Survival analysis for RFS and OS of high-risk group patients with or without adjuvant treatment in training cohort (**A** and **B**); and the validation cohort (**C** and **D**).

5-year RFS rates for EC patients. Subsequently, we proceeded with internal and external validation of the model. The ROC curves and calibration curves demonstrated that the model has promising prospects in terms of prediction accuracy and prognosis assessment. Additionally, through the evaluation of the C-index for model prediction accuracy, we observed that, in comparison to other risk stratification systems, the established model exhibits superior predictive accuracy and enhanced capability in identifying high-risk patients. Furthermore, based on a large sample cohort, we identified the optimal cut-off values for the MLR, NLR, PLR, and SIRI indexes. While previous studies have reported these cut-off values, notable discrepancies exist among them. Moreover, research conducted with small sample cohorts may introduce bias, highlighting the significance of our study in providing valuable reference and guidance for further related research.[24]

It is worth noting that p53 abnormal expression was identified as an independent predictor by multivariate analysis and incorporated into our models. With the development and application of genome-wide technologies, molecular analysis is currently being used in the diagnosis, treatment, and prognosis of EC. In the latest revised FIGO staging system, the TCGA molecular classification has been integrated to redefine EC.[25,26] According to this classification, patients with P53 abnormalities have the worst prognosis, while a limited number of patients harboring *POLE* mutations showed favorable outcomes regardless of differentiation degree and histological type.[27,28] However, the high cost of testing and technical barriers impeded the widespread application of this technology, particularly in underdeveloped medical resource areas and countries. This study utilized immunohistochemistry to detect P53 expression, addressing this limitation via incorporating the variable into the nomogram. Although the molecular subtypes in our model require further expansion, our model can serve as a transitional tool for future molecular prognostic models.

Due to the high heterogeneity and elevated mortality rate among recurrent EC patients, effectively predicting recurrence and planning tailored treatment has become an urgent issue in clinical practice. Although surgical resection has been performed, some patients with EC still experience local relapse or distant metastasis within years, so post-operative adjuvant therapy is particularly important.[13] According to the NCCN guidelines, patients with specific risk factors, such as age over 60 years, non-endometrioid carcinoma, deep myometrial invasion, cervical stromal invasion, extensive LVSI, or FIGO stage III–IV, are recommended to receive postoperative adjuvant radiotherapy or concurrent chemoradiotherapy.[29–32] In the present study, EC patients were stratified into low- and high-risk groups based on the optimal threshold of the model. Despite the majority of high-risk group patients receiving standard postoperative adjuvant therapy in line with current treatment guidelines, it is apparent that a significant number of high-risk patients succumbed to the disease due to the cumulative impact of various adverse prognostic factors, highlighting the necessity of prioritizing the care of high-risk individuals identified by the model. In light of the study findings, clinicians need to closely monitor and follow up with patients in the high-risk group, while also devising personalized and proactive treatment approaches, including targeted therapy, immunotherapy, and other interventions, to improve their prognosis and overall survival outcomes.

It is worth noting that, while this study utilized inflammatory indices and clinical pathological parameters to predict the prognosis of EC patients, it did not specifically focus on the status of lymph node metastasis. Accumulating evidence highlights nodal status as a crucial prognostic factor for EC. Research indicates that sentinel node mapping is comparable to conventional lymphadenectomy in the detection rate of positive nodes, and it does not have a negative impact on the prognosis of high-intermediate/high-risk EC patients.[33] Moreover, ultrastaging sentinel node mapping can detect low-volume node disease. Therefore, a judicious approach to lymph node dissection can assist EC patients in striking a balance between appropriate treatment and potential overtreatment.[34] Despite underscoring the significance of the inflammatory index in EC, it remains imperative to consider the status of lymph node metastasis.

Our study benefits from a large cohort of patients with EC, which helps alleviate concerns about selection bias. However, there are some limitations in the present research. Firstly, this study is retrospective. While external validation of the model by including patient cohorts from other centers has confirmed the reliability of the research conclusions, as well as the predictive accuracy and generalizability of the model, additional validation through prospective trials is still necessary. Furthermore, in comparison to the 2009 FIGO staging system, the newly proposed FIGO staging now incorporates the TGCA molecular classification, indicating a transition in EC staging from a pathological staging system to a molecular classification.[26,35] Given that this study is retrospective, the majority of patients did not undergo next-generation sequencing, thereby impeding our ability to effectively acquire mutation or abnormal gene information. Finally, as the treatment modalities for EC are continuously evolving, with an increasing number of immunotherapies and targeted drugs being administered in clinics, these advancements have a significant impact on patients' recovery. However, the clinical application time of these drugs is relatively short, and our current research lacks data on the treatment of these patients, necessitating further exploration in future studies.

In conclusion, our study identified pretreatment inflammatory indexes associated with RFS, providing new insights to improve the management and healthcare for EC patients. Furthermore, we have developed a novel nomogram model that integrates inflammatory indexes with traditional predictors. This predictive model demonstrated high accuracy and potential clinical utility, providing treatment recommendations for EC patients based on risk stratification.

Abbreviations

EC, endometrial cancer; BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; LVSI, lympho-vascular space invasion; RFS, recurrence-free survival; OS, overall survival; ROC, receiver operating characteristic; AUC, area under the curve; MLR, monocyte/lymphocyte ratio; NLR, neutrophil/lymphocyte ratio; PLR, platelet/lymphocyte ratio; SIRI, systemic inflammation response index; NCCN, National Comprehensive Cancer Network.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethics Committee of Chongqing Medical University approved this study (Institutional Review Board number, IRB No. 2021-676), Chongqing Maternal and Child Health Hospital (IRB No. 2023-02), Yubei District People's Hospital (IRB No. K2024-03-264). All patients provided their informed consent before starting the treatment and gave consent to have their data published. As it was a retrospective clinical study, all the patients were contacted by telephone to obtain verbal informed consent and it was approved by the ethics committee. All data about the patients was anonymized or maintained with confidentiality. This study complied with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declared no conflicts of interest in this study.

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