Original Article

The development and validation of a tumor-specific death predictive nomogram in patients with ovarian cancer: a cohort study

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Background: Ovarian cancer has a high mortality rate. Accurate identification of risk factors for mortality is crucial to improve treatment strategies. Regretfully, prognostication tools are limited. In recent years, quantitative parameters of contrast enhanced ultrasound have shown economic, reproducible, and highly accurate advantages in predicting the prognosis of ovarian cancer patients. The purpose of this study was to develop a nomogram prediction model for the oncological outcome of patients with ovarian cancer based on quantitative parameters of contrast-enhanced ultrasound.

Methods: Data from 357 patients with ovarian cancer admitted to The Fourth People's Hospital of Zhenjiang from January 2018 to December 2019 were retrospectively collected and constructed the training set. Data from 153 cases admitted to The People's Hospital of Zhaoyuan during the same period were collected and constructed the validation set. All patients were treated with primary cytoreductive surgery, and were followed up for 5 years after surgery. The differences in clinical characteristics and quantitative parameters of contrast-enhanced ultrasound were compared between patients who passed away within 5 years and those which did not.

Results: Peak systolic velocity (PSV), stage III, poor differentiation, and ascites were independent risk factors for tumor-specific mortality in patients with ovarian cancer, with their relative risk being 2.011 (95% confidence interval: 1.680–2.407), 13.480 (95% confidence interval: 4.540–40.022), 2.997 (95% confidence interval: 1.206–7.452), and 2.997 (95% confidence interval: 1.206–7.452), respectively. Time to peak (TTP) was a protective factor of tumor-specific mortality in patients with ovarian cancer, with a relative risk of 0.800 (95% confidence interval: 0.731–0.875). The area under the receiver operating characteristic (ROC) curve in the training set was 0.948 (95% confidence interval: 0.926–0.969), and the area under the ROC curve in the validation set was 0.860 (95% confidence interval: 0.802–0.917).

Conclusions: The nomogram prediction model for prognosis of patients with ovarian cancer based on quantitative parameters of contrast-enhanced ultrasound has good efficacy and reliability.

Keywords: Ovarian cancer; contrast-enhanced ultrasound; tumor-specific mortality; predictive models

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Introduction

Ovarian cancer is not uncommon, and ranks the fifth highest mortality rate among female malignant tumors (1). The reported mortality rate of ovarian cancer is higher than 50% (2), and despite some therapeutic improvements, the mortality rate of ovarian cancer remains high. Accurate classification of patients with ovarian cancer to identify those at high risk of postoperative mortality can contribute to the development of new treatment strategies. Although scholars have been continuously researching predictive models for ovarian cancer prognosis, previous studies have shown low predictive efficacy and high prices (3,4). In a study that included 478 patients with ovarian cancer, Barlin *et al.* constructed a nomogram prediction model for patients with ovarian cancer to predict the 5-year mortality post-surgical resection (5). More recently, quantitative parameters of contrast-enhanced ultrasound have demonstrated value for diagnosis and prognostication of patients with ovarian cancer (6,7).

We hypothesized that the addition of prognostic variables to the nomogram prediction model may improve its accuracy and thus potentially improve the ability of clinicians to ascertain the prognosis of patients diagnosed with ovarian cancer. Herein, we describe the construction a nomogram prediction model based on quantitative parameters of contrast-enhanced ultrasound, for predicting the long-term prognosis of patients with ovarian cancer. We present this article in accordance with the TRIPOD reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-2025-208/rc).

Highlight box

Key findings

- Quantitative parameters of contrast-enhanced ultrasound are valuable in predicting the long-term prognosis of patients with ovarian cancer.

What is known and what is new?

- Accurate identification of risk factors of postoperative ovarian cancer-related mortality is critical for the development of better treatment strategies.
- The nomogram prediction model for the 5-year survival of patients with ovarian cancer based on quantitative parameters of contrast-enhanced ultrasound has good accuracy and reliability.

What is the implication, and what should change now?

- The nomogram prediction model can be used to identify patients with ovarian cancer at high risk of 5-year mortality. This tool should be validated in other datasets for better delineation of its role.

