Am J Cancer Res 2025;15(1):168-181
www.ajcr.us /ISSN:2156-6976/ajcr0160425

Original Article

Pregnancy is associated with the prognosis of ovarian cancer patients with abdominal metastasis

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Received September 9, 2024; Accepted December 6, 2024; Epub January 15, 2025; Published January 30, 2025

Abstract: This study aims to explore a new approach to reduce the recurrence risk and improve the prognosis of ovarian cancer (OC) patients with abdominal metastasis by analyzing the clinical characteristics and prognostic factors. A total of 292 OC patients with abdominal metastasis, treated at Henan Provincial People's Hospital between 2021 and 2023 were included in this retrospective study. Follow-up was conducted for one year to observe the recurrence, with 285 patients completing the observation. The patients were then categorized into relapsing and non-relapsing groups based on whether they experienced a relapse within one-year follow-up. Independent sample t-tests and χ^2 tests were used for inter-group comparison. Both univariate and multivariate logistic regression analyses were utilized to screen factors affecting recurrence. The variance inflation factor (VIF) was used to analyze whether the variables in the model had multicollinearity. Receiver Operating Characteristic (ROC) curves and nomographs were used to construct models for predicting one-year recurrence in OC patients with abdominal metastasis. Area under curve (AUC) of ROC and Hosmer-Lemeshow goodness of fit test were used to evaluate the accuracy of the model. The prediction model was verified by internal verification and external verification. The number of pregnancies, the number of births, diabetes mellitus, tumor diameter, tumor reduction combined with intraperitoneal chemotherapy, CA-125, HE-4, NLR, PLR, MLR showed association with patient recurrence. Logistic regression analysis revealed that lower pregnancy frequency and elevated levels of CA-125, HE-4, PLR and MLR were independent risk factors for increased risk of recurrence. In addition, the nomogram-based model demonstrated strong predictive accuracy for one-year recurrence. OC patients with abdominal metastasis present diverse clinical manifestations, among which fewer pregnancies and elevated levels of CA-125, HE-4, PLR, and MLR may be independent risk factors for increased risk of recurrence. Individualized interventions based on these prognostic factors are essential to reduce risk and enhance patient quality of life.

Keywords: Ovarian cancer, abdominal metastasis, clinical characteristics, prognostic factors

Introduction

Ovarian cancer (OC), a prevalent gynecological malignancy, has long posed a serious threat to women's health [1]. Research shows a continual rise in global disease burden attributed to OC [2], with the OC burden in China surpassing global levels and accelerating in recent years [3]. Beyond invading the ovary itself, OC can also metastasize to other tissues and organs through various pathways [4]. Among these, abdominal metastasis is a particularly common form, where cancerous cells spread through ascites to organs such as intestine, liver, and spleen [5]. The abdominal metastasis results in the formation of ascites, increasing tumor load and causing a series of adverse symptoms like reduced mobility, appetite loss, and fatigue, which greatly diminish patient quality of life [6]. The accumulation of ascites can also lead to reduced tolerance to tumor treatments, protein imbalances, and other complications, further complicating treatment efforts [7, 8]. In addition, abdominal metastasis of OC often signifies advanced disease, and while surgical and chemotherapeutic interventions may improve outcomes, the overall survival rate remains low, with a bleak prognosis [9]. Hence, investigating the clinical characteristics and prognostic factors of abdominal metastasis in OC patients, as

https://doi.org/10.62347/JUJQ9225

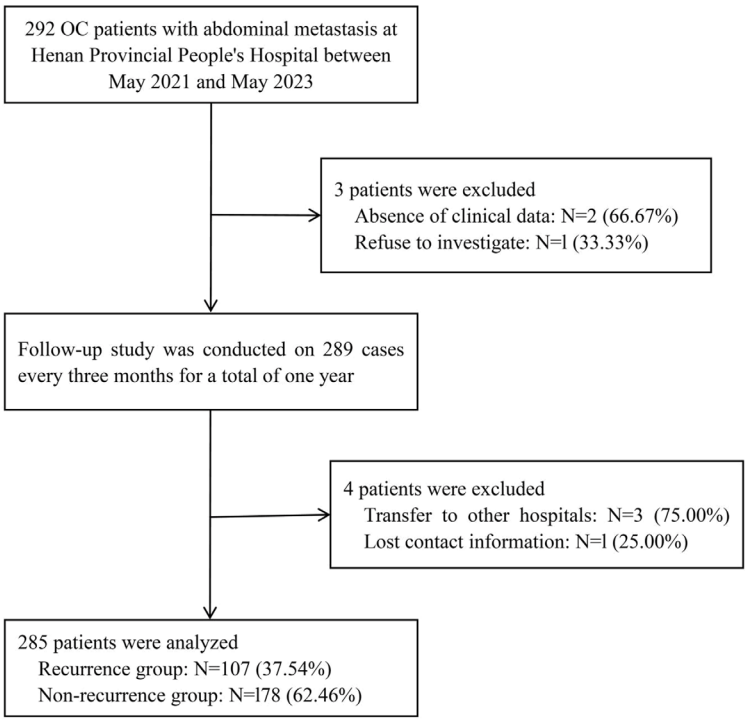

Figure 1. The flow diagram of this study.

well as identifying novel approaches to effectively enhance prognosis, has become a pressing concern for clinicians and researchers.

