# Novel prognostic nomograms to assess survival in high-grade serous ovarian carcinoma after surgery and chemotherapy: a retrospective cohort study from SEER database

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**Background:** Despite high-grade serous ovarian carcinoma (HGSOC) being the most common epithelial ovarian cancer, it is a heterogenous group of tumors with several histological subtypes. The goal of our study was to develop specifical models to predict the survival of actively treated, HGSOC.

**Methods:** This retrospective cohort study included patients with HGSOC who had undergone surgery and chemotherapy between the years of 2010 and 2016 using the Surveillance, Epidemiology, and End Results (SEER) database. A total of 3,788 cases were randomly divided into a training (n=2,591) and test set (n=1,197). Cox-LASSO algorithm and cross validation (based on lambda.1se) were used to identify survival factors in the training set. Nomograms were created and internally validated. We used Harrell's C-statistic to assess discrimination. The performance of each nomogram was evaluated using calibration plots. The clinical benefit of our models was evaluated using a decision curve analysis.

**Results:** The significant prognostic factors were marital status, age, lymph node (LN) dissection, tumor size, residual disease, and the International Federation of Obstetrics and Gynecology (FIGO) stage, which were utilized to develop the nomogram for accurately predicting 3- and 5-year overall survival (OS). Among the above factors, except for marital status, the others were included in the model for cancer-specific survival (CSS). The C-indices for OS and CSS achieved 0.679 [95% confidence interval (CI): 0.660 to 0.699] and 0.678 (95% CI: 0.658 to 0.698), respectively, in the training set and 0.662 (95% CI: 0.633 to 0.690) and 0.680 (95% CI: 0.653 to 0.707), respectively, in the test set. The good consistency was illustrated using calibration plots. In comparison with models including only FIGO or the AJCC staging system, C-index in our study were increased by 4.5–7.0% for the development test and by 6.7–7.9% for the validation test. In addition, the nomograms had a bigger range of threshold probabilities in the decision curve analysis (DCA) curves. The high-risk subgroup had significantly less favorable survival than the low-risk subgroup.

**Conclusions:** The present study indicated that the low-cost nomograms could be used as a potential prognostic tool specially for predicting survival in patients with HGSOC. Given the relatively small C-index, we still need to build a more accurate model to predict survival of HGSOC.

**Keywords:** High-grade serous ovarian carcinoma (HGSOC); Surveillance, Epidemiology, and End Results (SEER); nomogram; prognosis

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#### Introduction

In 2018, over 295,000 women were diagnosed with ovarian cancer and nearly 185,000 died from the disease worldwide (1). For patients and their families, decisions about active medical treatment versus palliative care inherently depend on survival expectations (2). Yet, accurate prediction of the prognosis of actively-treated patients remain a significant challenge for gynecologic oncologists.

It is well known that ovarian carcinoma consists of a heterogeneous group of neoplasms with multiple histologic subtypes, including epithelial and non-epithelial ovarian cancers (3,4). High-grade serous ovarian carcinoma (HGSOC) is the most common histological type with distinct biological features compared to other ovarian carcinomas, accounting for approximately 70–80% of all malignant ovarian neoplasms (5,6). Most HGSOC patients are diagnosed at stage III/IV (advanced stage) with a poor overall prognosis (7). Comprehensive staging surgery, primary cytoreductive surgery, or neoadjuvant chemotherapy combined with interval debulking surgery followed by adjuvant chemotherapy is the treatment used for most patients (8).

There are already some prognostic models for epithelial ovarian cancer that have been tested and externally validated; however, most are not specific to histologic subtypes (9). Although the International Federation of Obstetrics and Gynecology (FIGO) staging system has been incorporated in the existing prognostic models for HGSOC, some demographic and socioeconomic factors, such as younger age, have not been considered (10,11). Despite their previous omission, these easily assessed factors profiling the distinct specificities of functional status and social support may be prognostic indicators. Currently used prognostic models for HGSOC mainly focus on biomarkers (12-15), or clinical features with radiology (16,17). They reported the range of models' c-index of about 0.6-0.7. However, the associated expenses restrict access to these prognostic tools for decision making. And clinical data are still the major source of information regarding prognosis in large part because many biological factors have not yet been validated or are not readily measurable. Prediction nomograms based on easily accessible clinical information for patients with HGSOC need to be further studied.

