Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2025**; 52(12): 45342
https://doi.org/10.31083/CEOG45342

Original Research

Prediction and Validation of Influential Features in Prognostic Survival Against Serous Ovarian Cancer

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Academic Editor: Michael H. Dahan
Submitted: 28 July 2025 Revised: 25 September 2025 Accepted: 30 September 2025 Published: 24 December 2025

Abstract

Background: Current evidence on prognostic factors affecting outcomes in serous ovarian cancer (SOC) is limited, with many studies evaluating only a narrow range of variables. This study aimed to assess survival patterns and prognostic determinants among SOC patients treated at our institution. **Methods**: We conducted a retrospective analysis of women diagnosed with SOC based on histopathological and cytopathological analyses between January 2016 and December 2023. The collected data included demographic characteristics, comorbidities, laboratory parameters, histological grade, tumour stage, surgical approach, postoperative residual disease, chemotherapy regimens, targeted therapy use, postoperative complications, and clinical outcomes. The primary endpoints were overall survival (OS) and mortality. **Results**: A total of 302 patients with SOC were included, with a median age of 52 years (mean 51.4 $\pm$ 10.0 years). Of these, 116 patients (38.4%) had high-grade serous ovarian cancer (HGSOC), and 119 patients (39.4%) were at clinicopathological stages III/IV. Comorbidities were present in 32.1% of patients but did not significantly affect survival. Multivariate analysis identified the following independent prognostic factors (ranked by hazard ratio): human epididymis protein 4 (HE4) positivity (hazard ratio [HR] = 1.856), tumour stage (HR = 2.411), histological grade (HR = 3.415), achieving R0 resection status (HR = 3.316), use of targeted therapies (HR = 4.498), and adequacy of chemotherapy cycles (HR = 2.663). **Conclusions**: OS in SOC was significantly influenced by HE4 expression, tumour stage, histological grade, surgical resection status, targeted therapy, and the number of chemotherapy cycles ($p < 0.05$). These findings highlight the importance of early diagnosis, optimal cytoreduction, complete chemotherapy, and incorporation of targeted treatments to improve patient outcomes.

Keywords: serous ovarian cancer; influencing features; nomogram; overall survival; prognostic model; validation

1. Introduction

Epithelial ovarian cancer (EOC) remains a leading cause of mortality in gynecologic malignancies. Among its histological subtypes, serous ovarian cancer (SOC) is the most common, representing nearly 52% of cases [1]. Early detection of SOC is particularly difficult due to its largely asymptomatic course and the absence of reliable screening modalities. Consequently, a majority of patients are diagnosed at advanced stages, with approximately 51% presenting at stage III and 29% at stage IV [2]. Survival outcomes reflect this late presentation, with 5-year survival rates of only ~42% for stage III and ~26% for stage IV disease [1–3].

Although frequently grouped under the umbrella term "ovarian cancer", EOC comprises a diverse set of histopathological entities, each with distinct biological behaviors and therapeutic implications. Thus, given the predominance of SOC, elucidating its prognostic factors is essential to guide clinical decision-making and improve patient outcomes [4].

In oncology, nomograms have recently gained prominence as valuable tools for individualized risk assessment and clinical decision-making [5]. These models incorporate multiple prognostic variables to provide quantitative survival predictions and are extensively applied in cancers such as breast, lung, and prostate [6–8]. In contrast, their use in ovarian cancer, particularly in SOC remains limited. Prognostic heterogeneity and the absence of validated predictive models continue to restrict personalized treatment approaches in this setting. These gaps highlight the need for a robust, data-driven nomogram specifically designed for SOC patients.

In this study, our objective was to systematically identify and validate the prognostic determinants that influence overall survival (OS) in SOC patients. To this end, we constructed and validated a comprehensive prognostic nomogram that integrates a range of clinicopatholog-

ical variables. Unlike conventional staging systems, this model leverages patient-specific characteristics to generate individualized survival predictions, thereby providing clinicians with a practical tool to refine diagnostic evaluations, optimize treatment strategies, and guide postoperative follow-up. Thus, by addressing the current limitations in SOC prognostication, our findings contribute to the advancement of precision oncology, with the goal of improving risk stratification and enabling more personalized, evidence-based clinical management for SOC patients.

2. Materials and Methods

2.1 Patient Cohort and Eligibility Criteria

This retrospective study included 302 patients with a confirmed diagnosis of SOC who were treated at our institution between January 2016 and December 2023. Patients were eligible for inclusion if they met the following criteria: (1) SOC diagnosis confirmed through both histopathological and cytopathological evaluation; (2) availability of complete clinical records; (3) receipt of primary treatment at our institution; and (4) administration of adjuvant chemotherapy after surgery.

Exclusion criteria included: (1) presence of concurrent gynecologic or extragenital malignancies; (2) absence of surgical treatment; (3) fertility-preserving intent; (4) history of previous gynecologic surgery; and (5) severe comorbid conditions involving cardiac, hepatic, or renal function, or incomplete clinical data.

2.2 Data Collection and Quantification of Prognostic Factors

All 302 eligible patients were randomly assigned to either the development cohort (n = 202) or the validation cohort (n = 100) using a random number table method. The data collected encompassed key prognostic and survival-related variables, including demographic information, laboratory parameters, tumour stage, histological grade, residual disease following surgery, chemotherapy regimen, utilization of targeted therapies, and the total number of chemotherapy cycles administered.

This study evaluated OS outcomes in the training and validation cohorts. Follow-up time was defined as the interval between SOC diagnosis and either last contact or death. Comparisons of baseline clinical characteristics between the two cohorts were performed using independent-sample *t* tests and chi-square tests, as appropriate.

