

# A nomogram for predicting overall survival rate in patients with brain metastatic non-small cell lung cancer

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## Abstract

The purpose was to develop a nomogram for the prediction of the 1- and 2-year overall survival (OS) rates in patients with brain metastatic non-small cell lung cancer (BMNSCLC).

Patients were collected from the Surveillance Epidemiology and End Results program (SEER) and classified into the training and validation groups. Several independent prognostic factors identified by statistical methods were incorporated to establish a predictive nomogram. The concordance index (C-index), the area under the receiver operating characteristics curve (AUC), and calibration curve were applied to estimate predictive ability of the nomogram. To compare the clinical practicability of the nomogram and TNM staging system by decision curve analysis (DCA).

A total of 24,164 eligible patients were collected and assigned into the training (n = 16,916) and validation groups (n = 7248). Based on the prognostic factors, we developed a nomogram with good discriminative ability. The C-indices for training and validation group were 0.727 and 0.728. The AUCs of 1- and 2-year OS rates were both 0.8, and the calibration curves also demonstrated good performance of the nomogram. DCA illustrated that the nomogram provided clinical net benefit compared with the TNM staging system.

We developed a predictive nomogram for more accurate and comprehensive prediction of OS in BMNSCLC patients, which can be a useful and convenient tool for clinicians to make proper clinical decisions, and adjust follow-up management strategies.

**Abbreviations:** AUC = the area under the receiver operating characteristics curve, BMNSCLC = brain metastatic non-small cell lung cancer, C-index = concordance index, DCA = decision curve analysis, NSCLC = non-small cell lung cancer, OS = overall survival, SEER = Surveillance Epidemiology and End Results program.

**Keywords:** nomogram, non-small cell lung cancer, overall survival, SEER

## 1. Introduction

Lung cancer, an important public health issue worldwide, is the main cause of cancer-related mortality in most countries.<sup>[1–5]</sup> Non-small cell lung cancer (NSCLC), the most common type of histology, accounts for 85% of all diagnosed lung cancer cases. Even 40% of patients with NSCLC present with distant metastasis including the brain, liver, and bones.<sup>[2–10]</sup> Due to limited treatment success, most patients have a low 5-year overall survival (OS) rate, which is approximately 15% in NSCLC patients with brain metastasis.<sup>[5–11]</sup> Currently, immunotherapy is widely used for therapy of brain metastatic non-small cell lung cancer (BMNSCLC) patients, which has significantly increased the survival rate to as much as 45%,<sup>[5]</sup> however, immunotherapy has relatively a subset of side effects and requires a long cycle.<sup>[6]</sup> Furthermore, immunotherapy is extremely expensive.<sup>[5]</sup> Therefore, it is important for physicians to monitor and treat BMNSCLC patients as soon as possible.

Nomogram is a graphical predictive model that uses several continuous or discontinuous variables to estimate a survival rate or risk of a disease. It is mainly based on common statistical methods, such as Cox hazard regression or logistical regression. To date, nomograms have been widely applied to help clinicians to quickly and accurately predict the prognosis in patients. Majority of studies identified several prognostic factors of BMNSCLC.<sup>[4,9,11–14]</sup> However, most of those studies were limited by a small sample size,<sup>[4,9,11–14]</sup> and few studies constructed a nomogram for predicting the survival rate of patients with BMNSCLC based completely on common clinical findings. As a consequence, we selected common clinical risk factors, including sex, age, race, marital status, primary site, histology, grade, tumor size, T stage, N stage, radiation, and chemotherapy, from a public population-based database, to provide better understanding on the prognostic factors of personal OS rate in BMNSCLC patients.

SP and YX equally contributed to the study.

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The datasets generated during and/or analyzed during the current study are publicly available.

The authors have no conflicts of interest to disclose.

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In the present study based on the Surveillance Epidemiology and End Results program (SEER) database, the aim was to identify demographic and clinicopathological factors related with prognosis. Particularly, our study sought to establish a predictive nomogram for the 1- and 2-year OS rates of BMNSCLC patients.

## 2. Methods

### 2.1. Study population

The information were collected from the SEER. There are 18 cancer registries in the SEER database, encompassing

approximately 26% of the USA population. The available data include cancer patient demographic information (sex, age, race), tumor-related indexes (grade, histology, and TNM stage), and treatment strategies (surgery, chemotherapy, radiotherapy).