Methods

General information

Data from 357 patients with ovarian cancer admitted to The Fourth People's Hospital of Zhenjiang from January 2018 to December 2019 were retrospectively collected as the training set, and 153 patients with ovarian cancer admitted to The People's Hospital of Zhaoyuan during the same period were collected as the validation set. The inclusion criteria were the following: (I) histologically proven ovarian cancer; (II) age ≥18 years; (III) administration of surgical treatment in The Fourth People's Hospital of Zhenjiang; and (IV) preoperative contrast-enhanced ultrasound. Exclusion criteria were as follows: (I) concurrent second primary malignancy; (II) recurrent ovarian cancer; (III) distant metastasis; (IV) administration of neoadjuvant chemoradiotherapy, targeted therapy, or immunotherapy before admission; and (V) loss to follow-up. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. This study was approved by the Ethics Committee of The Fourth People's Hospital of Zhenjiang (No. 20250006) and The People's Hospital of Zhaoyuan was informed and agreed with this study. The requirement for individual consent was waived due to the retrospective nature of the analysis. The treatment for ovarian cancer was administered according to the accepted guidelines (8).

Sample size estimation

It was required to have at least 20 samples corresponding to one variable for constructing a prediction model; and it was expected to include 5 independent variables. The expected mortality rate was 30%, so the minimum sample size was: n=[(5×20)/30%]=333.

Data collection

Data on age, body mass index, International Federation of Gynecology and Obstetrics (FIGO) staging, human epididymal protein 4, quantitative parameters of contrast-enhanced ultrasound [resistance index (RI), pulsatility index (PI), peak systolic velocity (PSV), arrival time (AT), and time to peak (TTP)], pathological type, grade of nuclear differentiation, and the presence of ascites were collected. Additionally, patients were followed for at least 5 years through outpatient visits once every 6 months to enable the collection of the information regarding tumor-specific death events.

Examination method

Ultrasound examination was performed using the LOGIQ S8 device (GE HealthCare, Chicago, IL, USA). For ultrasound examination, patients were required to have an empty blader, and vaginal ultrasound examination was performed at a probe frequency of 5–9 MHz. The optimal section of the tumor was selected, and the blood flow parameters (RI, PI, and PSV) of the tumor site were observed and calculated via ultrasound imaging technology after the blood flow image was stabilized. A contrast-enhanced ultrasound mode was then adopted, and a suspension consisting of 25 mg of sulfur hexafluoride microbubbles and 5 mL of normal saline was prepared and rapidly injected through the cubital vein. Contrast agent distribution and lesion enhancement were observed and recorded in real time. The AT and TTP were calculated via software of the LOGIQ S8 device.

Statistical analysis

Continuous data were expressed as the mean ± standard deviation, with the independent samples *t*-test being used to analyze the differences between groups. Count data were expressed as numbers and percentages, with the Chi-squared test being used to analyze the differences between two groups. Multivariate logistics regression analysis was used to analyze the risk factors of tumor-specific mortality in patients with ovarian cancer within 5 years after surgery. SPSS 26.0 (IBM Corp., Armonk, NY, USA) was used to complete data analysis, with $P<0.05$ indicating a statistically significant difference (two-sided). R v. 4.0.3 statistical software (The R Foundation of Statistical Computing) was used to construct and validate a prediction model for tumor-specific mortality in patients with ovarian cancer within 5 years after surgery.

Results

Patient inclusion

Of 672 patients, 162 (24.11%) were excluded because they also met the exclusion criteria; consequently, 510 patients with ovarian cancer were ultimately included in the study, including 357 (70.00%) in the training set and 153 (30.00%) in the validation set. According to whether the patients had tumor-specific death, the training set was divided into a death group (n=122, 34.17%) and a control group (n=235, 65.83%). The flowchart of patient inclusion is provided in *Figure 1*.

Comparison of general clinical characteristics between the two datasets

Upon comparison of the training and validation datasets, there were no statistically significant differences in age, body mass index, human epididymal protein 4, RI, PI, PSV, AT, TTP, FIGO stage, pathological type, grade of nuclear differentiation, ascites, or 5-year tumor-specific mortality between the two groups ($P>0.05$) (*Table 1*).

Comparison of the primary clinical characteristics of the death group and the control group in the training set

There were statistically significant differences in human epididymal protein 4, PSV, TTP, FIGO stage, tumor cell differentiation degree, and ascites between the two groups (*Table 2*).