Current treatment options of OC patients with abdominal metastasis mainly includes surgery, radiotherapy, chemotherapy, immunotherapy, targeted therapy, among other means [10, 11]. Surgery is essential in OC treatment, especially in patients with peritoneal metastases [12]. Radical tumor cell reduction is a preferred choice, aiming to remove as much visible tumor tissue as possible and to reduce overall tumor load [13]. While these treatments can relieve symptoms to some extent, achieving ideal therapeutic outcomes remains challenging due to the high heterogeneity of OC and the complexity of intraperitoneal metastasis [14]. Wang et al. conducted an analysis on 454 patients diagnosed with epithelial OC and discovered that age, histological type, International Federation of Gynecology and Obstetrics (FIGO) stage, and lymph node count correlated with the postoperative survival time [15]. Similarly, Chan et al. identified that CA125 levels were associated with the survival of patients with epithelial OC [16]. Nevertheless, these studies did not specifically focus on the prognosis of OC patients with abdominal metastasis. Vizzielli et al. stated that intraperitoneal spread could significantly influence the prognosis in elderly patients with OC [17]. Therefore, it is of great significance to further investigate the clinical features and prognostic factors of patients with abdominal metastasis of OC to optimize treatment and improve the survival rate of patients.

This retrospective analysis focused on assessing prognosis quality in OC patients with abdominal metastases. Utilizing a large sample size, this study not only analyzed a range of clinical characteristics but also included some serological indicators to comprehensively explore the factors influencing prognosis. The results of this study can assist clinicians more accurately identify crucial prognostic factors in OC patients with peritoneal metastasis, enabling more targeted management strategies. For instance, for patients with a poor prognosis, monitoring and follow-up can be intensified, and treatment regimens can be adjusted promptly to prolong the survival period and enhance the quality of life of patients. This enables doctors to assess patients' conditions with greater accuracy and develop more individualized treatment plans, thereby enhancing both the quality and effectiveness of OC diagnosis and treatment.

Materials and methods

Patient population

This study retrospectively analyzed 285 OC patients with abdominal metastases who were treated in Henan Provincial People's Hospital between May 2021 and May 2023 (**Figure 1**). Inclusion criteria: (a) patients diagnosed with OC by pathological examination; (b) patients with FIGO stage III or IV; (c) age ≥18 years; (d) patients with abdominal metastases confirmed by histological diagnosis; (e) no serious underlying diseases or other cancers. Exclusion

criteria: (a) patients with severe organ failure or other cancers; (b) patients with immune system diseases; (c) patients with uterine fibroids, pelvic inflammatory disease or other serious gynecological diseases. This study was approved by the Ethics Committee of Henan Provincial People's Hospital.

Collection of clinical data

General demographics and clinical information of patients were obtained through direct interviews or the medical record system. Demographic information included age, body mass index (BMI), pregnancy history, and delivery history. Clinical information included underlying disease (hypertension, diabetes, and cardiovascular disease), tumor diameter, FIGO stage (III or IV), pathological type (high-grade serous cancer, non-high-grade serous cancer), differentiation degree of (low, medium, or high), neoadjuvant chemotherapy, satisfactory tumor reduction, abdominal chemotherapy, targeted therapy, among others. In addition, several important serological markers were collected and analyzed, including cancer antigen 125 (CA-125), human epididymal protein 4 (HE-4), alpha-fetoprotein (AFP), albumin (ALB), neutrophil to lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and monocyte to lymphocyte ratio (MLR).

Outcome measures

Relapse is an important marker of OC progression, especially in patients with abdominal metastases [18]. Relapse is closely related to survival, serving as both an indicator for monitoring disease progression and a reference for treatment decisions [19]. Therefore, using relapse as a prognostic evaluation index in this study holds significant practical value for improving the quality of life of patients. Patients included in the study were followed up every three months by telephone or outpatient visit over a one-year follow-up period. Patients were classified into a relapse group if they had a recurrence within one year, and a no recurrence group if they had not (dependent variable assignment: 1, relapsed group; 0, non-relapsed group). Relapse was defined as evidence of OC reoccurring by imaging, elevated tumor markers, clinical symptoms, or histology after a disease-free period following initial treatment, with confirmation that cancer cells had metastasized to one or more sites within the abdominal cavity. Relapse determination was jointly decided by two doctors. The primary outcome of this study was to identify factors influencing recurrence risk in OC patients with abdominal metastasis. The secondary outcomes included differences in baseline clinical characteristics and serological indicators, as well as the development of a clinical prediction model based on recurrence risk factors in the two groups.