Integration of the pivotal factors into a model to build a nomogram requires a statistic-based tool to evaluate the prognosis and quantify the risks in many cancer types (18-20). Accurate prognostic prediction is important for providing individualized therapy for patients. Therefore, we aimed to use the Surveillance, Epidemiology, and End Results (SEER) database to establish a novel, easy-to-use, and accurate prognostic nomogram for HGSOC patients. We present the following article in accordance with the TRIPOD reporting checklist (available at https://atm. amegroups.com/article/view/10.21037/atm-21-4383/rc).

# Methods

#### **Participants**

This study is a retrospective cohort study. For the development model, samples used for this study were obtained from the SEER database, encompassing approximately 35% of the total population in the United States (21). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). No personally identifying information was used in the study, which eliminated the requirement for Institutional Review Board approval or informed patient consent.

#### Clinical data extraction and measurement

Patients diagnosed with ovarian serous cancer between 2010 to 2016 were selected using the International Classification of Diseases for Oncology, third edition (ICD-O-3) primary site code of C56.9 (ovary) and morphology codes of 8441/3, 8442/3, 8460/3, and 8461/3. Patients with a diagnosis not confirmed by histology, ovarian serous carcinoma not as the primary tumor, survival time shorter than 1 month or unknown, and unknown staging information [according to the American Joint Committee on Cancer (AJCC), 7th edition], marital status, race, tumor grade, tumor laterality, tumor size, lymph node (LN), residual disease, or organ metastasis were excluded from the study cohort. Cases with poorly differentiated or undifferentiated carcinoma were classified as HGSOC. The detailed flow chart for patient inclusion and exclusion is shown in Figure 1. The study outcomes included overall survival (OS) and cancer-specific survival (CSS). The survival time was measured in months. OS was calculated from diagnosis to death of all causes or to date of last follow-up in November 2016. CSS was calculated from diagnosis to death of cancer-specific cause or to date of last follow-up in November 2016.

Marital status was classified into three types: currently married, never married, and separated/ divorced/ widowed (22). The FIGO stage was re-evaluated based on information from the database, which included the tumornode-metastasis (TNM) stage (according to the AJCC,



Figure 1 Flow chart of FIGO stage based on TNM stage, tumor size, lymph node status and distant metastasis. SEER, Surveillance, Epidemiology, and End Results; LN, lymph node; FIGO, International Federation of Gynecology and Obstetrics; TNM, tumor-node-metastasis.

 $6^{\text{th}}$  and  $7^{\text{th}}$  editions), tumor size, LN status and distant metastasis, tumor size (cm), tumor laterality (unilateral versus bilateral), performance of regional lymphadenectomy [no, adequate, and inadequate;  $\geq 10$  excised LNs was defined as adequate lymphadenectomy, according to the Gynecologic Oncology Group (GOG) criteria (23)]. The tumor size was divided into the following five categories, based on maximum diameter: <2,  $\geq 2$  and <4,  $\geq 4$  and <10,  $\geq 10$  and <16, and  $\geq 16$  cm. The type of resection performed was classified as: R0 no residual disease, R1 microscopic residual disease (0–1 cm), and R2 macroscopic residual disease (>1 cm). The different age categories at diagnosis were specified as: <50,  $\geq 50$  and <60,  $\geq 60$  and <70,  $\geq 70$  and <80, and  $\geq 80$  years.

#### Variable screening and nomogram model building

All cases in this study were randomly dichotomized into two groups for training and testing at a ratio of 7:3. The primary endpoints were OS and CSS. The comparison of clinicopathological characteristics between the two cohorts was performed using the *t*-test or chi-square test. Firstly, the most valuable predictive features of HGSOC among 11 parameters were primarily selected via the least absolute shrinkage and selection operator (LASSO) method. The partial likelihood deviance (binomial deviance) curve was plotted versus log (lambda). The two vertical dashed lines represented the minimum value and one standard deviation from the minimum value. The one standard deviation from the minimum value of lambda values, 0.030 and 0.036, were chosen for OS and CSS, respectively. Then, the nomograms were built on the final risk factors identified in the multivariate analysis from the Cox proportional hazards model in the training cohort.