Risk factors for cancer-specific mortality in patients with ovarian cancer of the training set within 5 years after surgery

Multivariate logistic regression analysis showed that PSV, FIGO stage III, poor differentiation, and ascites were independent risk factors for tumor-specific mortality in patients with ovarian cancer within 5 years after surgery, with relative risks of 2.011 (95% confidence interval: 1.680–2.407), 13.480 (95% confidence interval: 4.540–40.022), 2.997 (95% confidence interval: 1.206–7.452), and 3.652 (95% confidence interval: 1.253–10.640), respectively. TTP was a protective factor for tumor-specific mortality in patients with ovarian cancer within 5 years after surgery, with a relative risk of 0.800 (95% confidence interval: 0.731–0.875) (*Table 3*).

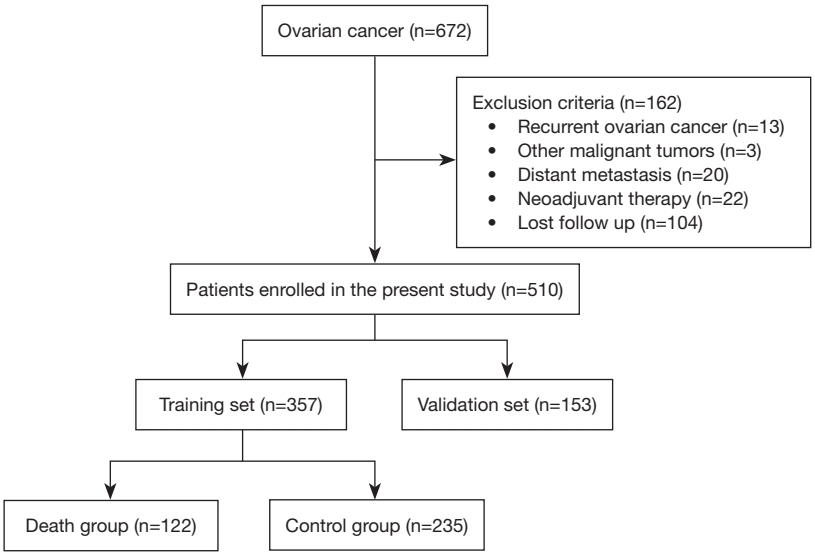

Figure 1 Flowchart of patient inclusion.

Table 1 Comparison of the general clinical characteristics between the two datasets

Variable	Training set (n=357)	Validation set (n=153)	t/χ^2 value	P value
Age (years)	59.10±12.49	58.18±12.28	0.767	0.44
Body mass index (kg/m^2)	24.60±3.77	24.57±3.97	0.096	0.92
Human epididymal protein 4 (pmol/L)	255.36±120.85	266.22±122.84	0.925	0.36
RI	0.41±0.07	0.41±0.06	0.109	0.91
PI	0.65±0.14	0.64±0.14	0.383	0.70
PSV (cm/s)	21.14±3.94	20.83±3.89	0.820	0.41
AT (s)	13.61±2.91	13.75±2.85	0.501	0.62
TTP (s)	23.76±5.04	23.54±4.94	0.457	0.65
FIGO stage			0.107	0.95
I	127 (35.57)	53 (34.64)		
II	171 (47.90)	73 (47.71)		
III	59 (16.53)	27 (17.65)		
Type of pathology			0.108	0.74
Epithelial ovarian cancer	292 (81.79)	127 (83.01)		
Sex cord stromal tumor	65 (18.21)	26 (16.99)		
Degree of differentiation			0.009	0.93
Poor differentiation	76 (21.29)	32 (20.92)		
Medium-to-high differentiation	281 (78.71)	121 (79.08)		
Ascites	46 (12.89)	22 (14.38)	0.207	0.65
5-year tumor-specific mortality	122 (34.17)	56 (36.60)	0.278	0.60

Data are presented as n (%) or mean ± standard deviation. AT, arrival time; FIGO, International Federation of Gynecology and Obstetrics; PI, pulsatility index; PSV, peak systolic velocity; RI, resistance index; TTP, time to peak.

