Development and Validation of Nomograms to Predict Lung Metastases in Patients with Ovarian Cancer: A Large Cohort Study

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Research

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Abstract

Background Lung metastasis, an independent risk factor affecting the prognosis of patients with ovarian cancer, is associated with poor survival. We tried to develop and validate a nomogram to predict the risk of lung metastases in newly diagnosed patients with ovarian cancer.

Methods Patients diagnosed with ovarian cancer from the surveillance, epidemiology and final results (SEER) database between 2010 and 2015 were retrospectively collected. The model nomogram was built based on logistic regression. The consistency index (C-index) was used to evaluate the discernment of the lung metastasis nomogram. Calibration plots was drawn to analyze the consistency between the observed probability and predicted probability of lung metastases in patients with ovarian cancer. The Kaplan-Meier method was used to estimate the overall survival rate, and the influencing factors were included in the multivariate Cox regression ($P < 0.05$) to analyze the independent prognostic factors of lung metastases.

Results A total of 16,059 eligible patients were randomly divided into training ($n = 11242$) and validation cohort ($n = 4817$). AJCC T, N stage, bone metastases, brain metastases and liver metastases were evaluated as predictors of lung metastases. Finally, a nomogram was constructed. The nomogram based on independent predictors was well calibrated and showed good discriminative ability. The C index is 0.761 (0.736-0.787) for the training cohort and 0.757-0.718-0.795 for the validation cohort. The overall survival rate of ovarian cancer patients with lung metastases was reduced. Mixed histological types, chemotherapy and primary site surgery were factors that affect the overall survival of ovarian cancer patients with lung metastases.

Conclusion: The clinical prediction model had high accuracy and can be used to predict the lung metastasis risk of newly diagnosed patients with ovarian cancer, which can guide the treatment of patients with lung metastases.

1. Introduction

Ovarian cancer is one of the most common malignant tumors in the female reproductive system. Ovarian cancer is the fifth most common cause of cancer-related deaths among American women. In 2018, there were an estimated 14,070 deaths in the United States¹. Because the symptoms are unclear and there is currently no effective screening method, most patients are already in the advanced stage (III and IV) at the time of diagnosis, accompanied by distant metastases².

Lung metastasis is the third most common distant metastatic site of ovarian cancer, accounting for 28.42% of the distant metastatic sites. The location of distant metastases is an independent prognostic factor for overall survival³. Previous studies had shown that the important risk factors for distant metastases are stage, grade, and lymph node involvement⁴. However, the sample size of the study is small. There are few studies on the risk factors of lung metastases and most of them are case reports^{5 6}.

The median interval between diagnosis of ovarian cancer and recording of metastatic disease was 44 months⁴. Identifying the risk factors for lung metastases can ensure that high-risk patients with lung metastases are thoroughly investigated and, if possible, treat these patients as early as possible or provide appropriate preventive treatment. Not only a large number of research samples are needed, but realistic evidence is still needed to determine the risk factors for lung metastases in patients with ovarian cancer.

The purpose of this study was to use surveillance, epidemiology, and end result (SEER) databases to characterize the prevalence, related factors, and prognostic factors of lung metastases in patients with ovarian cancer. At the same time, a nomogram based on clinical factors was established to predict the risk of lung metastases and may guide lung metastases screening.

2. Methods

2.1 Study population

Data were obtained from the Surveillance, Epidemiology, and End Results (SEER) database. The SEER *Stat 8.3.5 software (<https://seer.cancer.gov/data/>) was used to access the database. The site code was restricted to ovary. Since the details of metastases were not recorded before 2010, Patients with primary cancer of the ovarian cancer who were aged ≥ 18 years at diagnosis and between 2010–2015 were analyzed. The exclusion criteria for patient selection included (1) unknown grade; (2) unknown AJCC T,N stage and AJCC T0 stage; (3) unknown metastases information; (4) unknown tumor size; (5) unknown laterality; (6) unknown therapy information. The flowchart of the subjects' selection is listed in Fig. 1. According to the inclusion and exclusion criteria, 16059 patients with ovarian cancer were finally enrolled in our study. We further randomly divided the patients in a 7-to-3 ratio forming a training cohort (n = 11242) for nomogram construction and a validation cohort (n = 4817) for internal verification.