Baseline variables included smoking status, menopausal status, reproductive history, serum cancer antigen 125 (CA125) and human epididymis protein 4 (HE4) levels, risk of ovarian malignancy algorithm (ROMA) index, use of abortifacients, chemotherapy regimens, targeted therapies, comorbidities, family history of cancer, and postoperative complications. Residual tumour burden was assessed according to cytoreductive surgical outcomes, with R0 resection defined as the absence of visible residual disease. Additional parameters included treatment duration, International Federation of Gynecology and Obstetrics (FIGO) stage, histological grade, and tumour laterality. Continuous or ordinal variables such as age, body mass index (BMI), parity, and abortion history were converted into quartiles or appropriate categorical groups. Histological grade was classified as low, intermediate, or high. Patients were further stratified into early (stage I–II) and advanced (stage III–IV) groups based on FIGO staging. Survival analysis was conducted using Kaplan-Meier curves for both cohorts, with differences in OS assessed *via* the log-rank test. Prognostic factors were explored using univariate and multivariate Cox proportional hazards regression models to estimate hazard ratios (HRs) and standard errors (SEs). Non-significant variables were excluded from the multivariate model through forward stepwise selection.

The primary endpoint was OS, defined as the time from diagnosis to death or censoring at the last follow-up, and calculated using the life table method. Missing values in baseline characteristics were imputed using the K-nearest neighbor (KNN) approach. Independent variables were classified and coded as continuous, binary, or ordinal, depending on their distribution and clinical relevance.

2.3 Diagnosis, Surgery, Treatment, and Follow Up

Upon admission, all patients underwent standard laboratory testing and histopathological evaluation for clinical staging and tumour grading. For analysis, only complete laboratory datasets were considered, with emphasis on serum CA125 and HE4 levels. Postoperative staging was assigned according to the 2014 FIGO classification system [4], classifying patients into stages I through IV. Histological grading further classified cases as low-, intermediate-, or high-grade serous ovarian carcinoma.

Surgical management was tailored according to disease stage. In early-stage SOC, patients underwent comprehensive surgical staging, which included peritoneal and abdominal exploration, biopsy or excision of suspicious lesions, total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and pelvic and/or para-aortic lymphadenectomy. For advanced-stage disease, cytoreductive surgery was performed with the goal of complete removal of both primary and metastatic lesions, typically involving resection of the uterus, bilateral adnexa, omentum, and regional lymph nodes [5]. The study emphasized evaluation of residual disease after cytoreduction, particularly the achievement of R0 resection (absence of visible residual tumour). Postoperatively, patients were treated with platinum-based chemotherapy unless contraindicated. Two main chemotherapy regimens were administered:

TP regimen—paclitaxel (135–175 mg/m^2 IV) combined with cisplatin (70 mg/m^2 IV);

TC regimen—paclitaxel (135–175 mg/m^2 IV) combined with carboplatin (AUC = 5, IV).

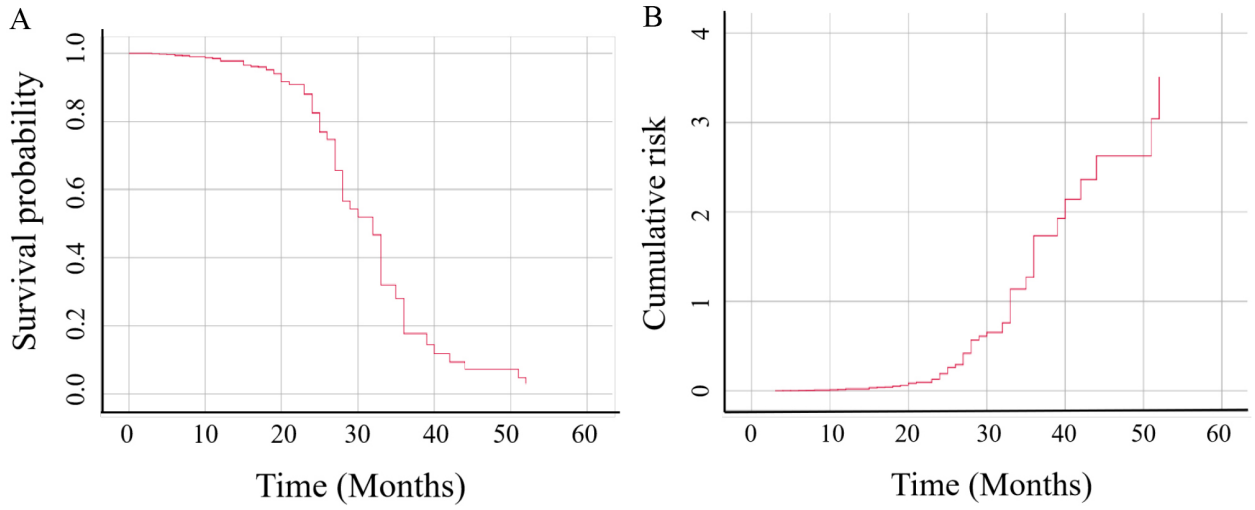

Fig. 1. Survival probability and cumulative risk of Training Set. (A) Survival probability curve of Training Set. (B) Cumulative hazard curve of Training Set.

Both regimens were administered on day 1 of each treatment cycle. Follow-up duration was calculated from the date of surgery, with patients monitored every six months. Survival time was recorded in months, from surgery until death or the last follow-up.