Table 2 Comparison of the primary clinical characteristics of the death group and the control group in the training set

Variable	Death group (n=122)	Control group (n=235)	t/χ^2 value	P value
Age (years)	58.32±12.44	59.51±12.52	0.854	0.39
Body mass index (kg/m^2)	24.56±3.58	24.63±3.88	0.162	0.87
Human epididymal protein 4 (pmol/L)	282.58±125.73	241.22±116.00	3.104	0.002
RI	0.41±0.07	0.41±0.07	0.395	0.69
PI	0.64±0.14	0.65±0.14	0.832	0.41
PSV (cm/s)	24.73±3.31	19.27±2.78	16.463	<0.001
AT (s)	13.67±3.06	13.58±2.83	0.252	0.80
TTP (s)	21.14±4.07	25.12±4.96	7.624	<0.001
FIGO stage			59.893	<0.001
I	14 (11.48)	113 (48.09)		
II	69 (56.56)	102 (43.40)		
III	39 (34.17)	20 (8.51)		
Type of pathology			2.272	0.13
Epithelial ovarian cancer	105 (86.07)	187 (79.57)		
Sex cord stromal tumor	17 (13.93)	48 (20.43)		
Degree of differentiation			10.751	0.001
Poor differentiation	38 (31.15)	38 (16.17)		
Medium-to-high differentiation	84 (68.85)	197 (83.83)		
Ascites	29 (23.77)	17 (7.23)	19.564	<0.001

Data are presented as n (%) or mean ± standard deviation. AT, arrival time; FIGO, International Federation of Gynecology and Obstetrics; PI, pulsatility index; PSV, peak systolic velocity; RI, resistance index; TTP, time to peak.

Table 3 Analysis of risk factors for tumor-specific mortality in patients with ovarian cancer 5 years after surgery

Variable	B value	Standard error	Wald value	P value	Relative risk (95% CI)
Human epididymal protein 4	0.002	0.002	2.130	0.14	1.002 (0.999–1.005)
PSV	0.699	0.092	58.040	<0.001	2.011 (1.680–2.407)
TTP	–0.223	0.046	23.874	<0.001	0.800 (0.731–0.875)
FIGO III stage	2.601	0.555	21.947	<0.001	13.480 (4.540–40.022)
Poor differentiation	1.098	0.465	5.581	0.02	2.997 (1.206–7.452)
Ascites	1.295	0.546	5.635	0.02	3.652 (1.253–10.640)
Constant	–12.282	2.097	34.291	<0.001	–

CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; PSV, peak systolic velocity; TTP, time to peak.

Construction and validation of a cancer-specific mortality prediction model for patients with ovarian cancer within 5 years after surgery

R v. 4.0.3 statistical software was used to construct and validate the model, and the outcome was 5-year tumor-specific death. The nomogram, receiver operating characteristic (ROC) curves, and calibration curves were drawn. The area under the ROC curve in the training set was 0.948 (95% confidence interval: 0.92–0.96), while the area under the ROC curve in the validation set was 0.86 (95% confidence interval: 0.80–0.91). The model was subjected to the Hosmer-Lemeshow goodness-of-fit test in

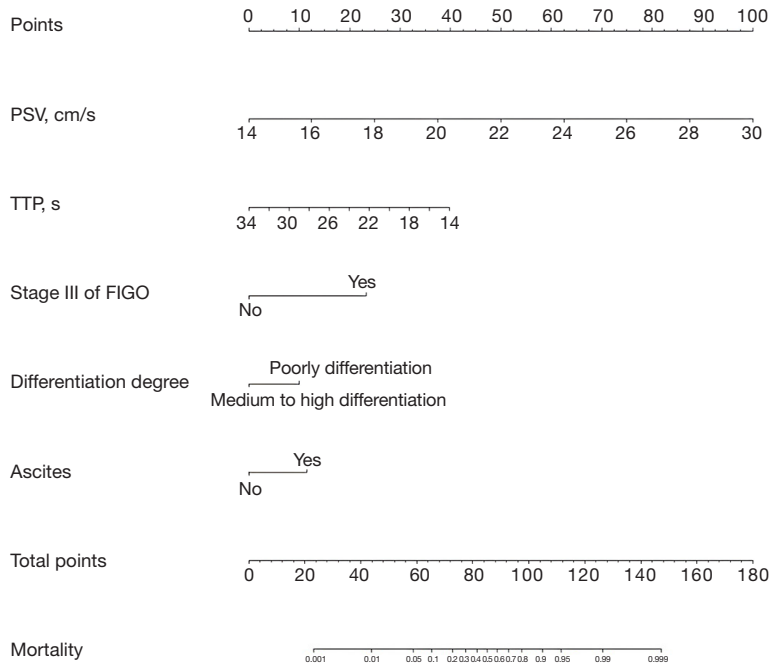

Figure 2 Nomogram of a 5-year tumor-specific mortality prediction model for patients with ovarian cancer. FIGO, International Federation of Gynecology and Obstetrics; PSV, peak systolic velocity; TTP, time to peak.