Data regarding clinical characteristics including age, race, marital status, insurance status, year of diagnosis, household income at the time of diagnosis, histological type, grade, laterality, clinical AJCC T, N stage, tumor size, metastatic status, and therapy information were collected from the SEER database. Since all information from the SEER database has been identified and no personal identifying information was used in this analysis, informed consent is not required for use of the SEER data. The present study complied with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

2.2 Statistical analysis

Statistical analysis was performed using SPSS 21 software. Categorical data were presented as frequency (%) and analyzed by the chi-squared test. Kolmogorov-Smirnov test was used to verify normality of variables. Normally distributed variables were expressed as mean $\pm$ standard deviation while non-normally distributed variables were expressed as median (interquartile range). Meanwhile, 95%

confidence intervals (CIs) and hazard ratios were calculated. Univariable and multivariable logistic regression analyses were used to determine risk factors of lung metastases of patients with ovarian cancer. Factors with a P-value less than 0.05 were incorporated into the multivariable logistics regression model.

A lung metastases nomogram formulated based on the results of multivariable logistic analysis using the rms package in R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria; www.r-project.org). The receiver operating characteristic (ROC) curves were drawn. Finally, we evaluated the stability of the prognostic nomogram and the lung metastases nomogram by internal validation with 1000 bootstrap samples. The nomograms were validated both internally and externally. The C-index (Harrell's concordance index) was used to assess the exact predicted values of nomograms. Calibration plots were drawn to analyze the consistency between observed probability and predicted probability. The overall survival was estimated by Kaplan-Meier method and the difference between distinct groups was compared using the log-rank test. Multivariable Cox regression model, incorporating the significant factors in Kaplan-Meier method ($P < 0.05$) was conducted for analyzing the independent prognostic factors for lung metastases.

3. Results

3.1 Patients' Basic Information

According to the inclusion and exclusion criteria, 16,059 of the 35,333 patients with ovarian disease registered between 2010 and 2015 were collected from the SEER database. The patients were divided into training group ($n = 11242$) and verification group ($n = 4817$). The basic information of the patients is listed in Table 1. The median age of these patients was 59 years. Among these patients, there were 13223 (82.3%) whites, 1057 (6.6%) blacks and 1711 (10.7%) other races. 3377 (21.0%) patients were unmarried, 8549 (53.2%) patients were married, and 3486 (21.7%) patients were separated. The number of insured and uninsured were 861 (3.5%) and 15337 (95.5%). The median household income was 6255. The numbers of those with tumor diameters < 2 , $2-5$, > 5 were 1311 (8.1%), 2678 (16.7%) and 12076 (75.2%). There were 4947 (30.8%) patients with tumors on the left. 5109 (31.8%) patients with tumors on the right and 6003 (37.4%) patients with tumors on both sides. The numbers of well differentiation, medium differentiation, poor differentiation and undifferentiation were 2011 (12.5%), 2758 (17.2%), 6395 (39.8%) and 4895 (30.5%). The number of T1, T2, and T3 stage were 5500 (34.2%), 2552 (15.9%), and 8007 (49.9%). The number of N0 and N1 stage were 12514 (77.9%) and 3545 (22.1%). Bone metastases occurred in 54 (0.3%) patients, brain metastases occurred in 15 (0.1%) patients, liver metastases occurred in 572 (3.6%) patients, and lung metastases occurred in 411 (2.6%) patients. The number of histology type serous, endometrioid, mucinous, clear cell, carcinosarcoma, malignant Brenner, carcinoma, NOS, mixed and other were 8644 (53.8%), 2367 (14.7%), 1071 (6.7%), 1124 (7.0%), 515 (3.2%), 18 (0.1%), 516 (3.2%), 1140 (7.1%) and 664 (4.1%). The chi-test for all of those variables between the two groups yielded $P > 0.05$.