2.4 Statistical Analysis

Statistical analyses were conducted using SPSS software (version 26.0; IBM Corp., Armonk, NY, USA). Categorical variables were coded as binary indicators (0/1), while continuous variables were categorized into ordinal levels and coded sequentially (1, 2, 3, etc.) according to predefined cut-off values. Detailed coding strategies for each variable are presented in the Results section. Comparisons of categorical variables were performed using the chi-square test. Survival analyses were first carried out with the Kaplan-Meier method to evaluate differences across clinical variables. Variables with $p < 0.05$ in univariate analysis were subsequently entered into a multivariate Cox proportional hazards regression model, with independent prognostic factors identified through forward stepwise selection. The proportional-hazards assumption was examined using Grambsch and Therneau's scaled Schoenfeld residual test (cox.zph in R). All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant. Internal and external validation of the predictive model were conducted using R software (version 4.0.3; R Foundation for Statistical Computing, Vienna, Austria). Model performance was evaluated based on discrimination, calibration, and clinical utility metrics, as described in subsequent sections.

3. Results

3.1 Clinical Characteristics and Baseline Comparison

The median age of the study population was 52 years (mean 51.4 $\pm$ 10.0 years), with a mean BMI of 23.8 $\pm$ 3.33 kg/m^2. Approximately 10% of patients reported a history of smoking, while 90% had a history of miscarriage. High-grade serous ovarian cancer (HGSOC) was diagnosed in 38.4% of patients (n = 116), and 39.4% (n = 119) presented with FIGO stage III or IV disease at the time of diagnosis. Comorbidities were present in 32.1% of patients but were not significantly associated with survival outcomes. In terms of treatment, about 70% of patients received paclitaxel-cisplatin (TP) chemotherapy, and only half of the cohort underwent targeted therapy. Baseline clinical variables included in the analysis are summarized in Table 1, with no significant differences in OS or mortality observed between the training and validation cohorts. Collectively, these results indicate that the study population was characterized by relatively early age, a high proportion of advanced-stage and high-grade disease, and frequent comorbidities. Despite variations in clinical features, comorbid conditions were not associated with survival outcomes. Treatment patterns showed that most patients received TP chemotherapy, but only half had access to targeted therapies.

3.2 Univariate Cox Regression and Feature Selection

Univariate Cox regression analysis revealed seven factors associated with OS: HE4, ROMA index, tumour stage, histological grade, residual tumour size, treatment objective, and chemotherapy cycles (Table 2). While an initial significance level of $p \leq 0.05$ was applied, the threshold was subsequently relaxed to $p \leq 0.10$ to avoid excluding variables with potential prognostic relevance. These findings highlight the multifactorial nature of SOC prognosis and provide a comprehensive foundation for subsequent multivariate modeling.

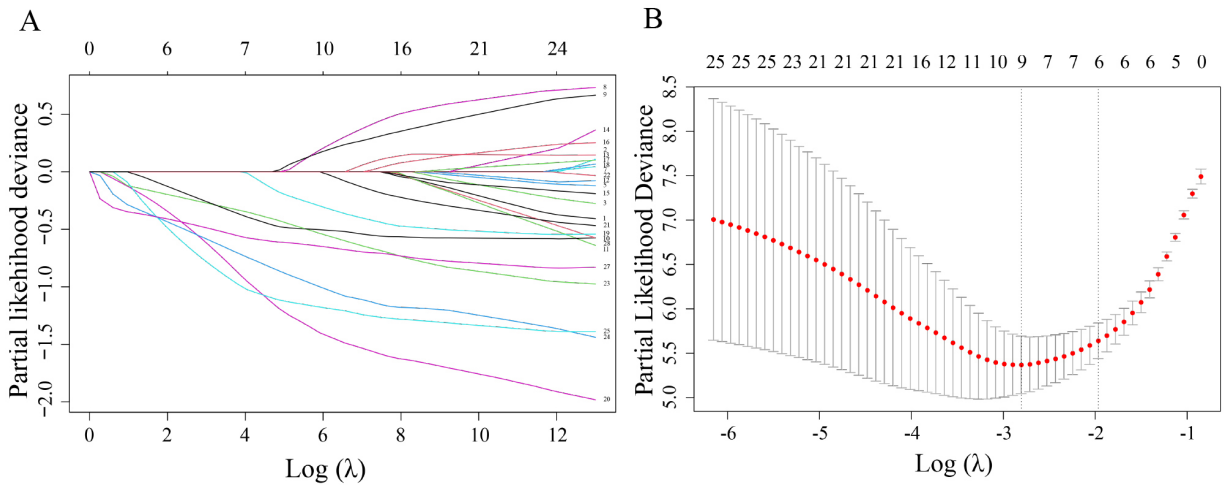

Fig. 2. Variable selection by using LASSO. (A) Selection of optimal prognostic variables using LASSO regression. (B) LASSO regression for variable shrinkage and optimal λ selection. LASSO, least absolute shrinkage and selection operator.

3.3 Proportional Hazards Assumption Test

A proportional hazards test was performed on the seven candidate variables to assess model suitability. The ROMA index failed to meet the proportional hazards assumption ($p < 0.001$; Table 3) and was excluded. Importantly, the remaining six variables satisfied the assumption (global $p = 0.083$; Table 4), ensuring their robustness for multivariate analysis and reliable prognostic modeling. Clinically, this strengthens the predictive accuracy of the nomogram by retaining only stable and valid prognostic indicators.

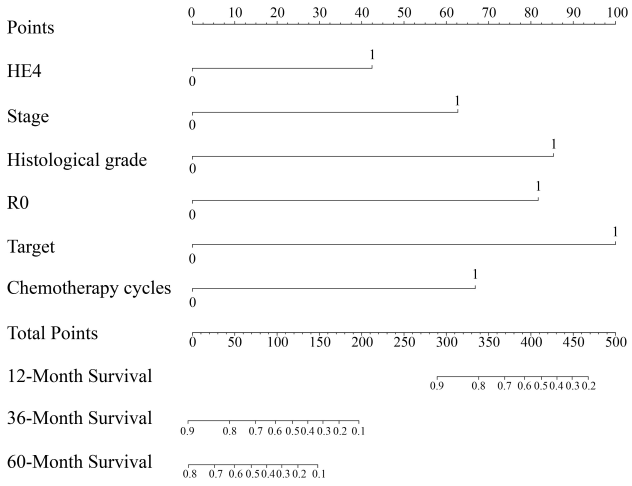

Fig. 3. Proposed SOC nomogram of final selected features.