Based on the restricted condition and the histology type in NSCLC, the clinicopathological findings and patients' status of BMSNCLC patients from 1973 to 2017 were extracted by the SEER\*Stat version 8.3.6 (username: 10883-Nov2019). The histologic types of NSCLC include adenocarcinoma (histologic codes 8244, 8245, 8250–8255, 8260, 8290, 8310, 8323, 8333, 8480, 8481, 8490, 8507, 8550, 8570, 8571, 8574, and 8576), squamous cell carcinoma (histologic codes 8052, 8070–8075,

**Table 1**

**The demographics and clinical characteristics for patients with BMNSCLC in different groups.**

Variable	Total(n = 24,164)(%)	Training group(n = 16,916)(%)	Validation group(n = 7248)(%)	P value
<b>Sex</b>				.4071
Female	11563(47.85)	8065(47.68)	3498(48.26)	
Male	12601(52.15)	8851(52.32)	3750(51.74)	
<b>Age</b>				.7301
<57	5310(21.97)	3710(21.93)	1600(22.08)	
57–76	15176(62.80)	10611(62.73)	4565(62.98)	
>76	3678(15.22)	2595(15.34)	1083(14.94)	
<b>Race</b>				.9325
White	18741(77.56)	13124(77.58)	5617(77.50)	
Black	3143(13.01)	2192(12.96)	951(13.12)	
Others	2280(9.43)	1600(9.46)	680(9.38)	
<b>Marital_status</b>				.0415
Married	12568(52.01)	8857(52.36)	3711(51.20)	
Unmarried	10610(43.91)	7400(43.75)	3210(44.29)	
Unknown	986(4.08)	659(3.89)	327(4.51)	
<b>Site</b>				.1652
Upper	12527(51.84)	8829(52.19)	3698(51.02)	
Middle	999(4.14)	704(4.16)	295(4.07)	
Lower	5940(24.58)	4154(24.56)	1786(24.64)	
Others	4698(19.44)	3229(19.09)	1469(20.27)	
<b>Histology</b>				.6611
ADC	16586(68.64)	11602(68.59)	4984(68.76)	
SCC	3253(13.46)	2264(13.38)	989(13.65)	
Others	4325(17.90)	3050(18.03)	1275(17.59)	
<b>Grade</b>				.3623
I	414(1.71)	282(1.67)	132(1.82)	
II	2492(10.31)	1750(10.35)	742(10.24)	
III	6754(27.95)	4707(27.83)	2047(28.24)	
IV	296(1.23)	194(1.15)	102(1.41)	
Other	14208(58.80)	9983(59.02)	4225(58.29)	
<b>Tumor_size</b>				.8142
0–3	19548(80.90)	13701(80.99)	5847(80.67)	
3.1–5	24(0.10)	17(0.10)	7(0.10)	
>5	24(0.10)	15(0.09)	9(0.12)	
Unknown	4568(18.90)	3183(18.82)	1385(19.11)	
<b>T_stage</b>				.4837
T0	216(0.89)	140(0.83)	76(1.05)	
T1	2632(10.89)	1820(10.76)	812(11.20)	
T2	6072(25.13)	4248(25.11)	1824(25.17)	
T3	5490(22.72)	3869(22.87)	1621(22.36)	
T4	6896(28.54)	4843(28.63)	2053(28.33)	
Tx	2858(11.83)	1996(11.80)	862(11.89)	
<b>N_stage</b>				.0573
N0	5344(222.12)	3825(22.61)	1519(20.95)	
N1	2026(8.38)	1421(8.40)	605(8.35)	
N2	10736(44.43)	7436(43.96)	3300(45.53)	
N3	4699(19.45)	3285(19.42)	1414(19.51)	
Nx	1359(5.62)	949(5.61)	410(5.66)	
<b>Radiation</b>				.0786
Non-radiation	5638(23.33)	4000(23.65)	1638(22.60)	
Radiation	18526(76.67)	12916(76.35)	5610(77.40)	
<b>Chemotherapy</b>				.8549
Non-chemotherapy	11268(46.63)	7895(46.67)	3373(46.54)	
Chemotherapy	12896(53.37)	9021(53.33)	3875(53.46)	

BAC = bronchioloalveolar carcinoma, BMNSCLC = brain metastatic non-small cell lung cancer, Nx = unknown T stage, other = other types or unknown information, SCC = squamous cell carcinoma, Tx = unknown T stage.