3.2 Risk factors for lung metastasis

Univariable logistic analysis showed that the following factors were closely related to the occurrence of lung metastasis: older patient age (OR = 1.015; 95% CI, 1.006–1.025; $P = 0.001$), bilateral tumors (OR = 1.556; 95% CI, 1.179–2.053; $P = 0.002$), lower differentiation grade (Poor differentiated OR = 5.288; 95% CI, 2.583–10.825; $P < 0.001$; Undifferentiated OR = 6.435; 95% CI, 3.139–13.195; $P < 0.001$), higher AJCC T stage (T2 OR = 4.991; 95% CI, 2.859–8.712; $P < 0.001$; T3 OR = 8.796; 95% CI, 5.432–14.243; $P < 0.001$), higher AJCC Stage N (OR = 2.863; 95% CI, 2.254–3.635; $P < 0.001$), bone (OR = 15.403; 95% CI, 7.355–32.256; $P < 0.001$), brain (OR = 17.443; 95% CI, 5.340–56.981; $P < 0.001$), liver metastases (OR = 10.483; 95% CI, 7.822–14.050; $P < 0.001$), Mucinous (OR = 0.425; 95% CI, 0.190–0.953; $P = 0.038$) and Clear cell (OR = 0.248; 95% CI, 0.077–0.794; $P = 0.019$).

Multivariable logistic regression analysis showed that higher T stage, higher N stage, and the presence of lung, liver, and brain metastases were significantly associated with the early development of lung metastases. (Table 2)

3.3 Nomogram development

A nomogram to predict lung metastases in patients with ovarian cancer was developed in the training cohort. The risk factors determined by multivariable logistic regression analysis, including higher T stage, higher N stage, the development of bone, liver, and brain metastases were developed and used as the final nomogram.(Figure 2)

3.4 ROC curves analysis and prediction value evaluation

The ROC curves were drawn to determine the predicted value of the nomogram of the lung metastases in the training cohort and the validation cohort. As shown in Figs. 3a and c, the receiver operating characteristic (ROC) curves were drawn. We verified the nomogram internally and externally. The C index was used to evaluate the prediction accuracy of the nomogram. As shown in Fig. 3b, internal verification of the nomogram was performed, and the C index was 0.761 (0.736–0.787). As shown in Fig. 3d, the external verification of the validation cohort showed that the C index was 0.757(0.718–0.795).

Verification of the nomogram showed good agreement with the predicted values.

3.5 Survival analysis and prognostic factors of lung metastases

The 3-year overall survival rate and 5-year overall survival rate of ovarian cancer patients were 72.2% and 58.1%, respectively. For the 411 patients with newly diagnosed lung metastases, the 3-year survival rate and 5-year survival rate were 33.8% and 22.8%, respectively (Fig. 4a). Kaplan-Meier analysis showed that the overall survival of married, (Fig. 4b, $dP = 0.021$), primary site surgery (Fig. 4c $P < 0.01$), chemotherapy (Fig. 4d $P < 0.01$) and *radiation* (Fig. 4e $P = 0.030$) is higher than the control group. Mixed histological type (Fig. 4f $0 < 0.001$), liver metastases (Fig. 4g, $P = 0.025$), bone metastases (Fig. 4h $P = 0.028$)and brain metastases (Fig. 4i $P = 0.003$)were negatively correlated to overall survival rate.

