

# Diagnostic and prognostic factors, and two nomograms for endometrial cancer patients with bone metastasis

## A large cohort retrospective study

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### Abstract

Patients with endometrial cancer (EC) who develop bone metastasis (BM) always imply a poorer prognosis. However, reliable predictive models associated with BM from EC are currently limited.

We retrospectively analyzed data on 54,077 patients diagnosed with primary EC in the Surveillance, Epidemiology, and End Results database. Multivariate logistic regression analysis was used to determine independent predictors of BM from EC. Univariate and multivariate Cox regression analyses were used to determine independent prognostic factors for EC with BM. Based on independent predictors and prognostic factors, we constructed a diagnostic nomogram and prognostic nomogram separately. Besides, calibration curves, receiver operating characteristic curves, and decision curve analysis were used to evaluate the models.

A total of 54,077 patients with EC from the Surveillance, Epidemiology, and End Results database were included in this study, 364 of whom had BM. Multivariate analysis in the logistic model showed that lung metastasis, liver metastasis, brain metastasis, N stage, T stage, histologic grade, and race were risk factors for BM from EC. Multivariate analysis in the Cox model showed that liver metastasis, brain metastasis, chemotherapy, surgery, and histologic type had a significant effect on overall survival. Moreover, the receiver operating characteristic curve, calibration curve, and decision curve analysis indicated the good performance of both diagnostic and prognostic nomograms.

Two clinical prediction model was constructed and validated to predict individual risk and overall survival for EC with BM, respectively. Diagnostic nomogram and prognostic nomogram are complementary, improving the clinician's ability to assess the patient's prognosis and enhancing prognosis-based decision making.

**Abbreviations:** AUC = area under the curve, BM = bone metastasis, DCA = decision curve analysis, EC = endometrial cancer, OS = overall survival, ROC = receiver operating characteristic, SEER = Surveillance, Epidemiology, and End Results.

**Keywords:** bone metastasis, endometrial cancer, nomogram, overall survival, SEER

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The research did not involve animal experiments and human specimens, no ethics related issues.

Consent for publication is not applicable.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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## 1. Introduction

Endometrial cancer (EC) is a group of epithelial malignancies originating in the endometrium and is the fourth most common cancer disease in the United States.<sup>[1]</sup> According to statistics, the number of new diagnoses and deaths in the United States in 2018 reached 63,230 and 11,350, respectively.<sup>[2]</sup> EC is usually confined to the uterus at the time of initial diagnosis and can be cured by surgery in some patients. However, there are still patients with advanced stages at diagnosis, or some patients develop extra-pelvic metastases after surgery. The common metastatic sites of EC include the lung, liver, brain, and bone.<sup>[3]</sup> Although bone metastasis (BM) is a common complication of cancer, they are generally less common in EC than in breast or prostate cancer.<sup>[4,5]</sup> The occurrence of BM in EC patients means a poor prognosis, with a 5-year survival rate of only 8.7%.<sup>[6,7]</sup> Hence, it is of great significance to identify risk factors and conditions for BM in EC patients as soon as possible.

It has been reported that histologic type, advanced age, unmarried, black, and uninsured are high-risk factors for BM from EC.<sup>[8]</sup> Furthermore, in previous studies, several factors have been found to correlate with the prognosis of EC patients with BM, including age at diagnosis, histologic type, tumor grade, marital status, race, insurance status, surgical status, and the number of distant metastatic sites.<sup>[9]</sup> However, these studies only analyzed different factors separately and did not focus on

constructing predictive models of the risk of BM from EC and the prognosis of EC patients with BM, which means that the probability of the outcome is not quantifiable.

Nomogram, a tool that combines multiple biological and clinical variables to predict specific endpoints, has been widely used in recent years to predict the prognosis of cancer patients.<sup>[10]</sup> The combination of these important variables enables the nomogram to individually estimate the probability of events over time, such as overall survival (OS) and the risk of metastasis in cancer patients.<sup>[11]</sup> Well-constructed clinical nomograms provide a prediction of individual outcomes, which is beneficial to both patients and clinicians.<sup>[12]</sup> Therefore, we aimed to use the information in the Surveillance, Epidemiology, and End Results (SEER) database to construct 2 nomograms to predict the risk of BM from EC patients and the OS of EC patients with BM, respectively.

**2. Methods**

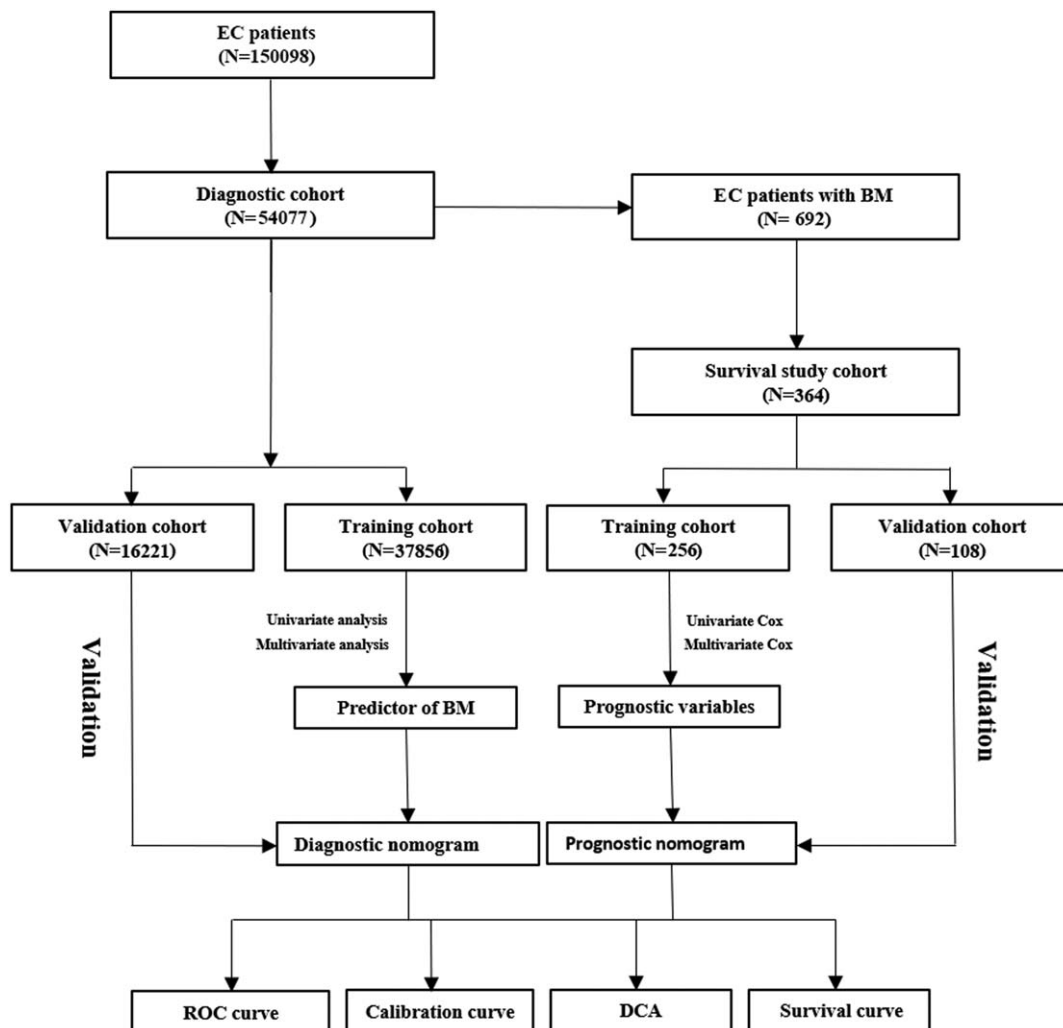
**2.1. Patient selection**

The workflow of our study is illustrated in Figure 1. With permission from the SEER program of the United States National