8083, 8084, 8123), large cell carcinoma (histologic codes 8012–8014), and other non-small-cell carcinoma (8046, 8050, 8003, 8004, 8022, 8031–8035, 8082, 8200, 8240, 8249, 8430, 8560, 8562, 8980). All methods were carried out in accordance with relevant guidelines and regulations. Data extraction and usage has been approved by SEER Program. All the data can be found in the SEER dataset. Analysis of data from SEER dataset was exempt from ethics review, and informed consent was not required.

**2.2. Selected variables**

In our study, the following common demographic and clinicopathological variables from the SEER database were obtained: sex, age, race, marital status, primary site, histology, grade, tumor size, T stage, N stage, radiation, chemotherapy, survival months, and vital status. We excluded cases with missing information and those younger than 18 years. X-tile, a tool for transforming a continuous variable into a categorical variable,<sup>[15]</sup> was used to divide the age into three groups as follows: <57 years, 57 to 76 years, and >67 years. Likewise, the tumor size was classified into 3 categories (0–3, 3.1–5, and >5 cm), in accordance with previous studies reported.<sup>[7,8,11]</sup>

**2.3. Nomogram construction**

The eligible patients were randomly divided into the training (70%) and validation groups (30%) by specific ratio. The candidate variables had to be confirmed as the independent prognostic factors by univariate and multivariate Cox regression analyses. In the training group, the identified prognostic factors were incorporated to construct a predictive nomogram for 1- and 2-year OS rates of BMNSCLC patients.

**2.4. Nomogram validation**

In the training group, internal validation of the nomogram was performed, and external validation was conducted in the validation group. The performances of nomogram validation include Harrell concordance index (C-index), calibration curve, the area under receiver operating characteristic (ROC) curve (AUC), and decision curve analysis (DCA). The Harrell C-index was used to estimate the discrimination ability of the nomogram. The Harrell C-index values fluctuate from 0.5 to 1.0,

with 0.5 indicating random opportunity and 1.0 representing perfect discrimination. In other words, higher Harrell C-index indicates better discrimination power of the nomogram. The calibration curve, comparing the concordance between the actual OS and the predicted OS probability, was conducted to estimate the nomogram’s performance. AUC was used to estimate the accuracy of the 1- and 2-year OS rate predictions. In brief, larger AUC reflects more accurate predictive performance of the nomogram. The DCA was conducted to show the clinical ability of the nomogram by quantifying the net benefit at disparate threshold probabilities. Furthermore, to compare the clinical net benefit between the nomogram and TNM staging system by the DCA.

**2.5. Statistical analysis**

Categorical variables were showed as frequencies and percentages, and they were compared using Chi-square test. Continuous variables were presented as median and range, and they were tested using Mann–Whitney U test. Univariate and multivariate analyses were applied to Cox proportional-hazards regression model, and we calculated the hazard ratio (HR) along with corresponding 95% confidence intervals (CI). Continuous variables were transformed into categorical variables using the X-tile software (Yale University, New Haven, Connecticut, USA).<sup>[15]</sup> Harrell C-index, calibration curve, AUC, DCA, and all of the statistical analyses were conducted in R software, version 3.6.3 and SPSS, version 26.0 (SPSS, Chicago, IL). The *P*-value <0.05 was considered statistically significant, and all analyses were two-sided.

**3. Results**

**3.1. Demographic and clinicopathological features of patients**

A total of 24,164 patients with BMNSCLC, aged more than 18 years, were eligible in the present study. They were randomly assigned into the training group (n = 16,916) and a validation group (n = 7248). Table 1 shows common demographic and clinicopathological features of the patients. Except marital status, there were no statistically significant differences in demographic and clinicopathological features between the training and validation groups. In total, 12,601 (52.15%) of the patients were