3.4 Multivariate Cox Regression Analysis

Multivariate Cox regression analysis was performed using six validated predictors, as shown in Table 5. Improved survival outcomes were independently associated with normal serum HE4 levels (HR = 1.856), early FIGO stage (HR = 2.411), low-grade histology (HR = 3.415), achievement of R0 resection postoperatively (HR = 3.316), receipt of targeted therapy (HR = 4.498), and completion of an adequate number of chemotherapy cycles (HR = 2.663) were all independently associated with improved survival outcomes. All six variables demonstrated statistical significance in the Cox model. On this basis, survival probability estimates and cumulative hazard curves were constructed for the Training Set (Fig. 1). Collectively, these findings provide a robust framework for individualized prognostication and treatment planning in clinical practice.

3.5 Development and Validation of a Personalized Prognostic Nomogram

Based on the multivariate Cox regression analysis, six independent prognostic variables were selected to develop a predictive model for OS. To verify the robustness of variable selection, we further applied the least absolute shrinkage and selection operator (LASSO) regression (with λ determined *via* cross-validation), and the results showed that its selected variables were consistent with those identified by multivariable Cox regression. At the optimal penalty parameter λ (Fig. 2), the same six variables were retained, confirming them as the most robust predictors.

The ROMA index was excluded after failing to meet the proportional hazards assumption. To finalize the model, a combination of univariate Cox regression, Wald testing, and forward stepwise selection guided by the Bayesian information criterion (BIC) was employed. Regression coefficients were then applied to generate individualized risk scores. Based on these results, a nomogram was constructed to provide a visual representation of the prognostic model and to estimate 1-, 3-, and 5-year survival probabilities in SOC patients (Fig. 3).

Table 1. Categorization scheme of influencing features.

Features	Categorization scheme	Training set (cases, %)	Validation set (cases, %)	χ^2	p
Age (year)	<40 coded as 1	29, 14.3	17, 17.0	1.601	0.659
	40∼50 coded as 2	64, 31.7	25, 25.0		
	50∼60 coded as 3	69, 34.2	38, 38.0		
	≥60 coded as 4	40, 19.8	20, 20.0		
BMI (kg/m^2)	<20 coded as 1	18, 8.9	10, 10.0	1.272	0.736
	20∼24 coded as 2	63, 31.2	34, 34.0		
	24∼28 coded as 3	102, 50.5	44, 44.0		
	≥28 coded as 4	19, 9.4	12, 12.0		
Smoke	No coded as 0	179, 88.6	90, 90.0	0.132	0.716
	Yes coded as 1	23, 11.4	10, 10.0		
Oral contraceptive use	No coded as 0	158, 78.2	80, 80.0	0.127	0.721
	Yes coded as 1	44, 21.8	20, 20.0		
Gestation (times)	<2 coded as 1	37, 18.3	18, 18.0	0.879	0.644
	3∼4 coded as 2	109, 54.0	59, 59.0		
	≥5 coded as 3	56, 27.7	23, 23.0		
Parity (times)	<2 coded as 0	74, 36.6	39, 39.0	0.160	0.689
	≥2 coded as 1	128, 63.4	61, 61.0		
Abortion (times)	None coded as 1	20, 9.9	10, 10.0	0.489	0.783
	1∼2 coded as 2	85, 42.1	38, 38.0		
	≥3 coded as 3	97, 48.0	52, 52.0		
Menopause	No coded as 0	75, 37.1	39, 39.0	0.100	0.752
	Yes coded as 1	127, 62.9	61, 61.0		
Comorbidity (DM/HL/HT)	No coded as 0	135, 66.8	70, 70.0	0.308	0.579
	Yes coded as 1	67, 33.2	30, 30.0		
FH (family history)	No coded as 0	170, 84.2	87, 87.0	0.426	0.514
	Yes coded as 1	32, 15.8	13, 13.0		
Complication	No coded as 0	159, 78.7	80, 80.0	0.067	0.796
	Yes coded as 1	43, 21.3	20, 20.0		
HE4 (pmol/L)	<140 coded as 0	66, 32.7	34, 34.0	0.053	0.818
	≥140 coded as 1	136, 67.3	66, 66.0		
CA125 (U/mL)	<35 coded as 0	75, 37.1	37, 37.0	0.000	0.983
	≥35 coded as 1	127, 62.9	63, 63.0		
ROMA	Premenopausal <11.4% coded as 0 Postmenopausal <29.9% coded as 1	44, 21.8	25, 25.0	0.393	0.531
	Premenopausal ≥11.4% coded as 0 Postmenopausal ≥29.9% coded as 1	158, 78.2	75, 75.0		
Location	One side coded as 0	68, 33.7	36, 36.0	0.162	0.688
	Two sides coded as 1	134, 66.3	64, 64.0		
Stage	I/II coded as 0	125, 61.9	58, 58.0	0.422	0.516
	III/IV coded as 1	77, 38.1	42, 42.0		
Histological grade	Low/Middle coded as 0	126, 62.4	60, 60.0	0.160	0.689
	High coded as 1	76, 37.6	40, 40.0		
R0	Yes coded as 0	148, 73.3	70, 70.0	0.356	0.551
	No coded as 1	54, 26.7	30, 30.0		
Chemotherapy regimen	TP coded as 0	130, 64.4	70, 70.0	0.952	0.329
	TC coded as 1	72, 35.6	30, 30.0		
Target	Yes coded as 0	111, 55.0	49, 49.0	0.951	0.330
	No coded as 1	91, 45.0	51, 51.0		

Table 1. Continued.