#### Assessment of nomogram performance and clinical use

The discriminative performance of the nomograms was evaluated using Harrell's concordance index (C-index). The maximum value of the Harrell's C-index, 1, indicates a perfectly discriminating model while a value of 0.5 indicates that discrimination is not better than chance (24). Calibration

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curves (1,000 bootstrap resamples) were generated to assess the consistency between the actual and predicted survival. Decision curve analysis (DCA) was applied to evaluate the clinical latent value of the nomograms (25). Risk stratification of HGSOC patients were evaluated. Firstly, the median risk score from the training cohort was deemed as the threshold for OS and CSS respectively. Secondly, we used the thresholds to distinguish high risk and low risk in both training cohort and test cohort.

## Statistical analysis

All statistical analyses were performed using R software (version 4.0.4; http://www.r-project.org/) and SPSS (version 24.0; SPSS, Chicago, IL, USA). Categorical variables were shown as numbers and proportions. Kaplan-Meier analysis and log-rank test were used to explore the survival difference between subgroups. Scaled Schoenfeld residuals was used to check the proportional hazards assumption. There are two endpoints including OS and CSS in our study, and we did not perform multiple test correction. A two-sided P value of <0.05 was considered statistically significant.

#### Results

#### Clinicopathological characteristics and survival

From the SEER database, a total of 3,788 individuals diagnosed with primary HGSOC were identified and included in the final analysis. Most of the cases (83.2%) had reached an advanced stage of cancer (stages III and IV) at their initial diagnosis, and more than half of the patients (53.9%) were older than 59 years. A total of 2,329 (61.5%) cases underwent LN dissection and 2,500 cases (66.0%) received R0 resection. The comparison of clinicopathological characteristics in the training cohort (n=2,591) and test cohort (n=1,197) is provided in *Table 1*. For all cases, the 3-year OS and CSS rates were 68.5%, and 69.5%, respectively. The 5-year OS and CSS rates were 49.0% and 50.5%, respectively.

# Identification of prognostic variables and construction of the nomograms

A total of 11 variables were included in the LASSO Cox regression analysis. We found that marital status, age, LN dissection, tumor size, residual disease, and FIGO stage were risk factors for OS and age, and LN dissection, tumor size, residual disease, and FIGO stage were risk factors for CSS, respectively (*Figure 2*). On multivariate Cox regression analysis, the factors independently associated with OS were marital status, age, LN dissection, tumor size, residual disease, and FIGO stage, whereas marital status was not significantly associated with CSS (*Table 2*). The nomograms were constructed to predict 3- and 5-year OS and CSS by combining the above prognostic factors (*Figure 3*).

# Testing of this novel nomogram and comparison with current models

The C-indices for the nomograms in the training cohort were 0.679 [95% confidence interval (CI): 0.660 to 0.699] and 0.678 (95% CI: 0.658 to 0.698) for OS and CSS, respectively, both of which were higher than that of the commonly accepted FIGO staging system [OS: 0.609 (95% CI: 0.591 to 0.627); CSS: 0.612 (95% CI: 0.593 to 0.630)] and the AJCC staging system [OS: 0.615 (95% CI: 0.595 to 0.636); CSS: 0.619 (95% CI: 0.598 to 0.640)]. The C-indices for the new models of OS and CSS [0.662 (95% CI: 0.633 to 0.690) and 0.680 (95% CI: 0.653 to 0.707), respectively] were also well presented in the test cohort compared with the FIGO [OS: 0.599 (95% CI: 0.573 to 0.624); CSS: 0.605 (95% CI: 0.579 to 0.630)] and AJCC [OS: 0.605 (95% CI: 0.576 to 0.634); CSS: 0.613 (95% CI: 0.585 to 0.642)] staging systems. In comparison with models including only the FIGO or the AJCC staging system, C-statistics using the nomogram were increased by 4.5-7.0% for the development test and by 6.7-7.9% for the validation test. The calibration curves showed sufficient agreement between the predicted and actual observed survival in both the training and test cohorts (Figure 4). The DCA curves indicated that our novel nomogram models achieved more accurate clinical prognosis predictions compared to survival predicted by the AJCC staging system and the FIGO staging system (Figure 5).