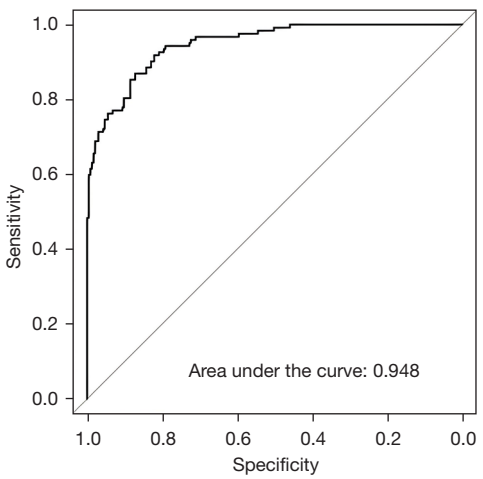

Figure 3 Predictive value of the prediction model for 5-year tumor-specific mortality in patients with ovarian cancer (training set).

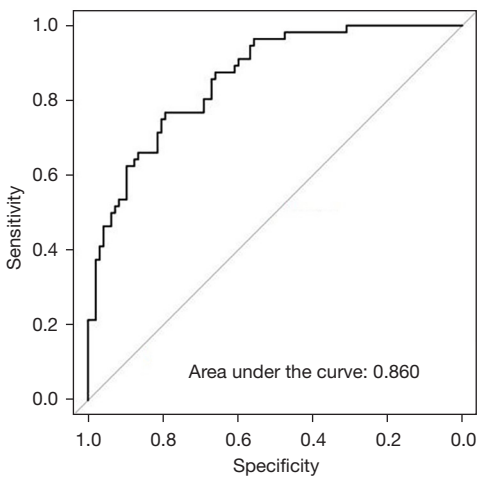

Figure 4 Predictive value of the prediction model for 5-year tumor-specific mortality in patients with ovarian cancer (validation set).

the validation set, the Chi-squared value was 18.2 (P=0.18) (*Figures 2-6*).

Discussion

Ovarian cancer is the leading cause of death among gynecologic malignancies and the fifth most common cause of cancer death in women, with a five-year survival rate of approximately 50% (9). Upon investigation of clinical, pathological, and radiological features associated with poor prognosis, we found that PSV, FIGO stage III, poor differentiation, and ascites were independent risk factors for cancer-specific mortality within 5 years after surgery in patients with ovarian cancer (P<0.05). A radiological feature,

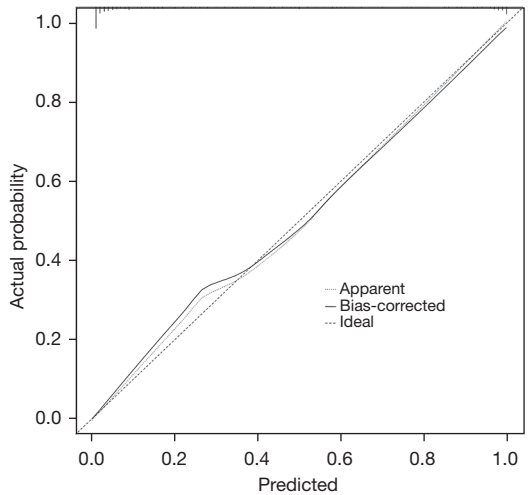

Figure 5 Calibration curve of a 5-year tumor-specific death prediction model for patients with ovarian cancer (training set).

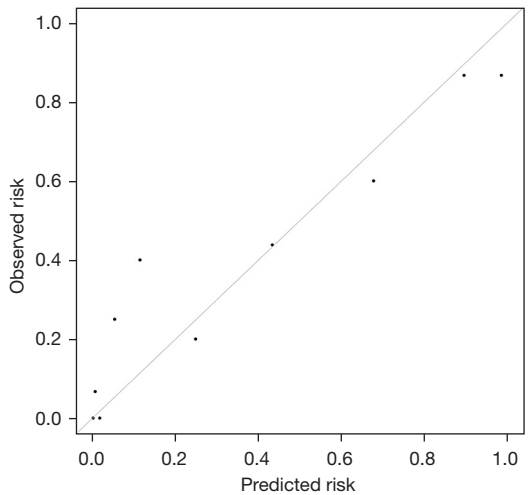

Figure 6 Calibration curves of a 5-year tumor-specific death prediction model in patients with ovarian cancer (validation set).