Cancer Institute, we collected information from patients diagnosed with EC between 2010 and 2015. The SEER program consists of 18 population-based cancer registries that collect statistical, oncological, diagnostic, and treatment information on approximately 28% of the United States population.<sup>[13]</sup> There is no medical ethics review and no informed consent required for the analysis of unidentified data in the SEER database. The inclusion criteria were as follows: primary EC patients, patients with BM, patients with complete clinicopathologic features, demographic data, and follow information. Finally, a total of 54,077 patients with EC who met the criteria were included to study their risk factors for developing BM. Subsequently, patients with BM with EC survival time  $\geq 1$  month and specific treatment information, including surgery, radiotherapy, and chemotherapy, were used to form a new cohort to explore prognostic factors in EC patients with BM. Ultimately, 364 patients were used to study prognostic factors.

**2.2. Variable definitions**

In this study, a total of 11 variables were used to identify risk factors for the development of BM from EC, including age, race, histologic type, grade, T stage, N stage, brain metastasis, liver



**Figure 1.** The workflow describing the schematic overview of the project. BM = bone metastasis, DCA = decision curve analysis, EC = endometrial cancer, ROC = receiver operating characteristic.

**Table 1**  
**Baseline demographics and clinical characteristics of patients with endometrial cancer patients.**

Variables	Training cohort N = 37,856		Validation cohort N = 16,221	
	n	%	n	%
Age				
<67	25,103	66.0	10,662	65.7
≥67	128,843	34.0	5559	34.3
Race				
Black	3684	9.7	1605	9.9
Other	3587	9.5	1500	9.2
White	30,585	80.8	13,116	80.9
Histological types				
Endometrioid	25,915	68.4	11,132	68.6
Non-endometrioid	8884	23.5	3776	23.3
Sarcomas	3057	8.1	1313	8.1
Grade				
I	15,950	42.1	6784	41.8
II	10,020	26.5	4435	27.4
III	8174	21.6	3440	21.2
IV	3712	9.8	1562	9.6
T stage				
T1	29,586	78.2	12,771	78.7
T2	2667	7.0	1164	7.2
T3	4194	11.1	1681	10.4
T4	667	1.8	295	1.8
Tx	742	1.9	310	1.9
N stage				
No	33,074	87.4	14,257	87.9
N1	2478	6.6	1033	6.4
N2	1690	4.4	666	4.1
Nx	614	1.6	265	1.6
Brain metastasis				
No	37,787	99.8	16,189	99.8
Yes	69	0.2	32	0.2
Liver metastasis				
No	37,504	99.1	16,071	99.1
Yes	352	0.9	150	0.9
Lung metastasis				
No	37,099	98.0	15,896	98.0
Yes	757	2.0	325	2.0
Insurance status				
No	1182	3.1	518	3.2
Yes	36,674	96.9	15,703	96.8
Marital status				
No	17,682	46.7	7715	47.6
Yes	20,174	53.3	8506	52.4

metastasis, lung metastasis, insurance status, and marital status. There were also 3 treatment variables included in the study of prognostic factors in EC patients with BM, including surgery, chemotherapy, and radiotherapy. In this section, OS was the primary outcome, which was defined as the time interval from the date of diagnosis to death (from any cause).

### 2.3. Statistical analysis

The optimal cutoff value of age in terms of OS was determined by the X-tile software. To process the data conveniently, we divided the patients into 2 groups (<67 and ≥67).<sup>[14]</sup> Patients were randomized in a 7:3 ratio into a training cohort and a validation cohort, respectively, and the classification process was performed in the R software. Univariate and multivariate logistic regression analyses were performed to identify risk factors for BM from EC.

Meanwhile, univariate and multivariate Cox regression analyses were used to identify independent prognostic factors in EC patients with BM. Diagnostic and prognostic nomograms were constructed separately based on corresponding risk factors and independent prognostic factors. Receiver operating characteristic (ROC) curves and area under the curve (AUC) were used to evaluate the discrimination of the nomogram. The calibration curve was used to measure the agreement of predicted probabilities with actual survival outcomes. The clinical application value of the nomograms was evaluated by decision curve analysis (DCA). In addition, we divided all patients into high-risk, middle-risk, and low-risk groups according to the best cutoff value of the risk score, and validated the prognostic value of the nomogram using Kaplan-Meier survival curves analysis and log-rank test. This study used SPSS 25.0 (NY, USA) and R software (version 4.0.3, Shanghai Jiao Tong University,

**Table 2**  
**Univariate and multivariate logistic regression analyses of risk factor of bone metastasis in patients with endometrial cancer.**

	Univariate Cox analysis				Multivariate Cox analysis		
	HR	95%CI		P	HR	95%CI	P
Age							
<67	1						
≥67	1.245	0.964	1.607	.093			
Race							
Black	1				1		
Other	0.941	0.585	1.512	.801	1.855	1.109	3.102
White	0.600	0.419	0.859	.005	1.198	0.812	1.768
Histologic type							
Endometrioid	1						
Non-endometrioid	3.731	2.809	4.955	.000			
Sarcomas	5.401	3.835	7.606	.000			
Grade							
I	1				1		
II	4.307	2.084	8.901	.000	3.145	1.495	6.617
III	27.172	14.291	51.663	.000	7.582	3.826	15.028
IV	32.870	16.975	63.649	.000	8.291	4.091	16.804
T stage							
T1	1				1		
T2	7.473	4.770	11.709	.000	2.965	1.839	4.781
T3	14.877	10.523	21.033	.000	3.226	2.158	4.822
T4	22.969	13.985	37.725	.000	3.473	1.992	6.054
TX	40.671	26.956	61.366	.000	7.592	4.539	12.696
N stage							
No	1				1		
N1	8.655	6.311	11.870	.000	2.162	1.516	3.082
N2	10.776	7.715	15.051	.000	2.667	1.828	3.890
NX	16.770	11.067	25.414	.000	2.029	1.212	3.397
Brain metastasis							
No	1				1		
Yes	57.381	33.017	99.724	.000	7.588	3.941	14.610
Liver metastasis							
No	1				1		
Yes	33.740	24.401	46.655	.000	3.433	2.332	5.055
Lung metastasis							
No	1				1		
Yes	44.406	34.167	57.715	.000	7.515	5.505	10.258
Insurance status							
No	1						
Yes	0.538	0.313	0.925	.025			
Marital status							
No	1						
Yes	0.715	0.557	0.918	.009			

Shanghai, China) for statistical analysis. In the present study, a *P* value < .05 was identified as statistical significance.

**3. Results**

**3.1. Baseline characteristics of EC patients**

A total of 54,077 EC patients from the SEER database were included. Furthermore, 37,856 and 16,221 patients were included in the training and validation cohorts, respectively. The baseline characteristics of 54,077 patients with EC were shown in Table 1.