# Risk stratification of HGSOC patients

The risk score of each feature was assigned by the nomogram and a total score was calculated for each individual case. The median risk score was 15 (range: 2 to 25) and 12 (range: 0 to 23) for OS and CSS in the training cohort, respectively. Based on the above scores, cases were divided into low- and high-risk groups, with

 Table 1 Demographics and clinicopathological characteristics of HGSOC patients

Variables	Training set, n (%)	Testing set, n (%)	All patients, n (%)	Ρ
Total	2,591 (70.0)	1,197 (30.0)	3,788 (100.0)	
Marital status				0.810
un-SDW	2,007 (77.5)	923 (77.1)	2,930 (77.3)	
SDW	584 (22.5)	274 (22.9)	858 (22.3)	
Race				0.482
White	2,201 (84.9)	999 (83.5)	3,200 (84.5)	
Black	159 (6.1)	83 (6.9)	242 (6.4)	
Other	231 (8.9)	115 (9.6)	346 (9.1)	
Age, years				1.000
<50	407 (15.7)	189 (15.8)	596 (15.7)	
50–59	787 (30.4)	363 (30.3)	1,150 (30.4)	
60–69	825 (31.8)	382 (31.9)	1,207 (31.9)	
70–79	461 (17.8)	211 (17.6)	672 (17.7)	
≥80	111 (4.3)	52 (4.3)	163 (4.3)	
Grade				0.537
Grade III	1,247 (48.1)	589 (49.2)	1,836 (48.5)	
Grade IV	1,344 (51.9)	608 (50.8)	1,952 (51.5)	
Laterality				0.479
Unilateral	1,064 (41.1)	477 (39.8)	1,541 (40.7)	
Bilateral	1,527 (58.9)	720 (60.2)	2,247 (59.3)	
Radiation				0.115
No/unknown	2,562 (98.9)	1,190 (99.4)	3,752 (99.9)	
Yes	29 (1.1)	7 (0.6)	36 (1.0)	
LN dissected				0.996
No or examined	997 (38.5)	462 (38.6)	1,459 (38.5)	
1–10	770 (29.7)	354 (29.6)	1,124 (29.7)	
≥11	824 (31.8)	381 (31.8)	1,205 (31.8)	
Organ metastas	sis			0.453
No	2,371 (91.5)	1,104 (92.2)	3,475 (91.7)	
Yes	220 (8.5)	93 (7.8)	313 (8.3)	
Tumor size, cm				0.924
<2	181 (7.0)	84 (7.0)	265 (7.0)	
≥2 and <4	291 (11.2)	143 (11.9)	434 (11.5)	

Table 1 (continued)

Training set, n (%)	Testing set, n (%)	All patients, n (%)	Ρ
1,110 (42.8)	508 (42.4)	1,618 (42.7)	
725 (28.0)	340 (28.4)	1,065 (28.1)	
284 (11.0)	122 (10.2)	406 (10.7)	
se			0.087
1,739 (67.1)	761 (63.6)	2,500 (66.0)	
566 (21.8)	283 (23.6)	849 (22.4)	
286 (11.0)	153 (12.8)	439 (11.6)	
			0.706
184 (7.1)	94 (7.9)	278 (7.3)	
252 (9.7)	107 (8.9)	359 (9.5)	
1,601 (61.8)	748 (62.5)	2,349 (62.0)	
554 (21.4)	248 (20.7)	802 (21.2)	
			0.698
227 (8.8)	113 (9.4)	340 (9.0)	
367 (14.2)	161 (13.5)	528 (13.9)	
1,997 (77.1)	923 (77.1)	2,920 (77.1)	
			0.907
1,692 (65.3)	784 (65.5)	2,476 (65.4)	
899 (34.7)	413 (34.5)	1,312 (34.6)	
			0.642
2,037 (78.6)	949 (79.3)	2,986 (78.8)	
554 (21.4)	248 (20.7)	802 (21.2)	
	Training set, n (%) 1,110 (42.8) 725 (28.0) 284 (11.0) 39 1,739 (67.1) 566 (21.8) 286 (11.0) 184 (7.1) 252 (9.7) 1,601 (61.8) 554 (21.4) 227 (8.8) 367 (14.2) 1,997 (77.1) 1,692 (65.3) 899 (34.7) 2,037 (78.6) 554 (21.4)	Training set, n (%)         Testing set, n (%)           1,110 (42.8)         508 (42.4)           725 (28.0)         340 (28.4)           284 (11.0)         122 (10.2)           Se         11739 (67.1)         761 (63.6)           1,739 (67.1)         761 (63.6)           566 (21.8)         283 (23.6)           286 (11.0)         153 (12.8)           184 (7.1)         94 (7.9)           252 (9.7)         107 (8.9)           1,601 (61.8)         748 (62.5)           554 (21.4)         248 (20.7)           227 (8.8)         113 (9.4)           367 (14.2)         161 (13.5)           1,997 (77.1)         923 (77.1)           1,692 (65.3)         784 (65.5)           899 (34.7)         413 (34.5)           2,037 (78.6)         949 (79.3)           554 (21.4)         248 (20.7)	Training set, n (%)Testing set, n (%)All patients, n (%) $1,110 (42.8)$ $508 (42.4)$ $1,618 (42.7)$ $725 (28.0)$ $340 (28.4)$ $1,065 (28.1)$ $284 (11.0)$ $122 (10.2)$ $406 (10.7)$ $39$ $122 (10.2)$ $406 (10.7)$ $39$ $283 (21.6)$ $849 (22.4)$ $286 (11.0)$ $153 (12.8)$ $439 (11.6)$ $184 (7.1)$ $94 (7.9)$ $278 (7.3)$ $252 (9.7)$ $107 (8.9)$ $359 (9.5)$ $1,601 (61.8)$ $748 (62.5)$ $2,349 (62.0)$ $554 (21.4)$ $248 (20.7)$ $802 (21.2)$ $227 (8.8)$ $113 (9.4)$ $340 (9.0)$ $367 (14.2)$ $161 (13.5)$ $528 (13.9)$ $1,692 (65.3)$ $784 (65.5)$ $2,476 (65.4)$ $899 (34.7)$ $413 (34.5)$ $1,312 (34.6)$ $2,037 (78.6)$ $949 (79.3)$ $2,986 (78.8)$ $554 (21.4)$ $248 (20.7)$ $802 (21.2)$