4. Discussion

Ovarian cancer is the seventh most common cancer among women and the eighth most common cause of cancer death in the world, with a 5-year overall survival rate of $< 50\%$ ⁷. Two-thirds of patients are already advanced at the time of diagnosis (Stage III/IV).⁸ When the lungs are affected by ovarian cancer, the main route of spread is from the pleura. Lung metastasis usually represents visceral pleura involvement and continuous infiltration. Occasionally, isolated substantial lesions are found, and the invasion of lymphatic vessels and blood vessels is also involved⁹. The incubation period from diagnosis of ovarian cancer to the development of lung metastases can be as long as 108 months¹⁰. Compared with standard chemotherapy treatment alone, early detection of lung metastases means earlier chances of receiving more aggressive treatments, which may lead to better survival³. Active chemotherapy can significantly reduce the tumor load and metastasis of ovarian cancer¹¹. Surgical removal of isolated lung metastatic lesions is reasonable¹². Targeted therapy is also a promising treatment for metastatic ovarian cancer¹³. Routine imaging studies, such as computed tomography (CT) or magnetic resonance imaging (MRI), have not shown high sensitivity and specificity when diagnosing micrometastasis $< 1\text{ cm}$ ¹⁴. Therefore, there is a need for a non-invasive method that can predict the likelihood of lung metastases in ovarian cancer patients. In this study, we used the SEER data set to develop and validate the predicted nomogram, which demonstrated significant discernment and calibration capabilities and provide a personalized estimate of the likelihood of lung metastases in ovarian cancer patients.

In order to solve this problem better, this study is the first to generate a risk model based on clinical and tumor characteristics through population-based surveillance, epidemiology, and final result databases to predict the risk of lung metastases in newly diagnosed ovarian cancer patients. We found that the higher of AJCC T and N stage, the more likely it is to metastasize, which is similar to the bone metastasis of ovarian cancer and other types of tumor metastases research^{15 16 17}. Previous studies have shown that poor differentiation and lymph node involvement are risk factors for distant metastasis³. We found that liver metastases, brain metastases and bone metastases are risk factors for lung metastases. If distant metastasis occurs in other parts, it means that cancer cells have spread¹⁸, and the possibility of lung metastases will be higher.

We constructed a nomogram of lung metastases from ovarian cancer and verified it internally and externally. It can predict the risk of lung metastases in patients with ovarian cancer. The nomogram of lung metastases included 5 factors, AJCC T stage, AJCC N stage, whether bone metastases, liver metastases and brain metastases occurs. The nomogram showed a good agreement between the predicted results and the observed results in the verification. In addition, the C indexes of internal verification and external verification of the nomogram were 0.761 (0.736–0.787) and 0.757 (0.718–0.795), respectively, indicating a good consistency with the predicted values. For patients with a higher risk of metastases predicted by this model, imaging examination should be performed on time to diagnose the occurrence of lung metastases in the first time, so as to better guide clinical procedures.

The determination of prognostic factors related to lung metastases in patients with ovarian cancer may help doctors provide targeted treatment strategies for patients at different risk levels and improve patient survival and quality of life. Previous studies had shown that lung metastases can significantly worsen the prognosis of patients.¹⁹ The median survival time for diagnosis of distant disease is 12 months.⁴ In this study, the 3-year and 5-year survival rates for 411 patients with newly diagnosed lung metastases were 33.8% and 22.8%, respectively, similar to other studies.^{20 21} It was found that primary site surgery treatment and chemotherapy can improve overall survival. Therefore, for patients with ovarian cancer with lung metastases, active surgery and chemotherapy are encouraged. At the same time, the mixed histological type is a high-risk factor for death, and physicians should attach great importance to it.

However, this study has several limitations that should be noted. The main limitation of this study is that the variables used to construct the nomogram had only some clinical pathological features, because there are no important tumor biomarkers in the SEER database. Another limitation is that although the established nomogram shows good discrimination and verification capabilities, it still requires further verification based on large-scale external queues. Third, in this study, only patients with a primary diagnosis of liver metastases were analyzed. Since they may not be recorded in the surveillance, epidemiology, and final results databases, liver metastases that occurred later in the disease cannot be analyzed.

Declarations

Conflict of Interest:

The authors declare that they have no conflicts of interest.

Ethics approval:

Since the data collected from the Surveillance, Epidemiology, and End Results database were anonymized and de-identified prior to release, informed patient consent was not required in our study.

Consent to participate:

Not applicable.