**3.2. Development and validation of a diagnostic nomogram for BM from EC**

Univariate and multivariate logistic regression analyses were performed to determine the risk factors for BM from EC. The results showed that 7 predictors were independent predictors of

BM from EC, including race, grade, T stage, N stage, brain metastasis, liver metastasis, and lung metastasis (Table 2). Based on the independent predictors selected in the training cohort, the diagnostic nomogram was constructed for the risk assessment of BM in EC patients (Fig. 2). The AUCs of the nomogram were 0.943 and 0.954 in the training and validation cohorts, respectively, showing good discrimination (Fig. 3). Furthermore, the ROC curves and AUC of each independent risk factor were also generated (Fig. 4). The results suggested that the discrimination of any single risk factor was lower than that of the nomogram in either the training or validation cohort. In both the training and validation cohorts, the calibration curves exhibit a high degree of agreement between observations and predictions (Fig. 5A and B). The DCA showed that the prognostic nomogram had a wider range of practical threshold probabilities, significantly increasing the net benefit and suggesting a high clinical value of the diagnostic nomogram (Fig. 5C and D).

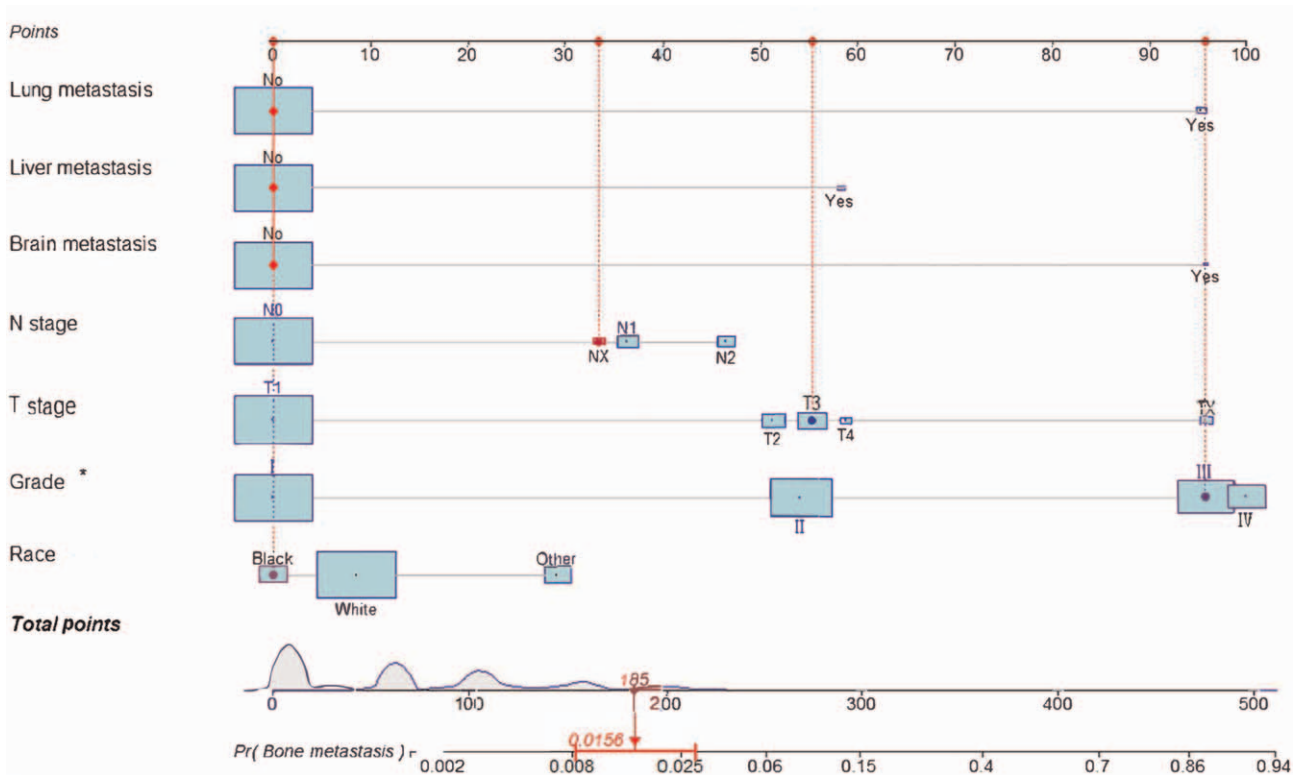


Figure 2. Nomogram to estimate the risk of BM in patients with EC. BM = bone metastasis, EC = endometrial cancer.