HGSOC, high-grade serous ovarian carcinoma; SDW, separated, divorced, and widowed; LN, lymph node; FIGO, International Federation of Gynecology and Obstetrics.

significant different prognoses for both OS (P<0.001) and CSS (P<0.001) in the training and test cohorts (*Figure 6*), showing the nomogram's good ability for prognostic and risk stratification.

# **Discussion**

Table 1 (continued)

Current European guidelines published in 2019 recommend BRCA genetic testing for all patients with non-mucinous ovarian cancer. In addition, other genes in homologous recombination pathways have been recognized, and biomarkers are now popular in ovarian cancer diagnosis and

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**Figure 2** The LASSO regression used to select prognostic factors for OS and CSS. (A) LASSO coefficient profiles of 11 variables for OS; (B) LASSO cox analysis identified 6 variables for OS; (C) LASSO coefficient profiles of 11 variables for CSS; (D) LASSO cox analysis identified 5 variables for CSS. LASSO, least absolute shrinkage and selection operator; OS, overall survival; CSS, cancer-special survival.

treatment. However, their real effect on the assessment of epithelial ovarian cancer risk is still uncertain (26) and due to their expense, not everybody has access to or can acquire these prognostic tools for decision making. For patients with HGSOC, there is still a lack of widely available, costeffective methods for predicting survival after surgery and chemotherapy. In our study, we identified prognostic risk factors from clinicopathological, demographic, and socioeconomic factors. Then, we developed novel nomograms using these easily accessible factors, with the aim of assessing the 3- and 5-year OS and CSS. The bigger range of threshold probabilities in DCA curves, higher C-index, and consistent calibration curve observed in both the training and test sets indicated better performances of the models compared with the FIGO staging system and the AJCC staging system. Additionally, the nomograms conveniently and successfully stratified patients with HGSOC according to their risk scores.

In our study, 6 independent prognostic factors were identified for OS: marital status, age, LN dissection, tumor size, residual disease, and FIGO stage. These factors also significantly played the same role in CSS, except for marital status. According to research, generally, younger patients are more likely to have a favorable prognosis because they are more likely to have tumors of less aggressive histology, lower grade, and better baseline performance status (11,27). We observed that the older the age, the less favorable the prognosis.

As for separated, divorced, and widowed (SDW) patients, their social support networks may reflect a lack of personal and social support and they appear to have more psychological distress and financial problems compared with non-SDW women (28). Among women at increased ovarian cancer risk, perceived threat was a unique predictor of cancer risk which influenced early performance behavior. This emphasized the close relationship between psychological state and the incidence of ovarian cancer. Our study found that compared with other patients, SDW patients had less favorable survival outcomes in HGSOC (29).

For patients with epithelial ovarian cancer (EOC), systematic lymphadenectomy is an important part of surgical treatment, because LN status is regarded as a significant prognostic factor (30). The GOG defined a 10-lymph-node cutoff as adequate lymphadenectomy criteria (23). In our study, patients with more than 10 LNs removed had better survival. In contrast, in another study, there was no significant survival improvement in advanced ovarian cancer patients with systematic retroperitoneal lymphadenectomy (31).