Statistical analysis

Quantitative data were presented as mean ± standard deviation, while qualitative data were reported in terms of frequency and percentage. For quantitative data following a normal distribution, the *t*-test was employed to analyze differences between the two groups. Qualitative data were analyzed using the χ^2 test. Univariate and multivariate Logistic regression models were used to identify prognostic factors and calculate odds ratios (ORs) and their 95% confidence intervals (*CI*). Variables with a *P* value <0.2 in univariate Logistic regression were included in the multi-factor Logistic regression analysis, and a backward stepwise regression method was used to construct the model. Nomograms and receiver operating characteristic (ROC) curves were used to construct clinical prediction models. Area under curve (AUC) of ROC, detection acceptability curve (DAC) and Hosmer-Lemeshow goodness-of-fit test were used to assess the model accuracy. The variance inflation factor (VIF) was used calculated to evaluate multicollinearity among variables in the model. For validation, the study applied both internal and external verification. First, the raw data were randomly split into a training set (70%) and an internal validation set (30%) at a ratio of 7:3. Differences between the training and validation sets were analyzed. The external validation set comprised patients subsequently recruited according to the same inclusion, exclusion, and follow-up criteria as the original cohort, resulting in 62 patients (21 in the relapse group and 41 in the non-relapse group). All statistical analyses were performed using SPSS23.0 and R4.2.1 software, with *rms, ResourceSelection, rmda*, *and pROC* packages in the R utilized to build and evaluate the prediction model. *P*<0.05 was considered statistically significant.

Results

Comparison of baseline characteristics between the two groups

A total of 292 OC patients with abdominal metastasis were initially included in the study, of whom 7 were lost to follow-up. Therefore, data from 285 patients were finally analyzed. Patients were divided into a recurrence group (107 patients, 37.54%) and non-recurrence group (178 patients, 62.46%) according to their recurrence within one year. The mean age was 57.14±11.63 years in the recurrence group and 57.13±11.51 years in the non-recurrence group. The mean BMI was 24.78±3.36 kg/m^2 in the recurrence group and 25.11±3.87 kg/m^2 in the non-recurrence group. There were no significant differences in age and BMI between the recurrence and non- recurrence groups (all P>0.05). However, significant differences were found in the number of pregnancies (χ^2=2.025, P=0.044) and births (χ^2=2.145, P=0.033) between the two groups. In addition, the prevalence of diabetes was significantly higher in the recurrence group (χ^2=4.625, P=0.032) (**Table 1**). No other significant differences were found in the basic characteristics between the two groups.

Comparison of clinical information between the two groups

The mean tumor size was (11.83±3.34) cm in the recurrence group, significantly larger than (10.93±3.18) cm in the non- recurrence group (t=3.340, P=0.024). Significant differences were also observed between the two groups in terms of whether they received tumor reduction surgery combined with intraperitoneal chemotherapy (χ^2=4.408, P=0.036). However, no statistical difference was found in FIGO stage, pathological type, histological differentiation, neoadjuvant chemotherapy and targeted therapy between the two groups, as shown in **Table 1**.

Comparison of serological markers between the two groups

The level of CA-125 was 110.52±5.49 U/mL in the recurrence group, significantly higher than 106.34±5.58 U/mL in the non-recurrence group (t=5.958, P<0.001). HE-4 level was 528.64±77.19 μg/L in the recurrence group and 483.48±65.27 μg/L in the non-recurrence group (t=5.276, P<0.001). In addition, significant differences were found in NLR (t=2.234, P=0.026), PLR (t=3.306, P=0.001), and MLR (t=3.413, P=0.001) between the two groups (**Table 1**). However, there was no significant difference in AFP and ALB levels between the two groups.

Univariate Logistic regression analysis between the two groups

Univariate Logistic regression analysis showed that patients with two (*OR*=0.40, 95% *CI*: 0.17-0.94, P=0.034) or three pregnancies (*OR*=0.34, 95% *CI*: 0.15-0.81, P=0.015) had a lower risk of OC recurrence compared to those with one pregnancy. Additionally, patients who underwent tumor reduction surgery combined with intraperitoneal chemotherapy had a significantly reduced recurrence risk compared to those who did not receive this treatment (*OR*=0.53, 95% *CI*: 0.29-0.96, P=0.037). Larger tumor size was also associated with a higher recurrence risk (*OR*=1.09, 95% *CI*: 1.01-1.18, P=0.025). In addition, elevated levels of CA-125 (*OR*=1.14, 95% *CI*: 1.09-1.19, P<0.001), HE-4 (*OR*=1.01, 95% *CI*: 1.01-1.01, P<0.001), NLR (*OR*=1.12, 95% *CI*: 1.01-1.24, P=0.027), PLR (*OR*=1.01, 95% *CI*: 1.01-1.01, P=0.001), and MLR (*OR*=17.78, 95% *CI*: 3.20-98.76, P=0.001) were all associated with an increased risk of OC recurrence (**Table 2**).

Multivariate Logistic regression analysis between the two groups

Multivariate logistic regression analysis, incorporating factors with P<0.20 from the univariate analysis revealed that compared with one pregnancy, two (*OR*=0.35, 95% *CI*: 0.12-0.99, P=0.050) pregnancies was a protective factor for OC prognosis. In addition, higher levels of CA-125 (*OR*=1.14, 95% *CI*: 1.08-1.20, P<0.001), HE-4 (*OR*=1.01, 95% *CI*: 1.01-1.01, P<0.001), PLR (*OR*=1.01, 95% *CI*: 1.01-1.01, P=0.038), and MLR (*OR*=18.19, 95% *CI*: 2.23-148.48, P=0.007) were identified as independent risk factors for disease recurrence. The details are shown in **Table 2**.