Consent for publication:

Not applicable

Availability of data and material:

Author contributions:

Yufei Yuan and Fanfan guo contributed equally to this manuscript .(I) Conception and design: Yufei Yuan;(II) Administrative support: Guiqin Bai ;(III) Provision of study materials or patients: Fanfan Guo;(IV) Collection and assembly of data: Yufei Yuan, Yidan Zhang;(V) Data analysis and interpretation: Ruoran Wang;(VI) Manuscript writing: All authors;(VII) Final approval of manuscript: All authors

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Tables

Table 1.

Demographical and clinical characteristics between patient with the training cohort and the validation cohort.

Variables	The training cohort(N=11242)		The validation cohort(N=4817)		Total(N=16059)		P value
	No.	%	No.	%	No.	%	
Age	59		59		59		0.360
Race							0.750
White	9267	82.4	3956	82.1	13223	82.3	
Black	725	6.4	332	6.9	1057	6.6	
Other (American Indian/AK Native, Asian/Pacific Islander)	1201	10.7	510	10.6	1711	10.7	
Unknown	49	0.4	19	0.4	68	0.4	
Marital status							0.363
Unmarried	2329	20.7	1049	21.8	3377	21.0	
Married	5987	53.3	2562	53.2	8549	53.2	
Separated	2473	22.0	1013	21.0	3486	21.7	
Unknown	453	4.0	194	4.0	647	4.0	
Insurance status							0.577
Uninsured	403	3.6	158	3.3	561	3.5	
Insured	10724	95.4	4613	95.8	15337	95.5	
Unknown	115	1.0	46	1.0	161	1.0	
Household income	6204 (5716-8008)		6325 (5716-8008)		6255 (5716-8008)		0.394
Year of diagnosis							0.210
2010	1783	15.9	755	15.7	2539	15.8	
2011	1850	16.5	806	16.7	2656	16.5	

2012	1825	16.2	816	16.9	2641	16.4
2013	1873	16.7	825	17.1	2698	16.8
2014	1951	17.4	759	15.8	2710	16.9
2015	19610	17.4	856	17.8	2816	17.5
Tumor size						0.892
<2 cm	906	8.1	399	8.3	1311	8.1
2-5 cm	1875	16.7	803	16.7	2678	16.7
>5 cm	8461	75.3	3615	75.0	12076	75.2
Laterality						0.628
Left	3471	30.9	1476	30.6	4947	30.8
Right	35965	32.0	1514	31.4	5109	31.8
Bilateral	4176	37.1	18287	37.9	6003	37.4
Grade						0.426
Well differentiated	1417	12.6	594	12.3	2011	12.5
Moderate differentiated	1904	16.9	854	17.7	2758	17.2
Poor differentiated	4460	39.7	1935	40.2	6395	39.8
Undifferentiated	34621	30.8	1434	29.8	4895	30.5
AJCC T stage						0.805
T1	3835	34.1	1665	34.6	5500	34.2
T2	1783	15.9	769	16.0	2552	15.9
T3	5624	50.0	2383	49.5	8007	49.9
AJCC N stage						0.497
N0	8747	77.8	37710	78.3	12514	77.9
N1	2498	22.2	1047	21.7	3545	22.1
Bone metastasis						0.592
No	11206	99.7	4799	99.6	16005	99.7
Yes	36	0.3	18	0.4	54	0.3
Brain metastasis						0.159
No	11229	99.9	4815	100.0	16044	99.9

Yes	13	0.1	2	0.0	15	0.1
Liver metastasis						0.681
No	10846	96.5	4641	96.3	15487	96.4
Yes	396	3.5	176	3.7	572	3.6
Lung metastasis						0.681
No	10959	97.5	4689	97.3	15648	97.4
Yes	283	2.5	128	2.7	411	2.6
Histological type						0.866
Serous	6016	53.5	2628	54.6	8644	53.8
Endometrioid	1662	14.8	705	14.6	2367	14.7
Mucinous	758	6.7	313	6.5	1071	6.7
Clear cell	779	6.9	345	7.2	1124	7.0
Carcinosarcoma	361	3.2	154	3.2	515	3.2
Malignant Brenner	14	0.1	4	0.1	18	0.1
Carcinoma, NOS	362	3.2	154	3.2	516	3.2
Mixed	813	7.2	327	6.8	1140	7.1
Other	477	4.2	187	3.9	664	4.1
Surgery[†]						0.292
No	149	72.0	58	70.0	207	70.0
Yes	11093	28.0	4759	30.0	15852	30.0
Radiation						0.493
No	11090	70.0	4751	69.7	15841	70.0
Yes	152	30.0	66	30.0	218	30.0
Chemotherapy						0.841
No	2753	70.1	1172	70.0	3925	70.0
Yes	8489	29.9	3645	30.0	12134	30.0