Features	Categorization scheme	Training set (cases, %)	Validation set (cases, %)	χ^2	p
Chemotherapy cycles	≥6 coded as 0	125, 61.9	60, 60.0	0.100	0.752
	<6 coded as 1	77, 38.1	40, 40.0		
Survive time	/	23 [14.5, 33]	23 [14, 34]	0.168	0.867
Survive outcome	Survive coded as 0	87, 43.1	43, 43.0	0.000	0.991
	Death coded as 1	115, 56.9	57, 57.0		

Note: All factors were quantified using binary (0/1) or ordinal (1/2/3) scales. Statistical analysis was performed using the chi-square test. A significance level of $\alpha = 0.05$ was used for all tests. Target, targeted drugs such as PARP inhibitors and anti-angiogenics have been used. R0, if R0 resection was not achieved at any surgical stage (primary or interval debulking), the patient was classified as "No". Survival time is presented as median [Q1, Q3] and compared between the two groups using the non-parametric Mann-Whitney U test.

BMI, body mass index; DM, diabetes mellitus; HL, hyperlipidemia; HT, hypertension; HE4, human epididymis protein 4; CA125, cancer antigen 125; ROMA, risk of ovarian malignancy algorithm.

Table 2. Kaplan-Meier survival estimates with log-rank comparisons across baseline variables ($p \leq 0.1$).

Features	Categorization scheme	Training set (cases, percentage)	χ^2	p
HE4 (pmol/L)	<140 = 0	66, 32.7	8.094	0.004
	≥140 = 1	136, 67.3		
ROMA	Premenopausal <11.4% = 0	158, 78.2	33.445	$p < 0.001$
	Postmenopausal <29.9% = 0			
	Premenopausal ≥11.4% = 1	44, 21.8		
	Postmenopausal ≥29.9% = 1			
Stage	1/2 = 0	125, 61.9	129.522	$p < 0.001$
	3/4 = 1	77, 38.1		
Histological grade	Low, Middle = 0	126, 62.4	145.431	$p < 0.001$
	High = 1	76, 37.6		
R0	Yes = 0	148, 73.3	163.596	$p < 0.001$
	No = 1	54, 26.7		
Target	Yes = 0	111, 55.0	130.061	$p < 0.001$
	No = 1	91, 45.0		
Chemotherapy cycles	≥6 = 0	125, 61.9	96.599	$p < 0.001$
	<6 = 1	77, 38.1		

Table 3. Proportional hazards test of selected features by Kaplan-Meier.

Features	χ^2	df	p
HE4 (pmol/L)	0.980	1	0.322
ROMA	16.714	1	<0.001
Stage	0.003	1	0.959
Histological grade	0.552	1	0.458
R0	3.811	1	0.051
Target	1.173	1	0.279
Chemotherapy cycles	0.840	1	0.359
Global	25.934	7	<0.001

Note: The proportional-hazards assumption was examined using Grambsch and Therneau's scaled Schoenfeld residual test (cox.zph in R); a p-value < 0.05 was considered evidence of non-proportionality.

Table 4. Proportional hazards test of final selected features.

Features	χ^2	df	p
HE4 (pmol/L)	1.660	1	0.198
Stage	0.054	1	0.817
Histological grade	1.008	1	0.315
R0	3.029	1	0.082
Target	1.962	1	0.161
Chemotherapy cycles	0.978	1	0.323
Global	11.172	6	0.083

Note: The proportional-hazards assumption was examined using Grambsch and Therneau's scaled Schoenfeld residual test (cox.zph in R); a p-value < 0.05 was considered evidence of non-proportionality.