Logistic regression analysis in age subgroups

In the age subgroup analysis, the mean age (approximately 57 years) was used as a cutoff

Table 1. Comparison of baseline characteristics between recurrence group and non-recurrence group

Variable	Number/mean		t/χ^2 value	*P* value
	Recurrence group (n=107)	Non-recurrence group (n=178)		
General characteristics				
Age	57.14±11.63	57.13±11.51	0.008	0.994
BMI	24.78±3.36	25.11±3.87	0.735	0.463
Number of pregnancies	2.24±0.72	2.41±0.64	2.025	0.044
Number of births	1.80±0.67	1.97±0.63	2.145	0.033
Family history	23	40	0.037	0.848
Hypertension	29	46	0.055	0.815
Diabetes	22	20	4.625	0.032
Cardiovascular disease	19	26	0.499	0.480
Clinical information				
Tumor size	11.83±3.34	10.93±3.18	3.340	0.024
FIGO staging			0.046	0.831
Phase 3	69	117		
Phase 4	38	61		
Pathological type			1.130	0.288
High grade serous	52	75		
Non-high grade serous	55	103		
Differentiation			1.690	0.194
Poorly	86	131		
Moderately and well	21	47		
Neoadjuvant chemotherapy	78	141	1.498	0.221
Tumor reduction + abdominal chemotherapy	80	151	4.408	0.036
Targeted therapy	16	29	0.090	0.764
Serological information				
CA125	110.52±5.49	106.34±5.88	5.958	0.000
HE4	528.64±77.19	483.48±65.27	5.276	0.000
AFP	60.08±8.68	58.79±8.67	1.226	0.221
ALB	28.30±2.53	28.15±2.18	0.564	0.573
NLR	3.13±2.44	2.49±2.29	2.234	0.026
PLR	227.42±115.39	182.77±107.33	3.306	0.001
MLR	0.39±0.17	0.33±0.13	3.413	0.001

Abbreviation: BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; CA125, Cancer Antigen 125; HE4, Human Epididymis Protein 4; AFP, Alpha-fetoprotein; ALB, Albumin; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio.

value for grouping. In the <57 years subgroup, multivariate Logistic regression results showed that diabetes (*OR*=11.34, 95% *CI*: 2.69-47.79, *P*<0.001), large tumor size (*OR*=1.24, 95% *CI*: 1.05-1.47, *P*=0.010), and high levels of CA-125 (*OR*=1.20, 95% *CI*: 1.10-1.30, *P*<0.001) and HE-4 (*OR*=1.01, 95% *CI*: 1.01-1.02, *P*<0.001) were independent risk factors for OC recurrence. In the ≥57 years subgroup, high levels of CA-125 (*OR*=1.12, 95% *CI*: 1.04-1.22, *P*=0.005), HE-4 (*OR*=1.01, 95% *CI*: 1.10-1.02, *P*<0.001) and MLR (*OR*=74.00, 95% *CI*: 2.58-2125.03, *P*=0.012) were identified as independent risk factors for recurrence. The details are shown in **Table 3**.

Logistic regression analysis in the BMI subgroups

In the BMI subgroup analysis, the average BMI (approximately 25 kg/m^2) was used as a cutoff value for grouping. In the BMI<25 subgroup,

Table 2. Logistic regression analysis of OC patients with abdominal metastasis

Variable	Univariate Logistic analysis		Multivariate Logistic analysis	
	OR (95% *CI*)	*P* value	*OR* (95% *CI*)	*P* value
Number of pregnancies				
Once	Ref		Ref	
Twice	0.40 (0.17-0.94)	0.034	0.35 (0.12-0.99)	0.050
Three times	0.34 (0.15-0.81)	0.015	0.38 (0.13-1.17)	0.092
Four times	0.34 (0.05-2.21)	0.261	0.30 (0.03-3.24)	0.322
Diabetes				
No	Ref		Ref	
Yes	1.63 (0.84-3.15)	0.147	1.29 (0.57-2.93)	0.540
Differentiation				
Poorly	Ref			
Moderately and well	0.68 (0.38-1.22)	0.195	0.76 (0.38-1.55)	0.456
Tumor reduction + abdominal chemotherapy				
No	Ref		Ref	
Yes	0.53 (0.29-0.96)	0.037	0.68 (0.32-1.44)	0.317
Tumor size	1.09 (1.01-1.18)	0.025	1.06 (0.97-1.16)	0.219
CA-125	1.14 (1.09-1.19)	<0.001	1.14 (1.08-1.20)	<0.001
HE4	1.01 (1.01-1.01)	<0.001	1.01 (1.01-1.01)	<0.001
NLR	1.12 (1.01-1.24)	0.027	1.06 (0.94-1.19)	0.360
PLR	1.01 (1.01-1.01)	0.001	1.01 (1.01-1.01)	0.038
MLR	17.78 (3.20-98.76)	0.001	18.19 (2.23-148.48)	0.007

Abbreviation: OC, ovarian cancer; OR, Odds Ratio; CI, Confidence Interval; CA125, Cancer Antigen 125; HE4, Human Epididymis Protein 4; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio.