Table 2.

Univariable and Multivariable Logistic Regression for analyzing the associated factors for developing liver metastases in training cohort.

Variables	Univariable			Multivariable		
	OR	95% CI	P value	OR	95% CI	P value
Age	1.015	1.006-1.025	0.001	1.010	0.999-1.021	0.086
Race			0.622			0.114
White	References			References		
Black	1.193	0.758-1.878	0.445	1.174	0.725-1.899	0.515
Other	1.236	0.865-1.767	0.244	1.595	1.089-2.336	0.016
Unknown	0.000	0.000	0.998	0.000	0.000	0.997
Marital status			0.287			0.144
Unmarried	References			References		
Married	1.034	0.761-1.404	0.832	0.868	0.626-1.203	0.396
Separated	1.074	0.751-1.535	0.697	0.770	0.520-1.139	0.191
Unknown	0.437	0.174-1.096	0.078	0.352	0.136-0.912	0.032
Insurance status			0.772			0.418
Uninsured	References			References		
Insured	0.913	0.496-1.683	0.772	0.730	0.378-1.411	0.349
Others/Unknown	1.284	0.401-4.111	0.674	1.221	0.357-4.174	0.750
Household income	1.000	1.000-1.000	0.794	1.000	1.000-1.000	0.622
Year of diagnosis			0.666			0.742
2010	References			References		

2011	1.293	0.835-2.001	0.250	1.283	0.817-2.015	0.278
2012	1.367	0.886-2.109	0.158	1.389	0.889-2.172	0.149
2013	1.140	0.729-1.784	0.565	1.166	0.736-1.847	0.51
2014	1.381	0.902-2.117	0.138	1.348	0.865-2.100	0.187
2015	1.323	0.860-2.033	0.202	1.197	0.765-1.873	0.432
Tumor size			0.080			0.207
<2 cm	References			References		
2-5 cm	1.291	0.717-1.822	0.303	1.026	0.620-1.696	0.921
>5 cm	0.925	0.541-1.240	0.726	0.796	0.505-1.255	0.326
Laterality			<0.001			0.082
Left	References			References		
Right	0.704	0.500-0.991	0.044	0.666	0.467-0.951	0.025
Bilateral	1.556	1.179-2.053	0.002	0.840	0.620-1.138	0.261
Grade			<0.001		0.000	0.246
Well differentiated	References			References		
Moderate differentiated	2.154	0.960-4.829	0.063	1.355	0.592-3.101	0.471
Poor differentiated	5.288	2.583-10.825	<0.001	1.590	0.736-3.437	0.238
Undifferentiated	6.435	3.139-13.195	<0.001	1.890	0.868-4.118	0.109
AJCC T stage			<0.001	References		<0.001
T1	References					
T2	4.991	2.859-8.712	<0.001	3.032	1.675-5.485	<0.001