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Table 2 Multivariate cox analysis of the training cohort based on the results of lasso regression

Variables -	OS	OS		CSS	
	HR (95% CI)	Р	HR (95% CI)	Р	
Marital status					
un-SDW	Reference				
SDW	1.313 (1.120–1.541)	0.001			
Age, years					
<50	Reference		Reference		
50–59	1.110 (0.879–1.402)	0.382	1.422 (1.109–1.823)	0.006	
60–69	1.418 (1.128–1.782)	0.003	1.683 (1.321–2.144)	<0.001	
70–79	1.522 (1.188–1.949)	0.001	1.830 (1.410–2.376)	<0.001	
≥80	1.914 (1.333–2.747)	<0.001	2.506 (1.702–3.691)	<0.001	
LN dissected					
No or examined	Reference		Reference		
1–10	0.895 (0.761–1.052)	0.178	0.877 (0.740–1.038)	0.126	
≥11	0.647 (0.538–0.777)	<0.001	0.677 (0560–0818)	<0.001	
Tumor size, cm					
<2	Reference		Reference		
≥2 and <4	0.795 (0.594–1.063)	0.021	0.853 (0615–1.182)	0.339	
≥4 and <10	0.710 (0.554–0.908)	0.006	0.835 (0.631–1.106)	0.209	
≥10 and <16	0.555 (0.425–0.726)	<0.001	0.671 (0.498–0.904)	0.009	
≥16	0.523 (0.376–0.726)	<0.001	0.697 (0.489–0.995)	0.047	
Residual					
R0	Reference		Reference		
R1	1.422 (1.207–1.676)	<0.001	1.602 (1.351–1.899)	<0.001	
R2	1.409 (10155–1.719)	0.001	1.601 (1.301–1.970)	<0.001	
FIGO stage					
Stage I	Reference		Reference		
Stage II	1.936 (1.047–3.579)	0.035	1.820 (0.934–3.547)	0.078	
Stage III	4.371 (2.604–7.339)	<0.001	4.413 (2.529–7.701)	<0.001	
Stage IV	5.900 (3.476–10.014)	<0.001	6.281 (3.556–11.094)	<0.001	

OS, overall survival; CSS, cancer-special survival; HR, hazard ratio; CI, confidence interval; SDW, separated, divorced, and widowed; LN, lymph node; R0, no residual disease; R1, microscopic residual disease (0–1 cm); R2, macroscopic residual disease (>1 cm); FIGO, International Federation of Gynecology and Obstetrics; OS, overall survival; CSS, cancer-special survival.

Therefore, the role of lymphadenectomy in EOC patients, including HGSOC patients, is still controversial and needs further research.

The extent of metastatic disease and metastasis size has

important significance for the postoperative pathological staging and prognostic evaluation of patients with ovarian cancer. However, there is no definite consensus on the prognostic influence of tumor size. Another potential

А	Points	0 1 2 3 4 5 6 7 8 9 10
		SDW
M	arital status	un-SDW <sub>50-59</sub> 70-79
	Age, years	<50 60–69 ≥80
Turr	ior size, cm	$\geq$ 10 and <16 $\geq$ 2 and <4
	FIGO stage	Stage II Stage II
LN	dissected,n	1-10 $\geq 11$ No or examined
Resid	ual disease	RO R2
	Total points	0 2 4 6 8 10 12 14 16 18 20 22 24 26 28
	3-year OS	0.95 0.9 0.85 0.8 0.75 0.7 0.6 0.5
	5-year OS	0.9 0.85 0.8 0.75 0.7 0.6 0.5
В	Points	0 1 2 3 4 5 6 7 8 9 10
	Age	50-59 70-79 <50 60-69 >80
	Tumor size	$\geq 10 \text{ and } < 16 \geq 2 \text{ and } < 4$ > 16 >4 and <10 <2
	FIGO stage	Stage II Stage IV
		Stage I Stage III
LI	V dissected	1-10
Resid	ual disease	
	Total points	KU K2
:	3-year CSS	0 2 4 6 8 10 12 14 16 18 20 22 24 26 0.95 0.9 0.85 0.8 0.75 0.7 0.6 0.5
:	5-year CSS	0.9 0.85 0.8 0.750.7 0.6 0.5