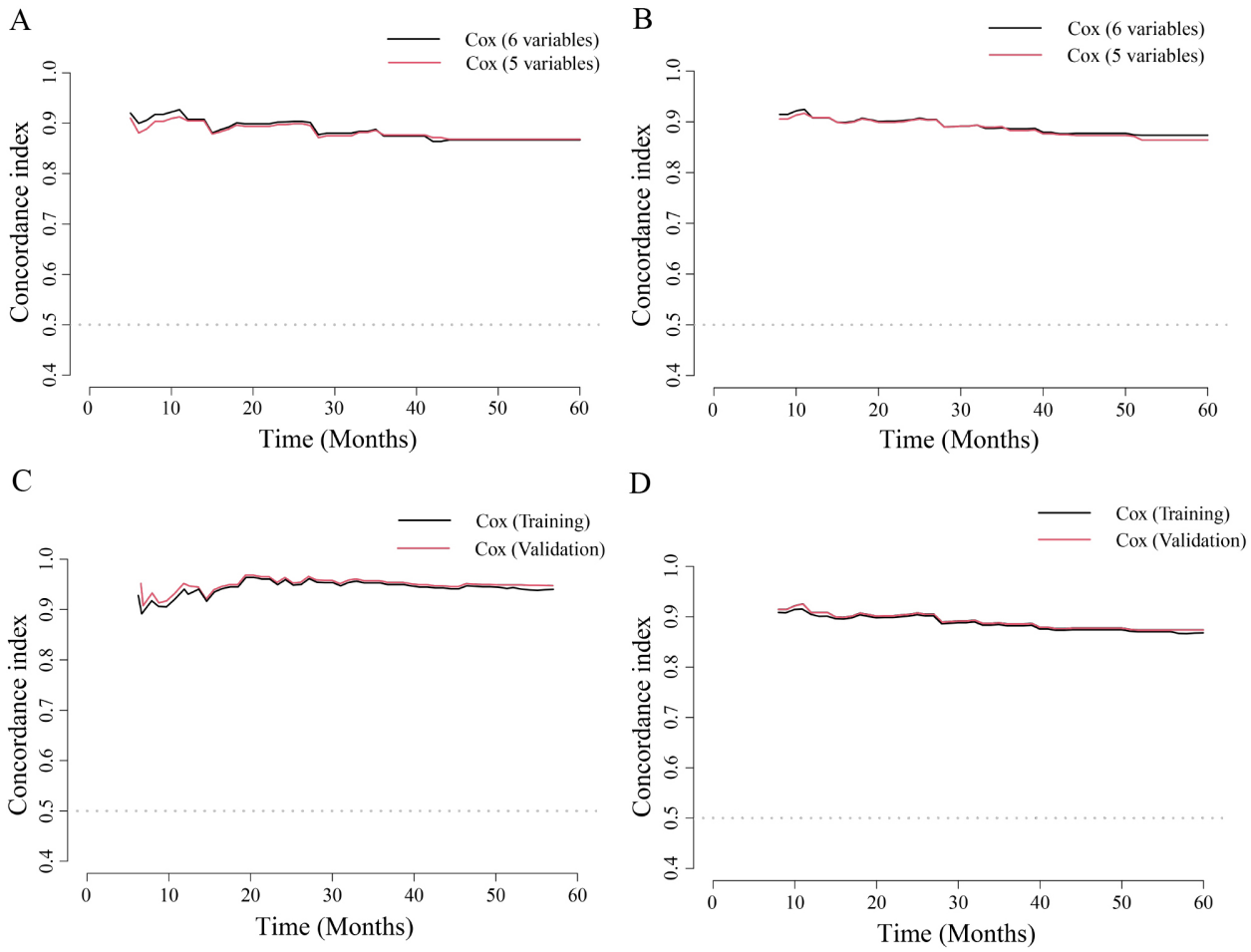

Fig. 4. C-index of Training Set and Validation Set. (A) C-index for internal validation in the Training Set. (B) C-index for cross-validation in the Training Set. (C) C-index for external validation in the Validation Set. (D) C-index for cross-validation in the Validation Set.

Table 5. Cox regression analysis of final selected features.

Features	β	SE	Wald	*df*	*p*	HR
HE4 (pmol/L)	0.618	0.270	5.260	1	0.022	1.856
Stage	0.880	0.361	5.955	1	0.015	2.411
Histological grade	1.228	0.380	10.439	1	0.001	3.415
R0	1.199	0.333	12.990	1	0.000	3.316
Target	1.504	0.405	13.809	1	0.000	4.498
Chemotherapy cycles	0.980	0.321	9.337	1	0.002	2.663

3.6 Model Performance and Validation Discrimination

3.6.1 Concordance Index (C-index)

The predictive accuracy of the nomogram was evaluated using the C-index, which reflects the model's discriminative capacity. The six-variable model achieved a C-index of approximately 0.9 in both internal validation (Fig. 4A) and cross-validation (Fig. 4B), demonstrating excellent predictive performance well above random chance. Comparative analysis further showed that this model outperformed the five-variable version that excluded chemotherapy cycles.

External validation with an independent cohort of 100 patients (Validation Set, Fig. 4C), along with additional cross-validation (Fig. 4D), produced C-index values approaching 0.9. These findings confirm the robustness and generalizability of the six-variable model, demonstrating consistently high predictive performance across both external datasets and multiple validation approaches.

3.6.2 Calibration

Calibration plots were constructed to evaluate the agreement between predicted and observed survival probabilities at 1, 2, 3, and 5 years. In the ideal scenario, pre-