T3	8.796	5.432-14.243	<0.001	4.055	2.343-7.019	<0.001
AJCC N stage			<0.001		<0.001	
N0	References			References		
N1	2.863	2.254-3.635	<0.001	1.696	1.313-2.190	<0.001
Bone metastasis			<0.001		<0.001	
No	References			References		
Yes	15.403	7.355-32.256	<0.001	5.945	2.373-14.894	<0.001
Brain metastasis			<0.001		<0.001	
No	References			References		
Yes	17.443	5.340-56.981	<0.001	13.375	3.449-51.865	<0.001
Liver metastasis			<0.001	<0.001	<0.001	
No	References			References		
Yes	10.483	7.822-14.050	<0.001	6.292	4.605-8.598	<0.001
Histological type			<0.001		0.503	
Serous	References			References		
Endometrioid	1.581	0.832-3.005	0.162	0.807	0.449-1.450	0.473
Mucinous	0.425	0.190-0.953	0.038	0.526	0.180-1.535	0.240
Clear cell	0.248	0.077-0.794	0.019	0.536	0.240-1.195	0.127
Carcinosarcoma	0.423	0.160-1.120	0.083	1.513	0.8792.605	0.135
Malignant Brenner	2.166	0.971-4.831	0.059	0.000	0.000	0.999
Carcinoma, NOS	0.000	0.000	0.999	1.184	0.659-2.125	0.572
Mixed	2.160	0.968-4.817	0.060	1.052	0.632-1.751	0.844
Other	1.057	0.484-	0.889	1.172	0.547-	0.682

Table 3.

Multivariable cox Regression for analyzing the associated factors for prognostic factors patients with lung metastases

Variables	Multivariable		
	OR	95% CI	P value
Histological type			0.003
Serous	References		
Endometrioid	1.391	0.764-2.532	0.280
Mucinous	1.081	0.391-2.990	0.880
Clear cell	1.106	0.515-2.374	0.797
Carcinosarcoma	1.457	0.854-2.488	0.167
Carcinoma, NOS	0.981	0.575-1.673	0.942
			0
Mixed	2.531	1.538-4.165	<0.001
Other	2.585	1.362-4.908	0.004
Surgery			<0.001
No	Reference		
Yes	0.315	0.190-0.522	<0.001
Chemotherapy			<0.001
No	Reference		
Yes	0.216	0.139-0.335	<0.001

Figures

Fig1.Flowchart of patient selection.

Figure 1

Flowchart of patient selection

Figure 2

Nomogram predicts lung metastases in patients with ovarian cancer. The first line shows the point assignment of each variable. Lines 2-6 indicate the variables included in the nomogram. For individual patients, each variable is assigned a point value based on tumor characteristics. The points assigned to each of the five variables are added, and the total point is displayed in the 7th line. The bottom row shows the possibility of lung metastases.

Figure 3

Identify and calibrate the nomogram in the training cohort and verification cohort. a and c Receiver operating characteristic (ROC) curve for discrimination in the training and validation cohorts. b and d Calibration plots for the actual (observed) and predicted probabilities of the nomograms in the training and verification cohorts. The x-axis represents the predicted probability of the nomogram measured by logistic regression analysis, and the y-axis represents the actual probability. The vertical line represents the frequency distribution of predicted probabilities. The dashed line represents the ideal reference line, where the predicted probability matches the observed probability. Calibration plots showed excellent calibration of the nomogram

Figure 4

Kaplan-Meier analysis of the overall survival (OS) of patients ovarian cancer with lung metastasis. (A) Study the overall survival (OS) of the total population. (B) Overall survival (OS) stratified by marital status. (C) Overall survival (OS) stratified by primary site surgery. (D) Overall survival (OS) stratified by chemotherapy (e) Overall survival (OS) stratified by radiation. (f) Overall survival stratified by histological type. (g) Overall survival (OS) Stratified by the presence of liver metastases. (H) Overall survival rate (OS) stratified by the presence of bone metastases. (I) Overall survival (OS) stratified by the presence of brain metastases. Multivariate Cox regression results incorporating the above important factors showed that mixed tissue type [hazard ratio (HR) = 2.531; 95% CI: 1.538-4.165; $P < 0.001$] was positively correlated to overall mortality. Primary site surgery [hazard ratio (HR) = 0.315; 95% CI: 0.190-0.522; $P < 0.001$] and chemotherapy [hazard ratio (HR) = 0.216; 95% CI: 0.139-0.335; $P < 0.001$] were beneficial for survival (Table 3).