patients with two (*OR*=0.13, 95% *CI*: 0.02-0.72, *P*=0.019) and three (*OR*=0.14, 95% *CI*: 0.02-0.89, *P*=0.037) pregnancies and tumor reduction combined with abdominal chemotherapy (*OR*=0.23, 95% *CI*: 0.07-0.79, *P*=0.020) were protective factors. High levels of CA-125 (*OR*=1.22, 95% *CI*: 1.11-1.35, *P*<0.001), HE-4 (*OR*=1.01, 95% *CI*: 1.01-1.02, *P*<0.001) and PLR (*OR*=1.01, 95% *CI*: 1.01-1.01, *P*=0.007) were risk factors for recurrence. In the BMI≥ 25 subgroup, neoadjuvant chemotherapy (*OR*= 0.36, 95% *CI*: 0.13-0.99, *P*=0.047) was a protective factor for prognosis in OC patients. However, high levels of CA-125 (*OR*=1.15, 95% *CI*: 1.06-1.24, *P*<0.001), HE-4 (*OR*=1.01, 95% *CI*: 1.01-1.02, *P*=0.005) and MLR (*OR*=356.77, 95% *CI*: 9.12-13959.55, *P*=0.002) were risk factors (**Table 4**).

Construction of clinical prediction model

In this study, five variables including number of pregnancies, tumor size, CA-125, HE-4, and MLR were used to construct a clinical prediction model for one-year recurrence in patients with OC with abdominal metastasis (**Figure 2**). The ROC curve for this prediction model, constructed with these variables demonstrated an AUC of 0.80 (95% CI: 0.73-0.86), indicating good accuracy (**Figure 3A**). The sensitivity and specificity of this prediction model were 0.69 (95% CI: 0.61-0.77) and 0.80 (95% CI: 0.71-0.90), respectively, with an accuracy rate of 0.73 (95% CI: 0.66-0.86) (**Table 5**).

Evaluation of clinical predictive models

The results of AUC showed that the model had strong differentiation ability. The Hosmer-Lemeshow goodness-of-fit test result was 0.395, suggesting that the predicted values were consistent with the actual value, and the model fit well (**Figure 3D**). The Decision Curve Analysis (DCA) further validated the model's clinical value. The DCA curve revealed that, when the threshold probability was 0.0-0.8, the net return rate was greater than 0, indicating that the risk prediction model provides good clinical application value (**Figure 3G**). Furthermore, the VIF values for all variables were less than 5, indicating the absence of multicollinearity in the model.

Table 3. Logistic regression analysis of OC patients with abdominal metastasis in the age subgroups

Variable	Univariate Logistic analysis		Multivariate Logistic analysis	
	OR (95% *CI*)	*P* value	*OR* (95% *CI*)	*P* value
Age <57				
Number of pregnancies				
Once	Ref		Ref	
Twice	0.44 (0.13-1.50)	0.189	0.36 (0.06-2.18)	0.264
Three times	0.32 (0.09-1.15)	0.081	0.39 (0.06-2.64)	0.334
Four times	0.71 (0.04-14.35)	0.826	3.13 (0.03-299.90)	0.624
Diabetes				
No	Ref		Ref	
Yes	4.96 (1.77-13.85)	0.002	11.34 (2.69-47.79)	<0.001
Tumor reduction + abdominal chemotherapy				
No	Ref		Ref	
Yes	0.43 (0.19-1.00)	0.050	0.38 (0.12-1.23)	0.106
Tumor size	1.19 (1.05-1.35)	0.007	1.24 (1.05-1.47)	0.010
CA-125	1.16 (1.08-1.25)	<0.001	1.20 (1.10-1.30)	<0.001
HE4	1.01 (1.01-1.02)	<0.001	1.01 (1.01-1.02)	<0.001
MLR	7.72 (0.78-76.31)	0.080	13.14 (0.45-383.26)	0.134
Age ≥57				
Number of pregnancies				
Once	Ref		Ref	
Twice	0.37 (0.12-1.18)	0.092	0.59 (0.11-3.19)	0.537
Three times	0.37 (0.12-1.17)	0.089	0.88 (0.12-6.37)	0.899
Four times	0.22 (0.02-2.67)	0.236	013 (0.00-5.12)	0.276
Number of births				
Once	Ref		Ref	
Twice	0.46 (0.20-1.06)	0.069	0.50 (0.14-1.76)	0.278
Three times	0.39 (0.14-1.05)	0.063	0.63 (0.12-3.47)	0.598
Differentiation				
Poorly	Ref		Ref	
Moderately and well	0.53 (0.24-1.15)	0.109	0.42 (0.15-1.76)	0.353
Neoadjuvant chemotherapy				
No	Ref		Ref	
Yes	0.53 (0.23-1.23)	0.142	0.60 (0.21-1.76)	0.353
CA-125	1.11 (1.04-1.19)	0.001	1.12 (1.04-1.22)	0.005
HE4	1.01 (1.01-1.01)	<0.001	1.01 (1.01-1.02)	<0.001
NLR	1.18 (1.02-1.35)	0.023	1.17 (0.99-1.39)	0.065
PLR	1.01 (1.01-1.01)	0.010	1.00 (1.00-1.01)	0.302
MLR	53.49 (3.77-758.17)	0.003	74.00 (2.58-2125.03)	0.012

Abbreviation: OC, ovarian cancer; OR, Odds Ratio; CI, Confidence Interval; CA125, Cancer Antigen 125; HE4, Human Epididymis Protein 4; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio.