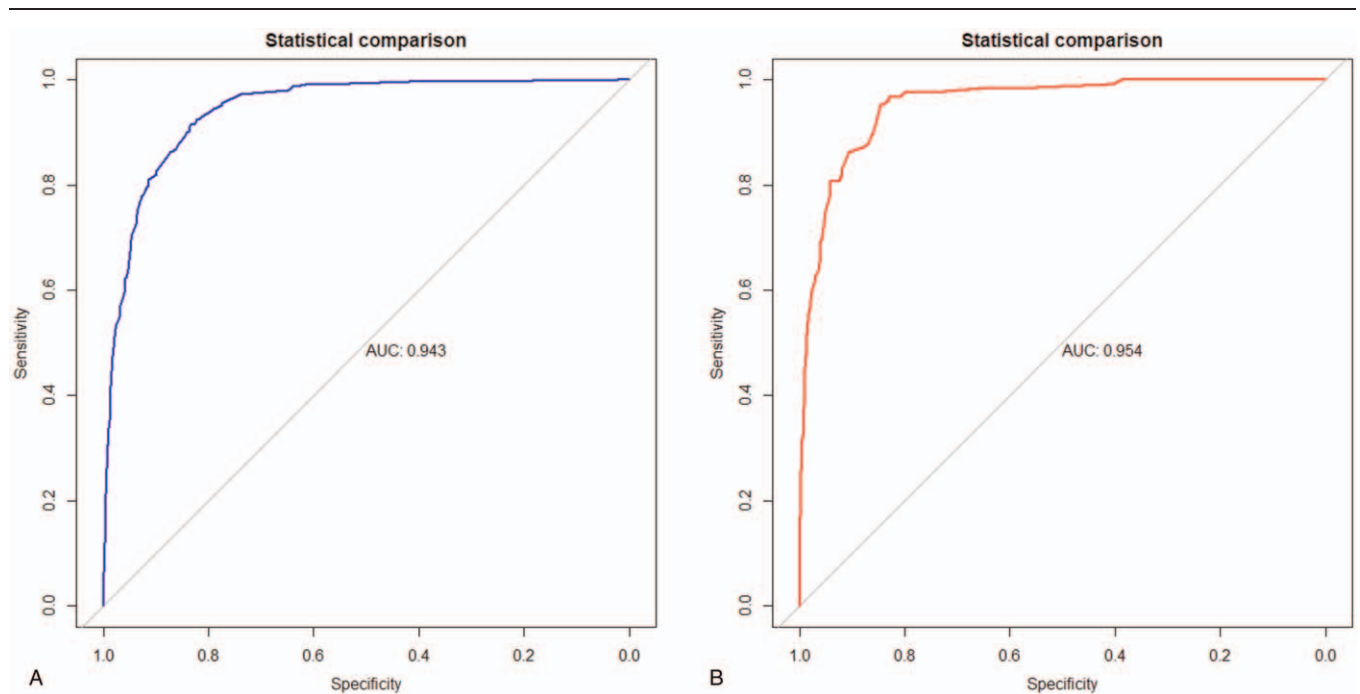
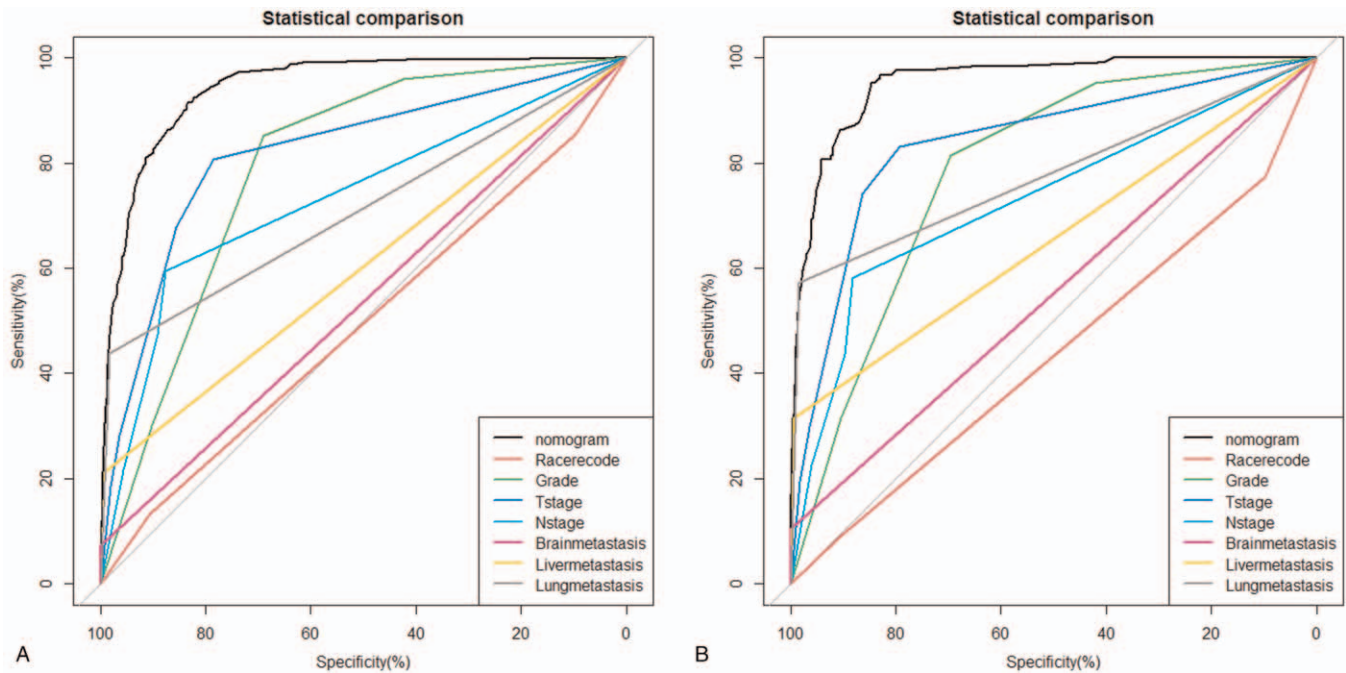


Figure 3. The ROC curves of the diagnostic nomogram in the training cohort (A) and the validation cohort (B). AUC = area under the curve, ROC = receiver operating characteristic.



**Figure 4.** Comparison of AUC between diagnostic nomogram and each independent predictor in the training cohort (A) and the validation cohort (B). AUC = area under the curve.

**3.3. Development and validation of a prognostic nomogram for EC patients with BM**

A total of 364 EC patients with BM were used to identify independent prognostic factors, as shown in Table 3. Meanwhile, 256 patients were incorporated into the training cohort, and the remaining 108 patients were incorporated into the validation cohort. Of the total patients included, 220 (60.4%) were aged less than 67 years. At the same time, the majority of patients were white (71.4%). A total of 175 (48.1%) patients had lung metastases, 30 (8.2%) patients had brain metastasis and 89 (24.5%) patients had liver metastases. As for treatment, nearly half of the patients received surgery (49.7%), 213 (58.5%) had chemotherapy and 159 (43.7%) had radiotherapy.

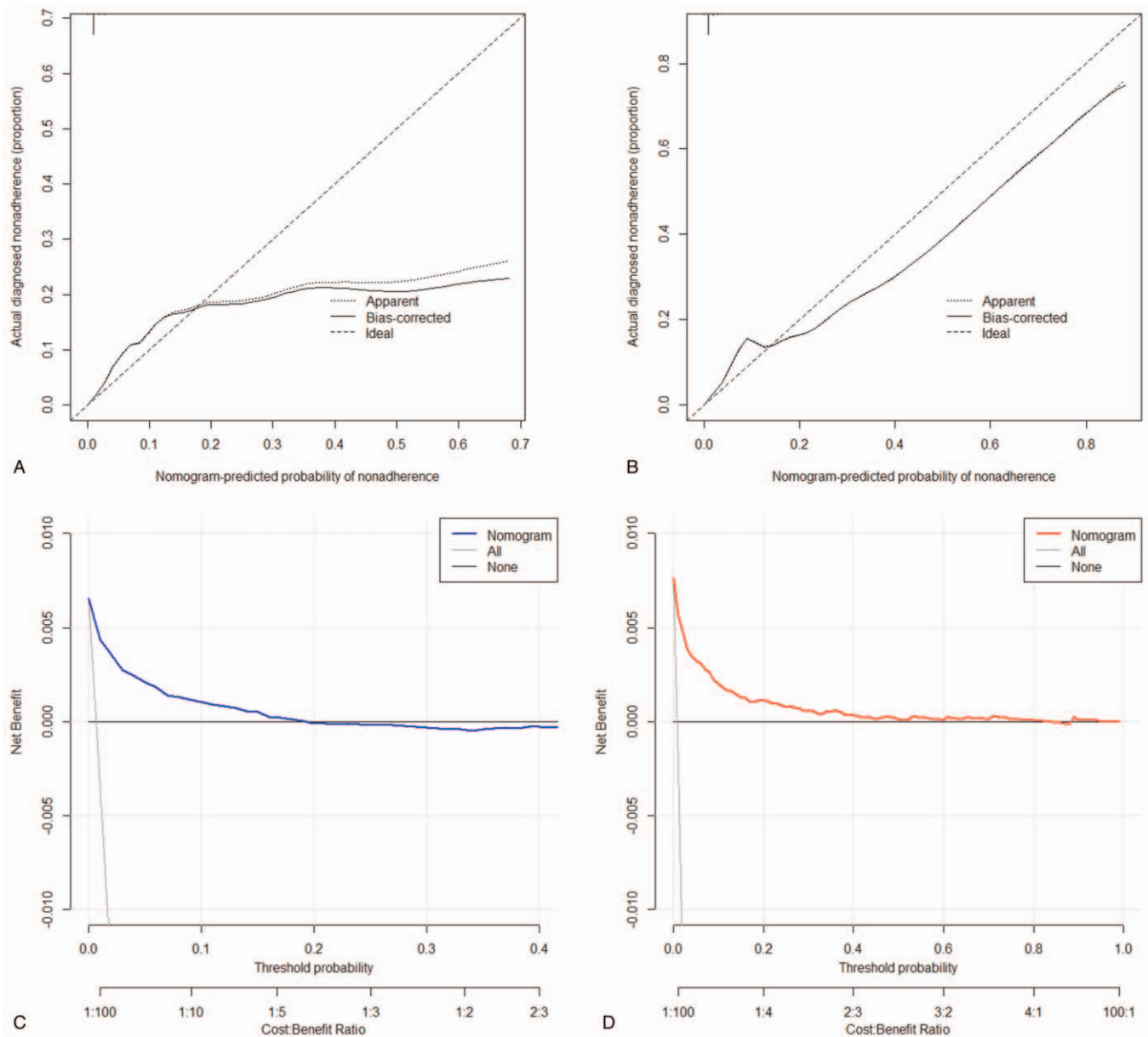
The results of the Cox regression analysis performed on all patients are shown in Table 4. The results of univariate Cox regression analysis indicated that age, race, histological type, T stage, surgery, chemotherapy, brain metastasis, and liver metastasis were correlates of OS. After controlling for confounding variables with multivariate Cox regression analysis, histologic type, surgery, chemotherapy, brain metastasis, and liver metastasis were identified as independent prognostic factors (Table 4). Then, the above-mentioned independent predictors were incorporated to construct the prognostic nomogram for predicting 1-, 2-, and 3-year OS (Fig. 6). ROC curves showed the AUCs of this prognostic nomogram at 1-, 2-, and 3-year OS reached 0.756, 0.788, and 0.775, respectively, in the training cohort (Fig. 7A) and 0.765, 0.779, and 0.808, respectively, in the validation cohort (Fig. 7B). The time-dependent ROCs showed that the nomogram has a higher prediction accuracy than a single independent prognostic factor (Fig. 8). The calibration curves of 1-, 2-, and 3-years showed significant consistency between the predictive survival and actual survival in both cohorts (Fig. 9).