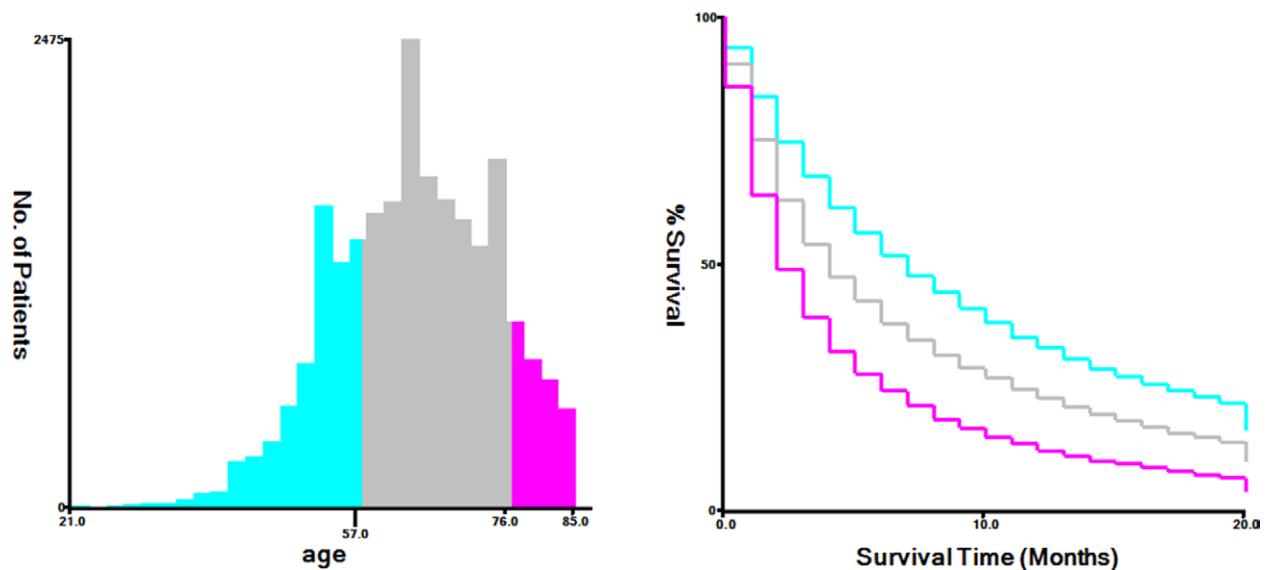


Figure 1. The optimal cutoff values for age were <57, 57 to 76 and >67 years old.

of male sex, and the most common race was White (18,741; 77.56%). With regard to the age, the optimal cutoff value of age were <57, 57 to 76, and >67 years old, 57 to 76-year-old patients (15,176; 62.8%) were most common (Fig. 1). The most common marital status was married; the most common location of the primary site was upper lung (12,527; 52.01%); the predominant histological type was adenocarcinoma (16,585, 68.64%), and the most common grade was others (14,208; 58.80%). Tumor size was most often in the category 0 to 3 cm (19,548; 80.90%). T stage was often T4 (6896, 28.54%), and

N stage was often N2 (10,736, 44.43%). The most common treatments were radiation (18,526; 76.67%) and chemotherapy (12,896; 53.37%).

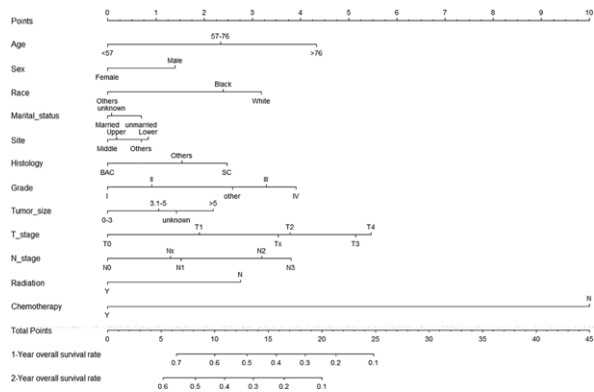
### 3.2. Independent prognostic factors in the training group

Univariate and multivariate Cox regression analyses were applied to select risk factors for predicting the OS rates. Sex, race, marital status, primary site, histology, tumor size, T stage, N stage, radiation, and chemotherapy were related with the