Validation of clinical predictive models

The results of difference analysis showed that the differences between the internal test set, the external test set and the training set were not statistically significant (data not shown). The internal validation set demonstrated an AUC of 0.77 (95% CI: 0.67-0.87) (**Figure 3B**). The Hosmer-Lemeshow goodness-of-fit test result for internal validation set was 0.629 (**Figure 3E**), confirming that the model fit well. The DCA diagram for internal validation set showed that the model had good application value (**Figure 3H**). The sensitivity and specifi-

Table 4. Logistic regression analysis of OC patients with abdominal metastasis in the BMI subgroups

Variable	Univariate Logistic analysis		Multivariate Logistic analysis	
	OR (95% *CI*)	*P* value	*OR* (95% *CI*)	*P* value
BMI<25				
Number of pregnancies				
Once	Ref		Ref	
Twice	0.23 (0.06-0.91)	0.036	0.13 (0.02-0.72)	0.019
Three times	0.18 (0.04-0.72)	0.016	0.14 (0.02-0.89)	0.037
Four times	0.17 (0.01-2.56)	0.199	0.11 (0.00-4.03)	0.227
Diabetes				
No	Ref		Ref	
Yes	2.17 (0.85-5.52)	0.105	1.25 (0.33-4.68)	0.744
Pathological type				
High grade serous	Ref		Ref	
Non-high grade serous	0.56 (0.29-1.09)	0.56	0.47 (0.18-1.25)	0.130
Differentiation				
Poorly	Ref		Ref	
Moderately and well	0.56 (0.25-1.24)	0.152	0.45 (0.15-1.37)	0.160
Tumor reduction + abdominal chemotherapy				
No	Ref		Ref	
Yes	0.33 (0.14-0.78)	0.012	0.23 (0.07-0.79)	0.020
Tumor size	1.10 (0.99-1.23)	0.082	1.03 (0.88-1.19)	0.734
CA-125	1.16 (1.08-1.24)	<0.001	1.22 (1.11-1.35)	<0.001
HE4	1.01 (1.01-1.02)	<0.001	1.01 (1.01-1.02)	<0.001
NLR	1.21 (1.04-1.41)	0.012	1.36 (1.10-1.67)	0.005
PLR	1.00 (1.00-1.01)	0.063	1.01 (1.01-1.01)	0.007
MLR	7.19 (0.74-69.46)	0.088	2.34 (0.10-57.49)	0.602
BMI≥25				
Neoadjuvant chemotherapy				
No	Ref		Ref	
Yes	0.39 (0.17-0.90)	0.027	0.36 (0.13-0.99)	0.047
Tumor size	1.08 (0.97-1.20)	0.151	1.10 (0.95-1.26)	0.203
CA-125	1.12 (1.05-1.20)	<0.001	1.15 (1.06-1.24)	<0.001
HE4	1.01 (1.01-1.01)	0.001	1.01 (1.01-1.02)	0.005
AFP	1.03 (0.99-1.08)	0.149	1.02 (0.97-1.08)	0.394
PLR	1.01 (1.01-1.01)	0.010	1.00 (1.00-1.01)	0.239
MLR	57.03 (3.98-817.85)	0.003	356.77 (9.12-13959.55)	0.002

Abbreviation: OC, ovarian cancer; OR, Odds Ratio; CI, Confidence Interval; CA125, Cancer Antigen 125; HE4, Human Epididymis Protein 4; AFP, Alpha-fetoprotein; ALB, Albumin; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; MLR, Monocyte-to-Lymphocyte Ratio.

city of internal validation set were 0.74 (95% CI: 0.62-0.86) and 0.61 (95% CI: 0.45-0.77) (**Table 3**), respectively.

For the external validation set, the AUC was 0.85 (95% CI: 0.75-0.96) (**Figure 3C**). The Hosmer-Lemeshow goodness-of-fit test for external validation set was 0.848 (**Figure 3F**). The DCA plot showed favorable intervention return within the range of 0.1-0.8 (**Figure 3I**). The sensitivity and specificity of external validation were 0.83 (95% CI: 0.71-0.94) and 0.81 (95% CI: 0.64-0.98), respectively (**Table 5**).

Discussion

Ovarian cancer (OC) is a malignant tumor that originates in ovarian tissue and can spread to