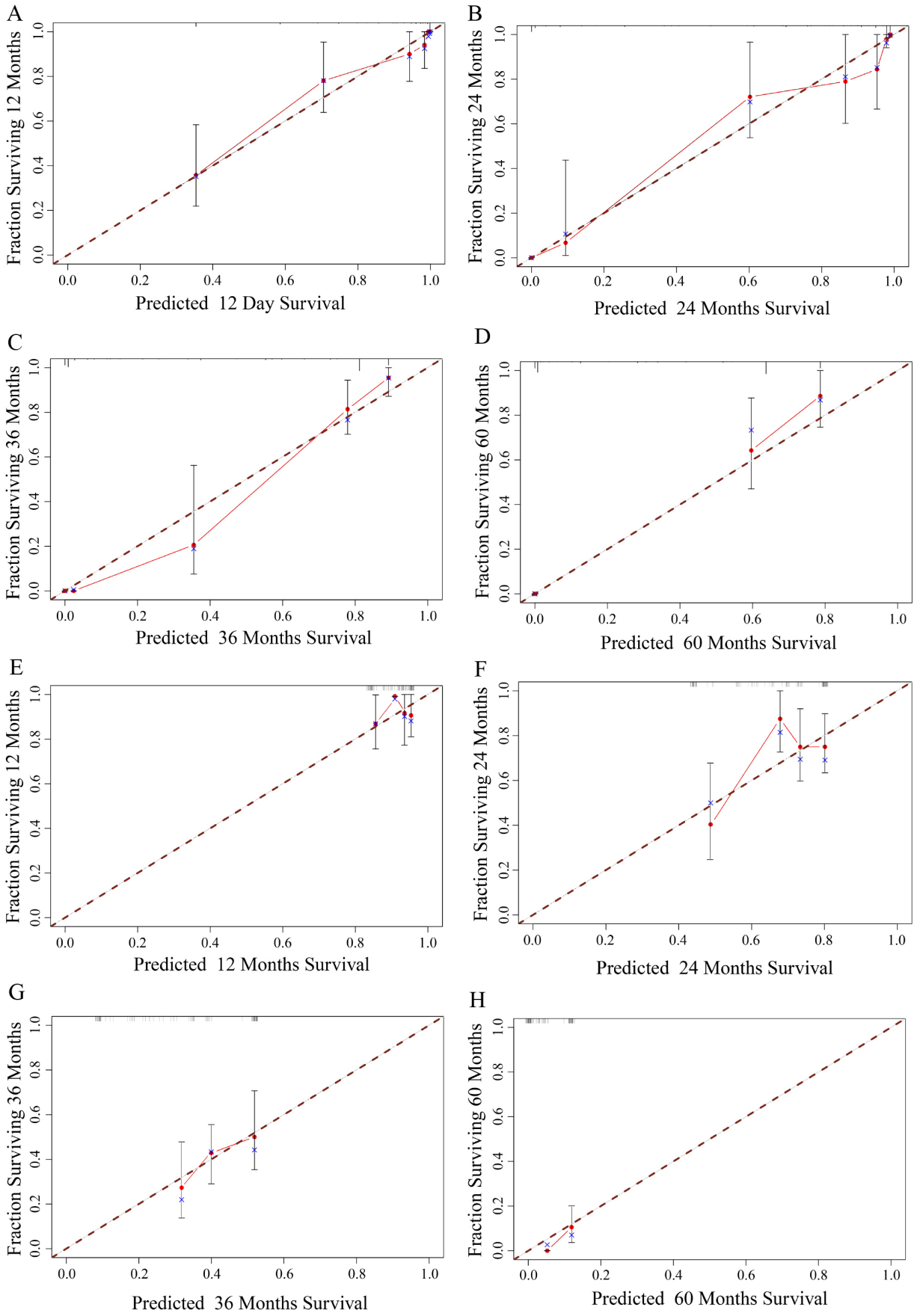

Fig. 5. Calibration curves of Training Set and Validation Set. (A–D) Training set at 12, 24, 36, and 60-months, respectively. (E–H) Validation set at 12, 24, 36, and 60-months, respectively.

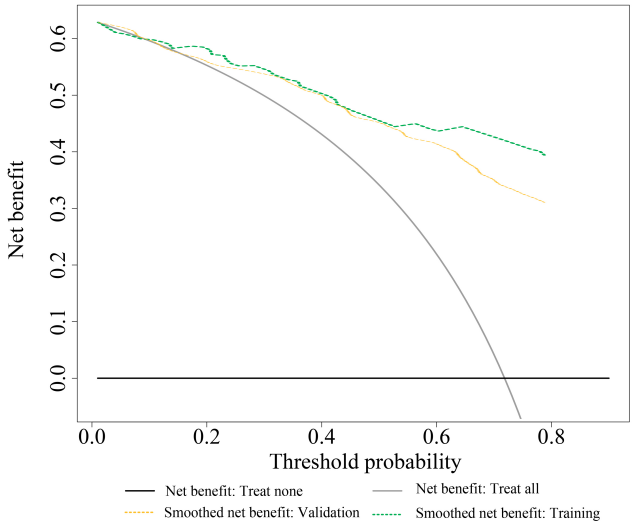

Fig. 6. Decision curve analysis for the model of Training Set and Validation Set.

dictions align along the 45-degree reference line, indicating perfect calibration. Despite the relatively limited sample size, the curves demonstrated strong concordance between predicted and actual OS in both the Training and Validation Sets (Fig. 5).

3.6.3 Decision Curve Analysis (DCA)

DCA was conducted to assess the clinical utility of the six-variable model by estimating net benefit across a range of threshold probabilities (Fig. 6). In both the Training Set and the external Validation Set, the model's decision curves consistently outperformed the 'treat-all' and 'treat-none' strategies, demonstrating clear clinical benefit. Within the threshold probability range of 0.1 to 0.8, the six-variable model also provided greater net benefit than the five-variable model excluding chemotherapy cycles, underscoring its strong applicability and value in guiding clinical decision-making across datasets.

4. Discussion

In this study, we developed and validated a prognostic nomogram that integrates multiple clinical variables to predict individualized OS probabilities in SOC patients. Beyond risk estimation, the model offers practical utility in guiding treatment planning and surgical decision-making. By stratifying patients into distinct risk groups, the nomogram supports personalized preoperative and postoperative management strategies. From an initial set of 21 clinical candidates, seven potential prognostic variables were identified using univariate Cox regression analysis. After confirming the proportional hazards assumption, six variables were retained. To strengthen model robustness and address multicollinearity, we applied the LASSO method, which effectively incorporates multiple predictors. The finalized nomogram demonstrated strong discriminative ability, with a C-index of approximately 0.9 in both the Training and Validation Sets. Although calibration was constrained by sample size, our model establishes a solid framework for the development of more refined predictive tools in SOC prognosis. Unlike earlier prognostic models for ovarian cancer, our study is tailored specifically to SOC patients. It uniquely incorporates HE4 status and assesses the influence of targeted therapies as well as the adequacy of chemotherapy cycles variables that are often absent from prior nomograms [9,10]. In addition, our model employs a LASSO-based variable selection approach, which minimizes the risk of overfitting compared with conventional stepwise methods, thereby enhancing its robustness and generalizability [11,12].