Moreover, the DCA also demonstrated the strong clinical applicability of the prognostic nomogram (Fig. 10). Interestingly, as shown in Figure 11, we found that as with the subgroup analysis of patients, when patients were classified in the low mortality risk subgroup, it always meant a better prognosis.

**4. Discussion**

EC is one of the most common gynecologic malignancies, with BM occurring in <1% of patients, and the median survival of EC patients with BM is only 10 to 17 months.<sup>[8,15,16]</sup> The most common site of BM in EC is the spine, and 70% of patients have multiple BM.<sup>[17]</sup> In the present study, 2 nomograms were constructed by analyzing relevant data from the SEER database to predict the risk of BM in patients with EC and the OS of EC patients with BM, respectively. In these nomograms, values for the individual patient are located along the variable axes, and a line is drawn upward to the points axis to determine the number of points assigned for each variable. There was a total points line at the bottom of the nomogram, and each variable score was summed to give the total points. And the accumulated total points can be used to predict the risk and OS of the patient. With the advantage of integrating all relevant factors, the model allows for an individualized risk assessment for each patient, which is often better than the subjective judgment of the clinician.<sup>[10]</sup>

It has been reported that patients with EC, including autopsy, have a 25% probability of BM, and the majority of patients have metastases in many sites, including the liver, lungs, and brain.<sup>[18]</sup> It was demonstrated in this study that T stage, N stage, race, grade, lung metastasis, liver metastasis, and brain metastasis were risk factors for EC with BM. The presence of metastases at distant sites indicates the presence of hematogenous transmission and



**Figure 5.** Calibration curves and DCA of the diagnostic nomogram for estimating the risk of BM in patients with EC. BM = bone metastasis, DCA = decision curve analysis, EC = endometrial cancer.

increases the probability of BM in the patient.<sup>[17]</sup> In previous studies, it has been shown that as tumor size and depth of invasion increase, the rate of lymph node involvement also increases, as does the incidence of BM, which is consistent with our results.<sup>[19]</sup> Also, we observed that currently for patients with a histologic grade of 1 or 2 (so-called low-risk patients), the risk of extrauterine tumor spread is relatively low, whereas, with a histologic grade of 3 or 4, patients have a relatively increased risk of BM. Based on the screened risk factors, the construction of a nomogram model to predict the risk of BM can enable early detection of BM, which is crucial for EC patients to receive appropriate treatment.

In addition, our study showed that histologic type, surgery, chemotherapy, brain metastasis, and liver metastasis were

independent prognostic factors for EC patients with BM. Based on 5 independent prognostic factors, a nomogram was constructed. The results showed that the nomogram can be used as an effective tool to identify high-risk patients while achieving an accurate prediction of OS. EC is a low-grade early-stage tumor and is more common, while non-endometrioid carcinoma and sarcoma are less common and have a stronger tendency to spread, resulting in a significantly poorer prognosis.<sup>[20]</sup> Stefano Uccella et al<sup>[16]</sup> found that the prognosis of patients with only a single BM was much better than that of patients with multiple organ metastases, which is consistent with our findings. There is still no standard treatment plan for EC patients with BM, but the available treatment options include surgery, chemotherapy, and radiotherapy.<sup>[6]</sup> The present results

**Table 3**  
**Baseline demographics and clinical characteristics of endometrial cancer patients with bone metastasis.**

Variables	Training cohort N = 256		Validation cohort N = 108	
	n	%	n	%
Age				
<67	159	62.1	61	56.4
≥67	97	37.9	47	43.5
Race				
Black	42	16.4	20	18.5
Other	25	9.8	17	15.7
White	189	73.8	71	65.8
Histological types				
Endometrioid	82	32.0	34	31.5
Non-endometrioid	110	42.9	53	49.1
Sarcoma	64	25.1	21	19.4
Grade				
I	9	3.5	7	6.5
II	30	11.7	13	12.0
III	134	52.3	59	54.6
IV	83	32.5	29	26.9
T stage				
T1	49	19.2	18	16.7
T2	30	11.7	12	11.1
T3	104	40.6	46	42.6
T4	28	10.9	9	8.3
Tx	45	17.6	23	21.3
N stage				
No	105	41.1	42	38.9
N1	60	23.4	29	26.8
N2	60	23.4	22	20.4
Nx	31	12.1	15	13.9
Surgery				
No	129	50.4	54	50.0
Yes	127	49.6	54	50.0
Radiotherapy				
No	146	57.0	59	54.6
Yes	110	43.0	49	45.4
Chemotherapy				
No	110	43.0	41	38.0
Yes	146	57.0	67	62.0
Brain metastasis				
No	233	91.0	101	93.5
Yes	23	9.0	7	6.5
Liver metastasis				
No	197	77.0	78	72.2
Yes	59	23.0	30	27.8
Lung metastasis				
No	146	57.0	43	39.8
Yes	110	43.0	65	60.2
Insurance status				
No	15	5.9	3	2.8
Yes	241	94.1	105	97.2
Marital status				
No	135	52.7	69	63.9
Yes	121	47.3	39	36.1

demonstrated the survival benefit of chemotherapy and surgery for EC patients with BM. EC is usually treated primarily by surgery, which has become part of the initial treatment of EC, with total hysterectomy being the standard.<sup>[21]</sup> In addition, there is an association between tumor clearance and patient survival,

with a 9.3-month improvement in OS, reported for patients who achieved complete local tumor resection compared to those with incomplete tumor resection.<sup>[6]</sup> Chemotherapy is a systemic treatment, and the combination of anthracyclines, purple shirts, and platinum is currently used for EC patients with BM.<sup>[22]</sup>