**Figure 3** Predictive nomograms. (A) Nomogram for predicting 3- and 5-year OS; (B) nomogram for predicting 3- and 5-year CSS. SDW, separated, divorced, and widowed; LN, lymph node; FIGO, International Federation of Gynecology and Obstetrics; R0, no residual disease; R1, microscopic residual disease (0–1 cm); R2, macroscopic residual disease (>1 cm); OS, overall survival; CSS, cancer-special survival.

reason for the inconformity is the histologic type. In ovarian malignant tumors, the significance of the size of the primary tumor has been demonstrated in sex cord-stromal tumors as follows: the smaller the tumor, the better the prognosis (28). However, in our study, we found that the larger the diameter of the primary tumor, the better the prognosis. We considered whether patients with larger sized tumors might be more prone to earlier diagnosis and treatment.

Residual disease is one of the most significant independent predictors of the prognosis of patients with ovarian cancer (10). Among the previously developed prognostic models or nomograms for ovarian cancer, the assessment of residual disease has not been sufficiently detailed (32,33). The difference was significant among the 3 classifications of residual disease in the nomogram.

Nomogram modelling has performed better than conventional staging systems, and researchers propose the nomogram as a promising tool for prognostic prediction (18,34). The nomogram area under the curve (AUC) used to predict the 5-year OS (0.72, 95% CI: 0.68 to 0.76) for all patients with extra-nodal, nasal-type NK/T-cell lymphoma was significantly higher than the AUC of other prognostic tools (34). Another nomogram was generated to predict the 2-year progression-free survival (PFS), 5-year OS, and pelvic recurrence for locally advanced cervical cancer limited to the pelvis, and achieved C-indices of 0.62, 0.64, and 0.73, respectively, which were well calibrated (18). The nomograms mentioned above demonstrated better



**Figure 4** Calibration plots. (A) 3-year and (B) 5-year OS for training cohort; (C) 3-year and (D) 5-year OS for testing cohort; (E) 3-year and (F) 5-year CSS for training cohort; (G) 3-year and (H) 5-year CSS for testing cohort. OS, overall survival; CSS, cancer-special survival.



Figure 5 DCA curve of the nomogram, FIGO stage, and TNM (AJCC) stage. (A,B) 3-year OS DCA curve for training cohort and testing cohort; (C,D) 3-year CSS DCA curve for training cohort and testing cohort. DCA, decision curve analysis; FIGO, International Federation of Gynecology and Obstetrics; TNM, tumor-node-metastasis; AJCC, American Joint Committee on Cancer; OS, overall survival; CSS, cancer-special survival.



**Figure 6** Kaplan-Meier curves. (A,B) OS for patients stratified by the risk stratification system in training cohort and testing cohort; (C,D) CSS for patients stratified by the risk stratification system in training cohort and testing cohort. OS, overall survival; CSS, cancer-special survival.

performance in prediction than did the staging systems. The nomograms also showed better prediction capacity compared with the FIGO staging system (9) and the AJCC (7<sup>th</sup> edition) staging system. Via our models, individual treatment plans and follow-up schedules can be made by integrating risk stratification in patient assessment. It may be feasible to use a prediction model to formulate and perform a realistic follow-up plan.

There were several limitations to this study. Firstly, detailed information on chemotherapy was not provided in the SEER database. The SEER data were also lacking details of tumor recurrence, reoperation, and molecular genetic testing. Secondly, because of the nature of the SEER data, some well-known prognostic factors, such as performance status, presence of ascites, and etc. were not included in our study. This might lead to the relative low C-index. Nomogram with a C-index less than 0.8 was not so good and we still need to build a more accurate model to predict survival in the future. Finally, in the present condition of only achieving internal validation, our models need external validation to confirm their performance.

# Conclusions

We have set up novel and accurate prognostic prediction models based on the most common histologic type of epithelial ovarian cancer (HGSOC). On the basis of the FIGO staging system, incorporating easy-to-obtain clinicopathological features makes our model low-cost and convenient to use. Our models will help to guide clinical decision-making about individual treatment plans and follow-up schedules using accurate assessments.

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#### Footnote

*Reporting Checklist*: The authors have completed the TRIPOD reporting checklist. Available at https://atm. amegroups.com/article/view/10.21037/atm-21-4383/rc

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). No personally identifying information was used in the study, which eliminated the requirement for Institutional Review Board approval or informed patient consent.

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