Although previous studies have examined a range of prognostic factors for ovarian cancer, many lacked rigorous validation or failed to report discrimination metrics such as the C-index, which limits cross-study comparability [13–16]. The ROMA index, while recognized as a valuable biomarker for detecting ovarian malignancies, did not show predictive utility for OS in our cohort, indicating its function may be primarily diagnostic rather than prognostic in this setting. Interestingly, other studies have highlighted that combining serum biomarkers such as CA125 with clinicopathological parameters can enhance survival prediction [17]. For example, the addition of CA125 improved the hazard ratio prediction (HR = 0.35, 95% confidence interval [CI]: 0.16–0.77) in a previous study [18]. In contrast, our multivariate model did not demonstrate a similar prognostic benefit from CA125 or ROMA, which may be attributable to differences in study populations, endpoint definitions, or statistical methodologies. Compared with more complex or molecular-based models, our six-factor nomogram provides a streamlined and clinically practical tool for risk prediction, relying solely on routinely available variables. Notably, histological subtype determined through preoperative biopsy emerged as an independent prognostic factor [19]. Although the non-random allocation of patients to histological categories may introduce sampling bias, the integration of multiple clinical predictors within the nomogram helps mitigate this limitation, ultimately supporting its reasonable discriminatory performance.

The nomogram demonstrated outstanding predictive accuracy, with C-indices approaching 0.9 in both internal and external validation cohorts, reflecting strong discriminative power in distinguishing survival outcomes among SOC patients. The C-index, a widely accepted benchmark for model performance in oncology, indicates that our tool performs on par with, or even surpasses, other validated prognostic models for ovarian and various solid tumours [20–22]. Calibration analyses at 1, 2, 3, and 5 years showed close agreement between predicted and observed survival probabilities, supporting the reliability of the model's absolute risk estimates despite the relatively modest sample size. Overall, achieving accurate calibration predictions is

essential for clinical implementation, as it ensures that estimated risks mirror real-world outcomes, an aspect often lacking in earlier ovarian cancer models [23–25].

Beyond discrimination and calibration, DCA further reinforced the clinical utility of our model, showing consistent net benefit across threshold probabilities ranging from 0.1 to 0.8. As DCA is increasingly recognized as a benchmark for evaluating decision-support tools, it provides insight into the net clinical value of this model beyond conventional statistical measures [26,27]. The notable gain in net benefit, particularly around the 0.7 threshold, underscores the model's potential to optimize treatment decisions compared with default strategies of treating all or none, a finding consistent with recent prognostic nomograms developed for gynecologic cancers [28,29]. Together, these complementary validation measures—C-index, calibration, and DCA—highlight the robustness, reproducibility, and clinical relevance of the nomogram, establishing it as a practical precision medicine tool for individualized OS prediction and risk-adapted treatment planning in SOC patients.

Limitations

Several limitations should be acknowledged. First, the absence of genomic data constrains the model's capacity to capture molecular heterogeneity. In real-world settings, many patients lack access to targeted therapies due to financial constraints or limited testing availability, particularly in resource-limited regions. Although our findings reinforce the clinical relevance of targeted therapies, future studies that integrate genetic and transcriptomic markers (e.g., *AKR1C3*, *Calponin-3*) are warranted to further improve predictive precision [30,31]. Details on adjuvant chemotherapy regimens, maintenance therapies (e.g., PARP inhibitors, bevacizumab), or surgical completeness (optimal vs. suboptimal debulking) have not been fully captured. These treatment-related factors significantly impact survival outcomes. Although clinicopathological factors are useful, important biomarkers such as CA125 kinetics, HE4, or homologous recombination deficiency (HRD) status were not incorporated. These markers are increasingly used in SOC management.

The model primarily uses baseline clinicopathological variables at diagnosis. However, dynamic predictors such as treatment response, recurrence patterns, and toxicity profiles were not considered. Comorbid conditions (e.g., diabetes, cardiovascular disease) and performance status play a critical role in OS and treatment tolerability. However, as these variables were not adequately included, the model may underestimate their impact. Moreover, while the model demonstrated consistent performance in both internal and external validations, the modest C-index and relatively small sample size emphasize the need for validation in larger, prospective, multicenter cohorts to ensure broader applicability. Finally, it remains uncertain whether gene-based models will ultimately surpass integrated clinical models such as ours, representing an ongoing challenge in predictive oncology.

5. Conclusions

In summary, we established a clinically applicable nomogram incorporating six easily obtainable clinicopathological variables to predict OS in patients with SOC. The model demonstrated strong discriminative power and consistent calibration, providing a practical and reliable tool for individualized risk stratification in both preoperative and postoperative contexts. Moreover, by integrating factors that reflect tumour biology, surgical outcomes, and treatment response, the nomogram supports more precise prognostication and may guide tailored therapeutic decisions. Importantly, its performance across internal and external validation cohorts highlights its robustness and potential clinical utility. However, future studies should focus on validating the model in larger, multi-center cohorts and across diverse populations to enhance its generalizability. Incorporating molecular and multi-omics data, such as genomic, transcriptomic, and proteomic profiles, may further refine its predictive accuracy and help capture the biological complexity of SOC. Overall, these efforts will strengthen the integration of nomogram-based approaches into precision oncology, enabling clinicians to deliver more personalized and evidence-based management strategies for SOC patients.

Availability of Data and Materials

The raw data supporting the findings of this study are available from the corresponding authors upon reasonable request.

Author Contributions

ZJ contributed to the interpretation of the data. WH was responsible for data management. YL contributed to data interpretation. XZ critically revised the manuscript for important intellectual content and data analysis. GH made substantial contributions to the conception of the work. ZH contributed to the conception of the work and provided funding support. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was carried out in accordance with the guidelines of the Declaration of Helsinki and was approved by the Medical Ethics Committee of the Second People's Hospital of Jingdezhen (Approval Number: 2025-LLLW-03). All patients or their families guardians gave their informed consent for inclusion before they participated in the study.

Acknowledgment

We would like to express our gratitude to all those who helped us during the writing of this manuscript. Thanks to all the peer reviewers for their opinions and suggestions.

Funding

This research was supported by the Project of Science and Technology of Jiangxi Provincial Health Commission (Award Number: 202311671).

Conflict of Interest

The authors declare no conflict of interest.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used ChatGPT-5.1 in order to check spelling and grammar. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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