**Table 4**  
**Univariate and multivariate Cox analysis for endometrial cancer patients with bone metastasis.**

	HR	Univariate Cox analysis			HR	Multivariate Cox analysis		
		95%CI		P		95%CI		P
Age								
<67	1							
≥67	1.321	1.003	1.739	.048				
Race								
Black	1							
Other	0.539	0.311	0.935	.028				
White	0.706	0.497	1.004	.053				
Histological types								
Endometrioid	1				1			
Non-endometrioid	1.379	1.004	1.895	.047	1.437	1.043	1.980	.027
Sarcoma	1.428	0.996	2.047	.053	1.974	1.356	2.874	.000
Grade								
I	1							
II	0.734	0.325	1.657	.457				
III	1.366	0.666	2.800	.395				
IV	1.183	0.569	2.461	.653				
T stage								
T1	1							
T2	1.384	.831	2.305	.212				
T3	1.433	0.976	2.104	.066				
T4	1.825	1.103	3.018	.019				
Tx	1.467	0.937	2.297	.094				
N stage								
No	1							
N1	1.094	0.776	1.543	.608				
N2	1.039	0.735	1.469	.827				
Nx	1.094	0.710	1.687	.683				
Surgery								
No	1				1			
Yes	0.592	0.451	0.776	.000	0.543	0.409	0.720	.000
Radiotherapy								
No	1							
Yes	0.829	0.634	1.085	.173				
Chemotherapy								
No	1				1			
Yes	0.438	0.334	0.575	.000	0.391	0.295	0.518	.000
Brain metastasis								
No	1				1			
Yes	1.979	1.253	3.126	.003	1.905	1.193	3.042	.007
Liver metastasis								
No	1				1			
Yes	1.518	1.120	2.057	.007	1.665	1.219	2.273	.001
Lung metastasis								
No	1							
Yes	1.098	0.840	1.435	.494				
Insurance status								
No	1							
Yes	0.903	0.515	1.582	.720				
Marital status								
No	1							
Yes	0.892	0.683	1.165	.402				

Chemotherapy can act to kill cancer cells in both primary tumor lesions and BM, so in patients with first diagnosed advanced EC (including those with BM), chemotherapy significantly improves the prognosis of patients and increases the survival rate as the number of chemotherapy cycles increase.<sup>[23]</sup> Radiotherapy failed to improve the prognosis of EC patients with BM, which may be

explained by the reduced responsiveness of the aggressiveness of these cancers to treatment and the rapid progression of the disease.<sup>[10]</sup> However, in our clinical work, we can control bone destruction and prevent fracture by local radiotherapy and application of phosphate or denosumab to the BM lesions, thus relieving pain and improving the quality of life of patients.<sup>[19]</sup>

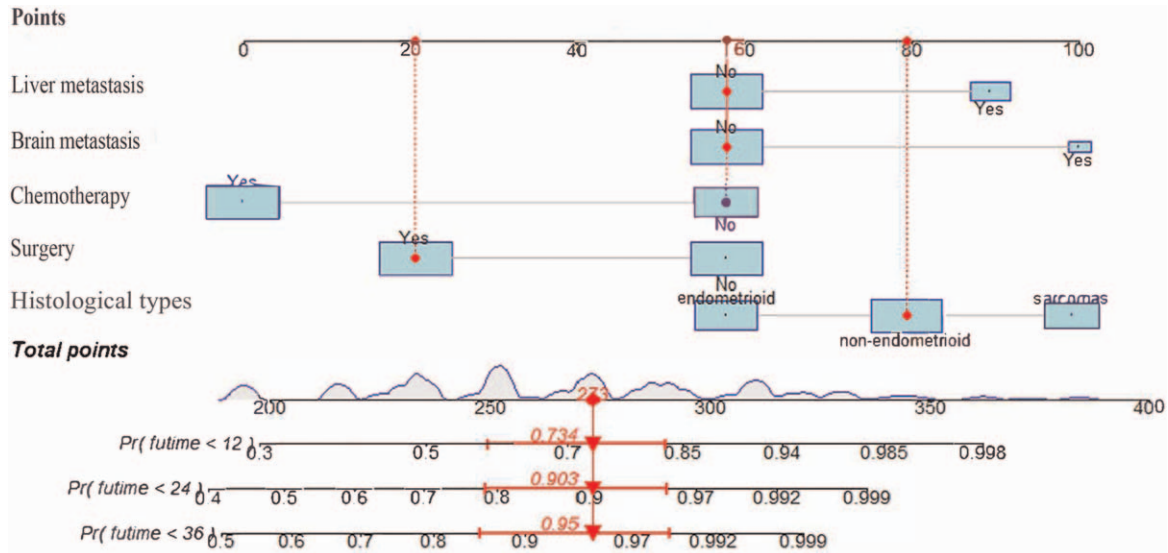


Figure 6. Nomogram to predict the OS of EC patients with BM. BM = bone metastasis, EC = endometrial cancer, OS = overall survival.

Recently, there have been few studies on nomograms to predict OS in patients with EC. Although some genetically based nomograms to predict prognosis in patients with EC have been reported previously, the difficulty and expense of obtaining relevant genetic data on patients have reduced the clinical utility of the models.<sup>[24–26]</sup> In the present study, we constructed diagnostic and prognostic nomograms to predict the risk of BM in EC patients and the OS of EC patients with BM by analyzing a large number of data, respectively. We believe that 2 nomograms representing OS and distant metastasis, respectively, are complementary and can increase their clinical value in

patients with EC. The total score can be calculated by obtaining data for the corresponding variable on the nomogram for each EC patient. The risk of BM can then be easily identified on the diagnostic nomogram, identifying patients in the high-risk group, and guiding clinical practice in early intervention. Similarly, the prognosis of EC patients with BM can be determined from the prognostic nomogram. In the validation of the 2 nomograms, the 2 nomograms showed excellent performance in BM risk assessment and OS prediction in EC patients, respectively, which will enable more accurate personalized clinical decision-making and monitoring. Inevitably, of course, this study has some