TTP, was associated with better prognosis, and therefore lower the 5-year cancer-specific mortality ($P<0.05$). We created a prediction model based on relevant risk factors, which was efficacious and consistent in predicting cancer-specific death in patients with ovarian cancer within 5 years after surgery.

FIGO staging is the standard staging system used for gynecological tumors set by the FIGO for cervical, endometrial, and ovarian cancer. FIGO staging has been widely implemented in the classification of ovarian cancer, and studies have confirmed that higher staging is associated with poor long-term prognosis in patients with ovarian cancer (10,11). Additionally, according to the microscopic morphology, growth rate, and degree of malignancy of tumor cells, tumor cells can be divided into poor, medium, and high differentiation, with a lower grade of nuclear differentiation corresponding to a higher degree of malignancy and a higher mortality rate (12). In terms of clinical presentation, ascites is a common comorbidity of ovarian cancer and is mainly caused by ovarian cancer cells infiltrating surrounding tissues and blood vessels, causing fluid to leak from the blood vessels and lymphatic system into the abdominal cavity and resulting in ascites (13-15). Therefore, while still curable, patients with ovarian cancer with ascites are often at locally advanced stage, and the mortality rate of these patients is high (16,17). In addition to the above clinical-pathological features, we revealed that quantitative parameters of contrast-enhanced ultrasound such as PSV and TTP were associated with cancer-specific mortality within 5 years in patients with ovarian cancer. Contrast-enhanced ultrasonography is a technique that uses contrast agents to enhance the backscattered echo and thus significantly improves the resolution, sensitivity, and specificity of ultrasound diagnosis. Contrast-enhanced ultrasound can also determine the degree of malignancy of tumors by observing the blood flow signal of tumor cells, which correlates with growth rate and metastatic potential (18-20). The application of contrast-enhanced ultrasound in patients with ovarian cancer has gradually become more common and it plays an important role in the diagnosis and assessment (7). The higher the PSV and the smaller the TTP are, the richer the tumor blood flow signal, which in turn increases the risk of tumor growth and metastasis, resulting in an increased risk of death.

Because diseases are often affected by multiple factors (21), the use of a single biological indicator to predict the prognosis of patients often does not fully capture the complexity and heterogeneity of diseases, especially for ovarian cancer. Therefore, numerous types of prediction models have been developed, among which the nomogram has emerged as one of the most commonly used clinical prediction models, due to its advantages of intuitive and simple use for predicting the prognosis of patients with different diseases (22,23). In order to more accurately assess the long-term prognosis of patients with ovarian cancer, we also established and validated a 5-year tumor-specific mortality prediction model. We found that the model had good efficacy. In

Barlin *et al.*'s study, a prediction model for ovarian cancer mortality was also established (5). In Sun *et al.*'s study, a prediction model for the prognosis of ovarian cancer patients was also constructed based on the SEER database, and the influencing factors of prognosis, such as race, age, histological grade, and FIGO stage, were determined, and the prediction model constructed according to the relevant influencing factors was valuable for predicting the prognosis of patients, with an area under the curve of 0.752 (24). The predictive values of the models constructed in previous studies were lower when compared with the model presented herein (5,24). This may be due to the incorporation of ultrasound quantitative parameters in the present study, which further improved the performance of the model.

Limitations

This study employed a retrospective design, and the efficacy of this model needs to be further confirmed in larger-sample, multicenter clinical studies. Moreover, the expression of Breast Cancer Susceptibility Gene and other factors in patients may have an impact on their prognosis, but we were unable to study these factors. We could not account for the different chemotherapy protocols given and this should also be acknowledged. In addition, compared to patients with FIGO stage I or II, patients with stage III have a higher mortality rate. However, due to the relatively small number of stage III patients, we were unable to develop a subgroup model.

Conclusions

The nomogram prediction model for the 5-year mortality rate of patients with ovarian cancer based on quantitative parameters of contrast-enhanced ultrasound demonstrated excellent performance.

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None.

Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-2025-208/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-2025-208/dss

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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 and its subsequent amendments. This study was approved by the Ethics Committee of The Fourth People's Hospital of Zhenjiang (No. 20250006) and The People's Hospital of Zhaoyuan was informed and agreed with this study. The requirement for individual consent was waived due to the retrospective nature of the analysis.

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