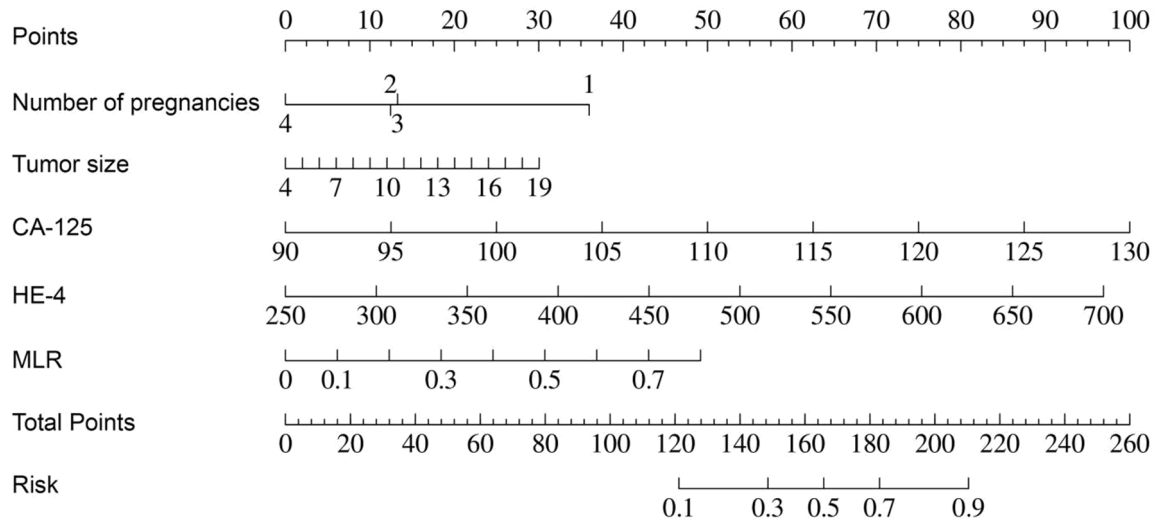

Figure 2. Nomogram for predicting disease relapse in OC patients with abdominal metastasis.

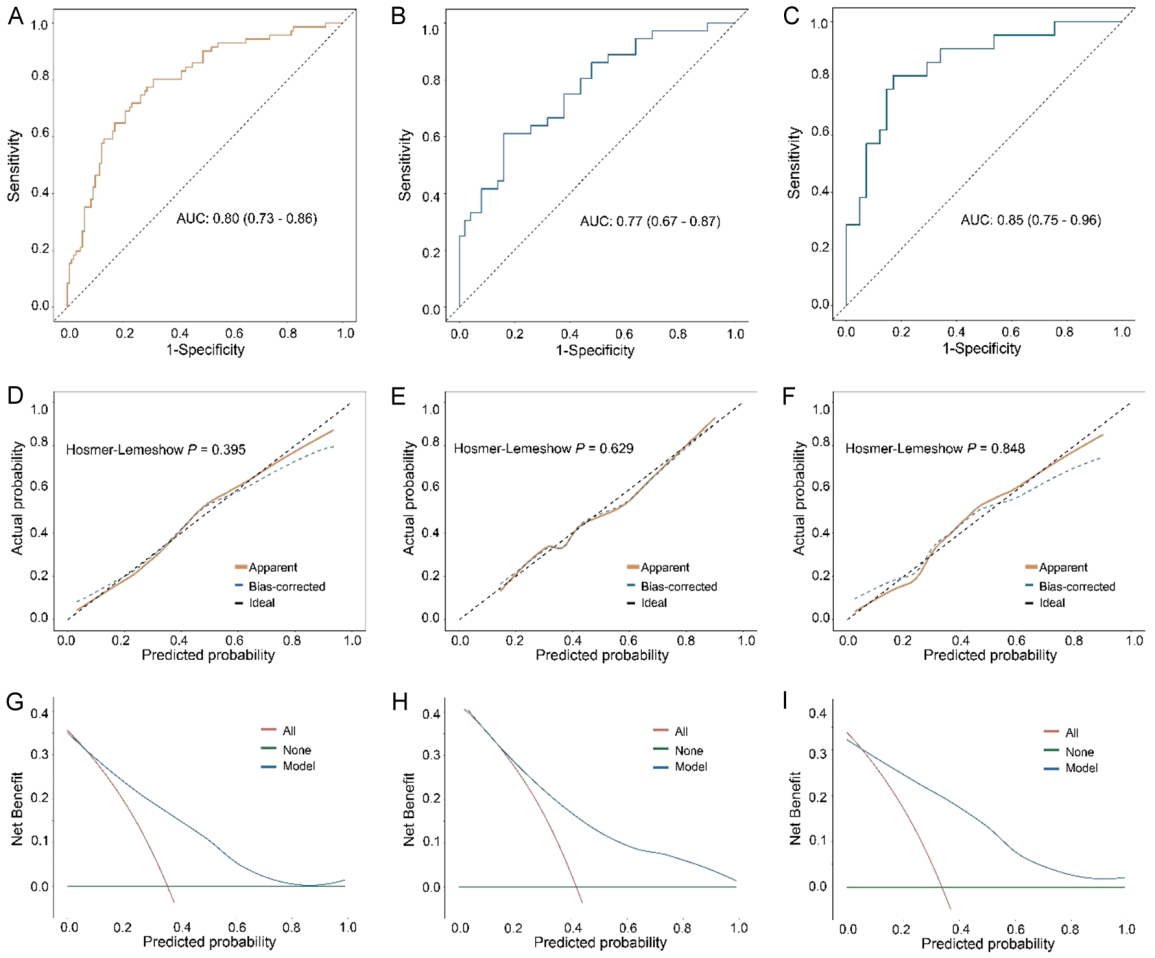

Figure 3. ROC curves, calibration curves, and DCA curves for training sets (A, D, G), internal validation sets (B, E, H), and external validation sets (C, F, I). ROC, Receiver Operating Characteristic; DCA, Decision Curve Analysis.