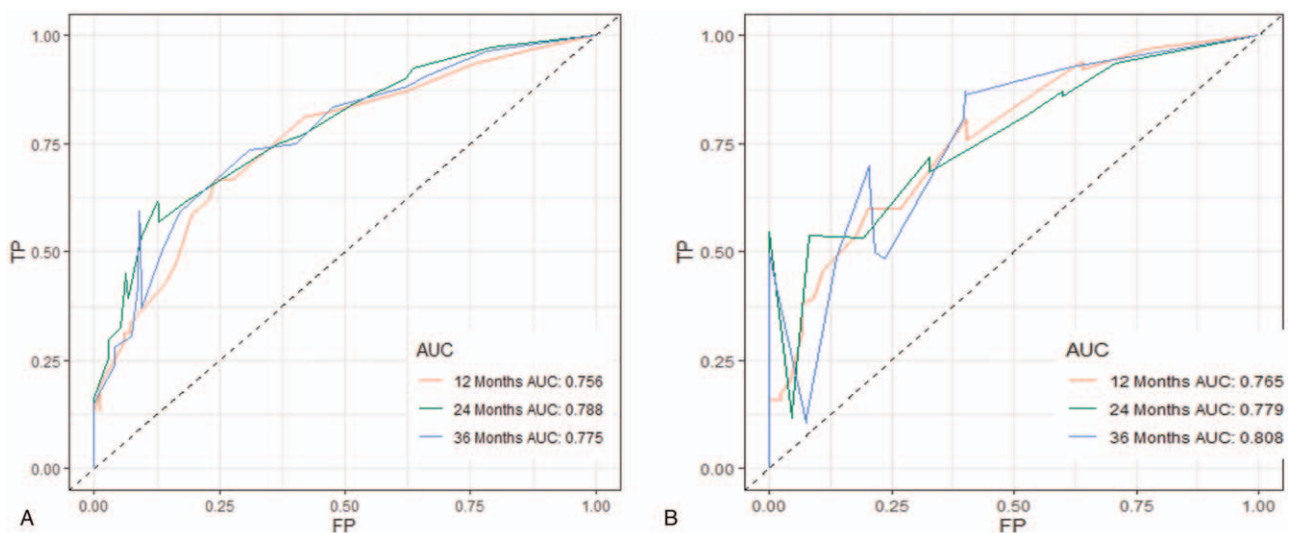
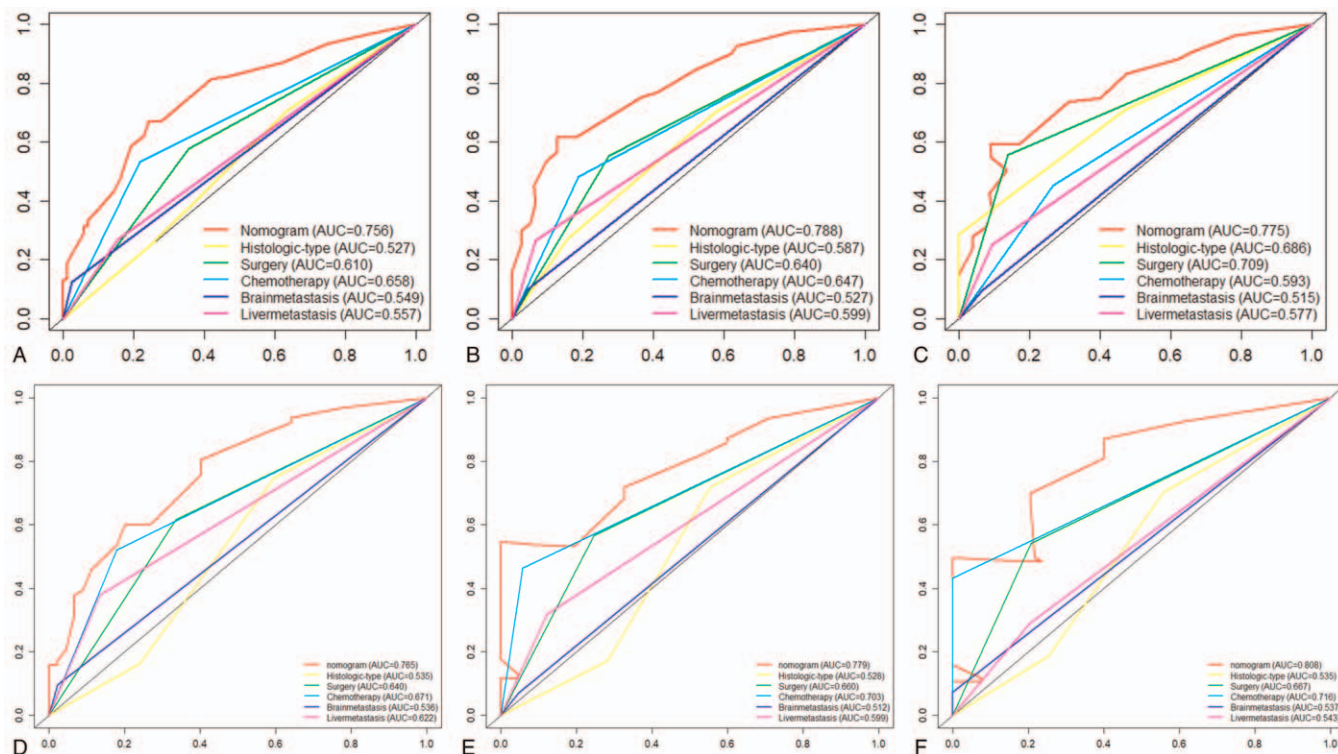


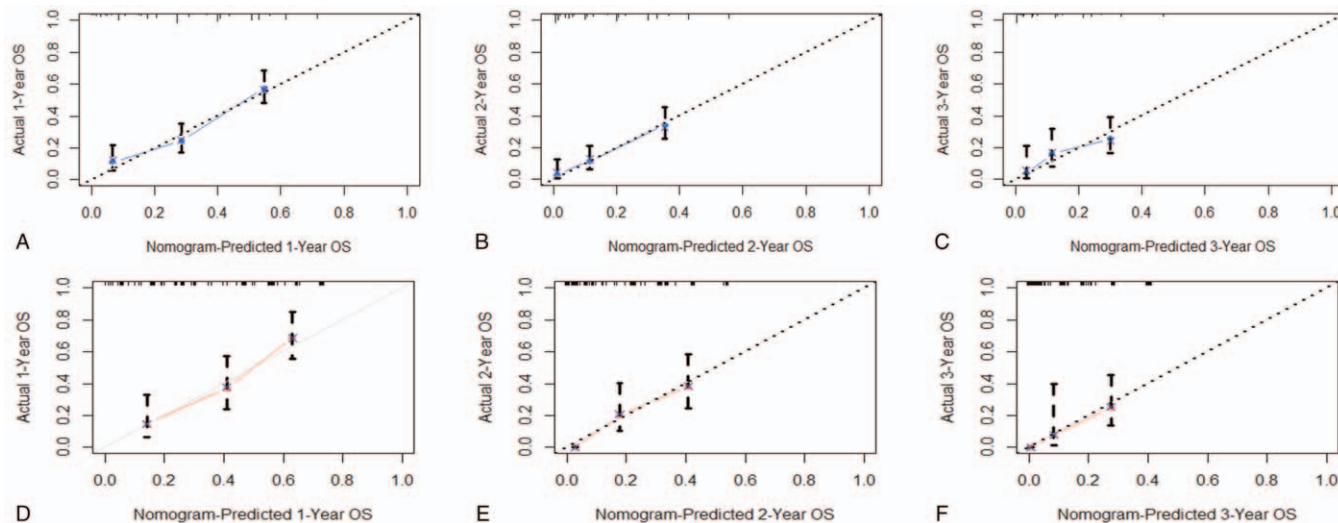
Figure 7. The ROC curves of nomogram at 1-, 2-, and 3-years in the training cohort and validation cohort. AUC = area under the curve, ROC = receiver operating characteristic.



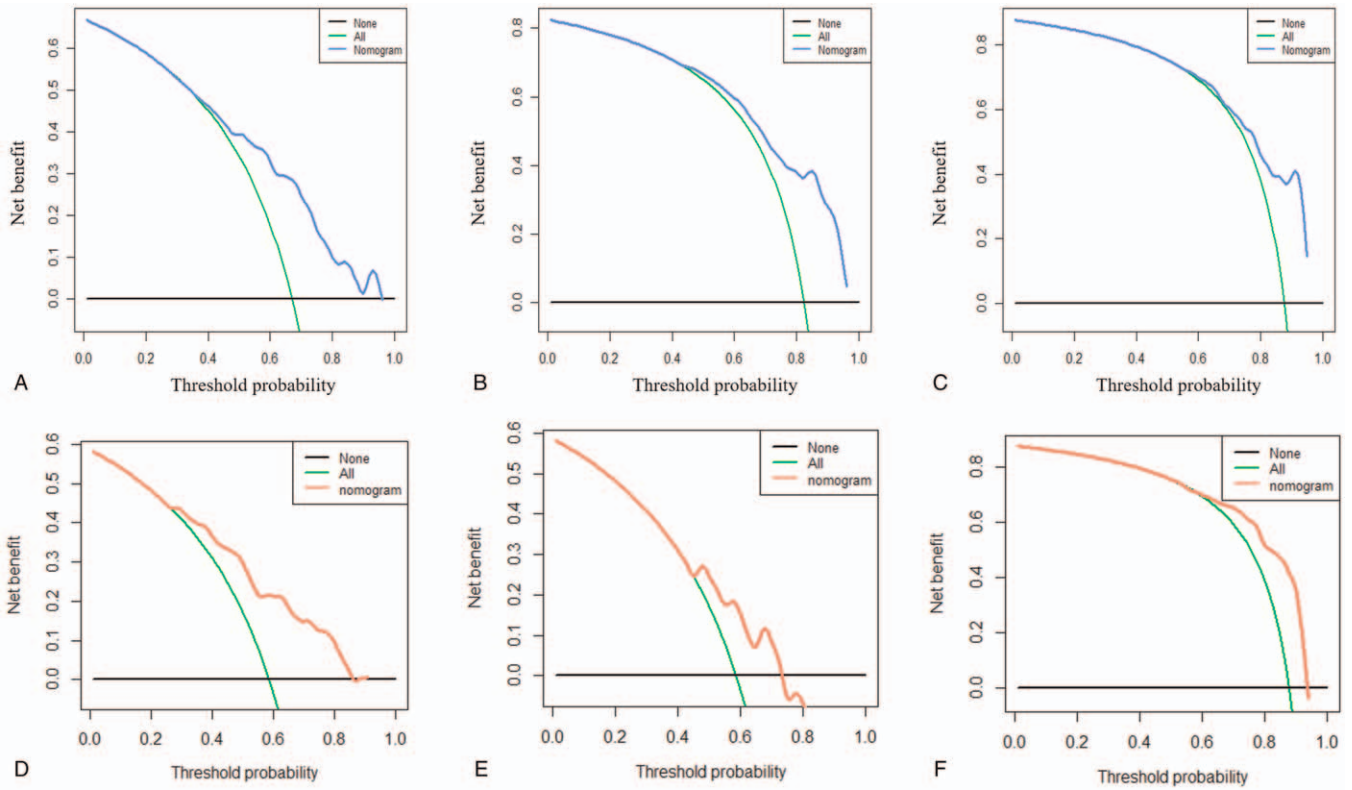
**Figure 8.** ROC curves of the prognostic nomogram and each independent predictor in predicting prognosis at the 1-, 2-, and 3-year points in the training cohort (A–C), validation cohort (D–F). AUC = area under the curve, ROC = receiver operating characteristic.

limitations. First, this was a retrospective study in which selection bias was inevitable. Secondly, the database does not reflect the complete process of treatment and does not clarify the sequence of treatment means and specific information related to treatment, such as the cycle of chemotherapy and the dose of radiotherapy.

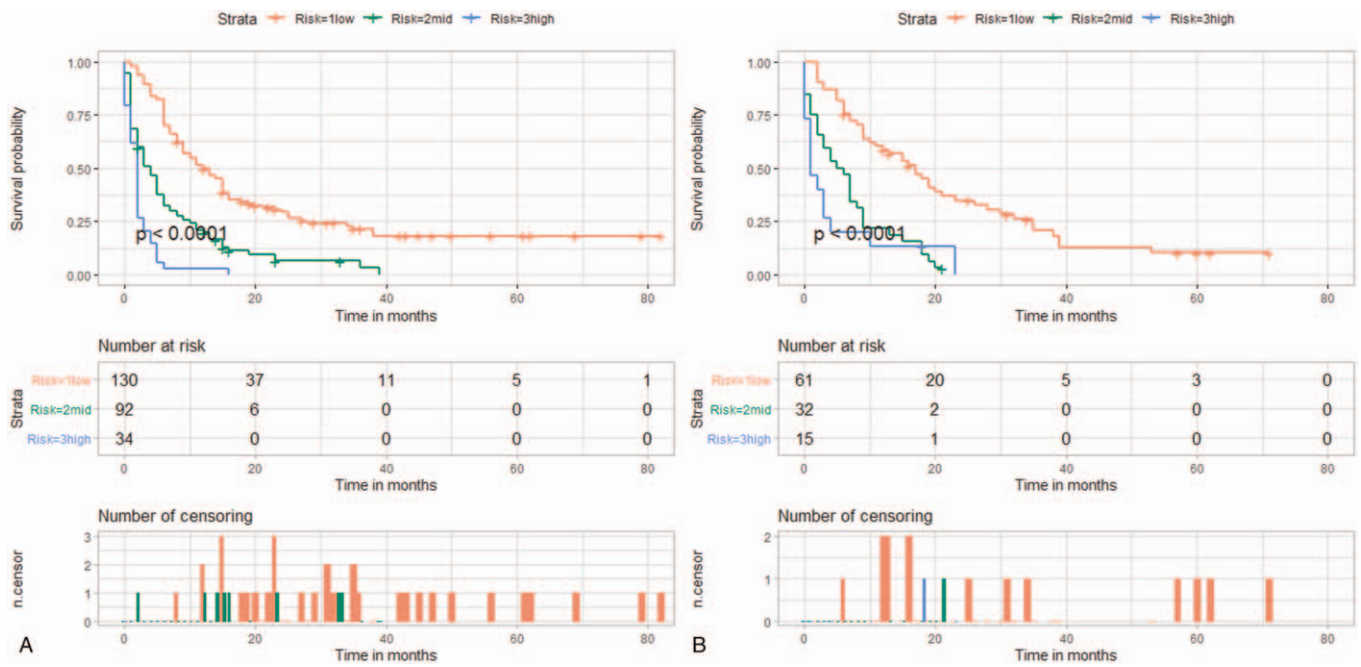
Third, information collected in the SEER database is about the disease at the time of the first diagnosis and does not record BM that occurred later. Fourthly, since 80% of the individual are “White”, this analysis could be a biased representation for the White population.



**Figure 9.** (A–C) The calibration curves of the prognostic nomogram in the training cohort; (D–F) The calibration curves of the prognostic nomogram in the validation cohort. OS = overall survival.



**Figure 10.** (A–C) The DCA of the prognostic nomogram in the training cohort; (D–F) The DCA of the prognostic nomogram in the validation cohort. DCA = decision curve analysis.



**Figure 11.** The Kaplan-Meier survival curve analysis of the training cohort (A) and validation cohort (B).

## 5. Conclusion

The risk factors for the development of BM in patients with EC and independent prognostic factors for EC patients with BM were identified in this study. On this basis, we created 2 nomograms that can be used as predictive tools for EC patients to help clinicians differentiate, assess, and evaluate the risk and prognosis of EC patients with BM.

## Author contributions

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**Writing – original draft:** Fengkai Yang.

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