Table 5. Performance metrics of the predictive model across training, internal validation, and external validation sets

Data	AUC (95% CI)	Accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	cut off
Training set	0.80 (0.73-0.86)	0.73 (0.66-0.79)	0.69 (0.61-0.77)	0.80 (0.71-0.90)	0.86 (0.80-0.93)	0.59 (0.49-0.69)	0.323
Internal validation set	0.77 (0.67-0.87)	0.69 (0.58-0.78)	0.74 (0.62-0.86)	0.61 (0.45-0.77)	0.73 (0.60-0.85)	0.63 (0.47-0.79)	0.323
External validation set	0.85 (0.75-0.96)	0.82 (0.70-0.91)	0.83 (0.71-0.94)	0.81 (0.64-0.98)	0.89 (0.80-0.99)	0.71 (0.53-0.89)	0.373

Abbreviation: AUC, Area under the Curve; PPV, Positive Predictive Value; NPV, Negative Predictive Value.

other parts of the body as the disease progresses [20]. Abdominal metastasis, as one of the most common forms of OC metastasis, can cause direct damage to abdominal organs and lead to various complications, increasing the difficulty of treatment [21-23]. Therefore, accurately identifying prognostic factors and predicting patient outcomes is of great importance for the individualized, comprehensive treatment and for improving prognosis. In this study, the general, clinical, and serological characteristics of 285 OC patients with abdominal metastasis were retrospectively analyzed, and the factors affecting patient prognosis were comprehensively examined.

This study found a significant correlation between the number of pregnancies and OC prognosis, potentially linked to hormonal changes during pregnancy. Previous studies have also reported that changes in hormone levels during pregnancy, particularly in estrogen and progesterone, may affect the activity of OC cells [24]. Novichkov et al. reported that progesterone receptor was a favorable prognostic factor in OC patients [25]. Similarly, a review by Liu et al. found infertility to be an important prognostic risk factor for OC patients [26]. Additionally, Camilla Skold et al. found that high-grade serous OC patients with a history of menorrhagia exhibit greater progesterone receptor expression, suggesting that pregnancy may have a lasting impact on OC development [27]. Changes in estrogen and progesterone levels during pregnancy may help reduce certain risk factors for OC or promote the health of ovarian tissue, though more in-depth research is needed to confirm this hypothesis. During pregnancy, a woman's immune system also adapts to accommodate the fetus [28], increasing immune tolerance and activating immune cells. This immune regulation may help reduce the escape and spread of OC cells, thereby reducing the risk of recurrence [29]. Its immunological mechanism needs further investigation.

This study also found that OC patients with diabetes were more likely to relapse, aligning with previous study. Lee et al. found a significant association between diabetes and an increased risk of OC [30]. Diabetes was significantly associated with increased mortality in OC patients [31]. Diabetes may lead to elevated blood sugar, which in turn causes molecular changes, such as increased oxidative stress and inflammation that favor tumor growth [32]. Moreover, some of these diabetes-induced changes may be irreversible, potentially promoting cancer progression even when blood sugar levels are controlled [33]. OC patients with diabetes face additional treatment challenges, as they have to control blood sugar and cancer treatment simultaneously. This dual management can complicate treatment options, affecting treatment effectiveness and overall patient prognosis. Additionally, Zhao et al. found through a retrospective study that larger tumor size is associated with a poorer prognosis in OC patients, which is consistent with the findings of this study [34]. Larger tumors tend to be more aggressive and metastatic, making them more difficult to treat. In addition, previous studies have found a significant correlation between tumor reduction surgery and increased survival rates in patients with advanced OC [35]. This approach not only removes as much tumor tissue as possible, reducing tumor load, but also enables the direct delivery of chemotherapy into the abdominal cavity. This high concentration drug environment in the metastasis area enhances the efficacy of chemotherapy. These findings suggest that tumor reduction combined with intraperitoneal chemotherapy has substantial clinical value for improving the prognosis of patients with advanced OC.

This study also found that elevated levels of CA-125, HE-4, PLR, and MLR were associated with an increased risk of OC recurrence. CA-125 and HE-4 are commonly used biomarkers for monitoring disease progression and evaluating prognosis in OC patients, and their elevated levels often reflect aggressive tumor behaviors, such as accelerated growth and enhanced aggressiveness [36]. The rise in PLR may be related to the inflammatory response caused by the tumor [37]. Tumor cells may release thrombopoietic factors that stimulate thrombocytosis, promoting tumor growth and angiogenesis. As for MLR, previous studies have shown that monocytes in the tumor microenvironment can differentiate into macrophages with tumor promoting activity (M2 macrophages), which can secrete cytokines and growth factors to facilitate tumor cell proliferation, migration and invasion [38]. In addition, a high MLR may indi-

cate an immune imbalance, with a relative decrease in lymphocytes, which weakens the immune system's ability to detect and clear cancer cells, thereby increasing the risk of recurrence [39]. The precise mechanism by which these serological markers influence OC prognosis deserves further study.

Of course, there are some limitations to this study. First, the single source of cases restricts the generalizability of the results. Second, the retrospective design may introduce selection and information biases that could affect the study findings. In addition, retrospective studies may have residual confounding factors that are difficult to completely eliminate during analysis, thereby affecting the accuracy of causal inference. Finally, the nomogram model constructed in this study needs further validation and improvement.

Conclusion

In conclusion, fewer pregnancies and elevated levels of CA-125, HE-4, PLR, and MLR are independent risk factors for increased risk of recurrence. In addition, the clinical prediction model constructed in this study has a high predictive value. These findings are clinically significant, providing insights into OC characteristics, facilitating early identification and intervention for high-risk patients, and supporting personalized treatment approaches.

Disclosure of conflict of interest

None.

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