**Table 2**  
Univariate and multivariate Cox regression analyses for patients with BMNSCLC.

	Univariate HR(95%CI)	P value	Multivariate HR(95%CI)	P value
<b>Selected variables</b>				
<b>Sex</b>				
Female	Reference	NA	Reference	NA
Male	1.24(1.20,1.28)	<.001	1.15(1.12,1.19)	<.001
<b>Age</b>				
<57	Reference	NA	Reference	NA
57–76	1.36(1.31,1.42)	<.001	1.27(1.22,1.32)	<.001
>76	1.99(1.89,2.10)	<.001	1.55(1.47,1.64)	<.001
<b>Race</b>				
White	Reference	NA	Reference	NA
Black	0.99(0.95,1.04)	.699	0.92(0.88,0.97)	<.001
Others	0.70(0.66,0.74)	<.001	0.72(0.68,0.77)	<.001
<b>Marital status</b>				
Married	Reference	NA	Reference	NA
Unmarried	1.20(1.16,1.24)	<.001	1.07(1.04,1.11)	<.001
Unknown	1.12(1.04,1.22)	.005	1.00(0.93,1.09)	.86
<b>Site</b>				
Upper	Reference	NA	Reference	NA
Middle	0.97(0.90,1.05)	.469	0.98(0.91,1.06)	.66
Lower	1.06(1.02,1.10)	.003	1.07(1.03,1.11)	<.001
Others	1.20(1.15,1.25)	<.001	1.05(1.01,1.10)	.027
<b>Histology</b>				
ADC	Reference	NA	Reference	NA
SCC	1.53(1.46,1.60)	<.001	1.29(1.23,1.35)	<.001
Others	1.33(1.28,1.39)	<.001	1.17(1.12,1.22)	<.001
<b>Grade</b>				
I	Reference	NA	Reference	NA
II	1.04(0.91,1.19)	.539	1.10(0.96,1.26)	.176
III	1.42(1.25,1.61)	<.001	1.40(1.23,1.59)	<.001
IV	1.62(1.33,1.95)	<.001	1.49(1.23,1.80)	<.001
Other	1.29(1.13,1.46)	<.001	1.30(1.15,1.48)	<.001
<b>Tumor_size</b>				
0–3	Reference	NA	Reference	NA
3.1–5	1.32(0.82,2.12)	.254	1.11(0.69,1.79)	.658
>5	1.78(1.07,2.96)	.025	1.25(0.75,2.07)	.389
Unknown	1.28(1.23,1.33)	<.001	1.16(1.10,1.21)	<.001
<b>T_stage</b>				
T0	Reference	NA	Reference	NA
T1	0.97(0.81,1.16)	.732	1.21(1.00,1.47)	.044
T2	1.19(0.99,1.43)	.056	1.47(1.22,1.77)	<.001
T3	1.37(1.14,1.64)	<.001	1.69(1.40,2.03)	<.001
T4	1.44(1.20,1.72)	<.001	1.74(1.45,2.09)	<.001
Tx	1.47(1.22,1.76)	<.001	1.43(1.18,1.73)	<.001
<b>N_stage</b>				
N0	Reference	NA	Reference	NA
N1	1.08(1.01,1.15)	.019	1.17(1.09,1.24)	<.001
N2	1.24(1.19,1.29)	<.001	1.38(1.33,1.44)	<.001
N3	1.23(1.17,1.29)	<.001	1.47(1.40,1.55)	<.001
Nx	1.39(1.29,1.49)	<.001	1.14(1.06,1.23)	<.001
<b>Radiation</b>				
Non-radiation	Reference	NA	Reference	NA
Radiation	0.58(0.56,0.61)	<.001	0.76(0.72,0.79)	<.001
<b>Chemotherapy</b>				
Non-chemotherapy	Reference	NA	Reference	NA
Chemotherapy	0.34(0.33,0.35)	<.001	0.36(0.35,0.38)	<.001

BAC = bronchioloalveolar carcinoma, BMNSCLC = brain metastatic non-small cell lung cancer, Nx = unknown T stage, other = other types or unknown information, SCC = squamous cell carcinoma, Tx = unknown T stage.



**Figure 2.** A nomogram for prediction of 1- and 2- year OS rates in patients with brain metastases in non-small cell lung cancer. BAC = bronchioloalveolar carcinoma, Nx = unknown T stage, other = other types or unknown information, OS = overall survival, SCC = squamous cell carcinoma, Tx = unknown T stage.

prognosis of BMNSCLC patients (Table 2). These prognosis-related factors were identified as the independent prognostic factors by multivariate Cox regression analyses.

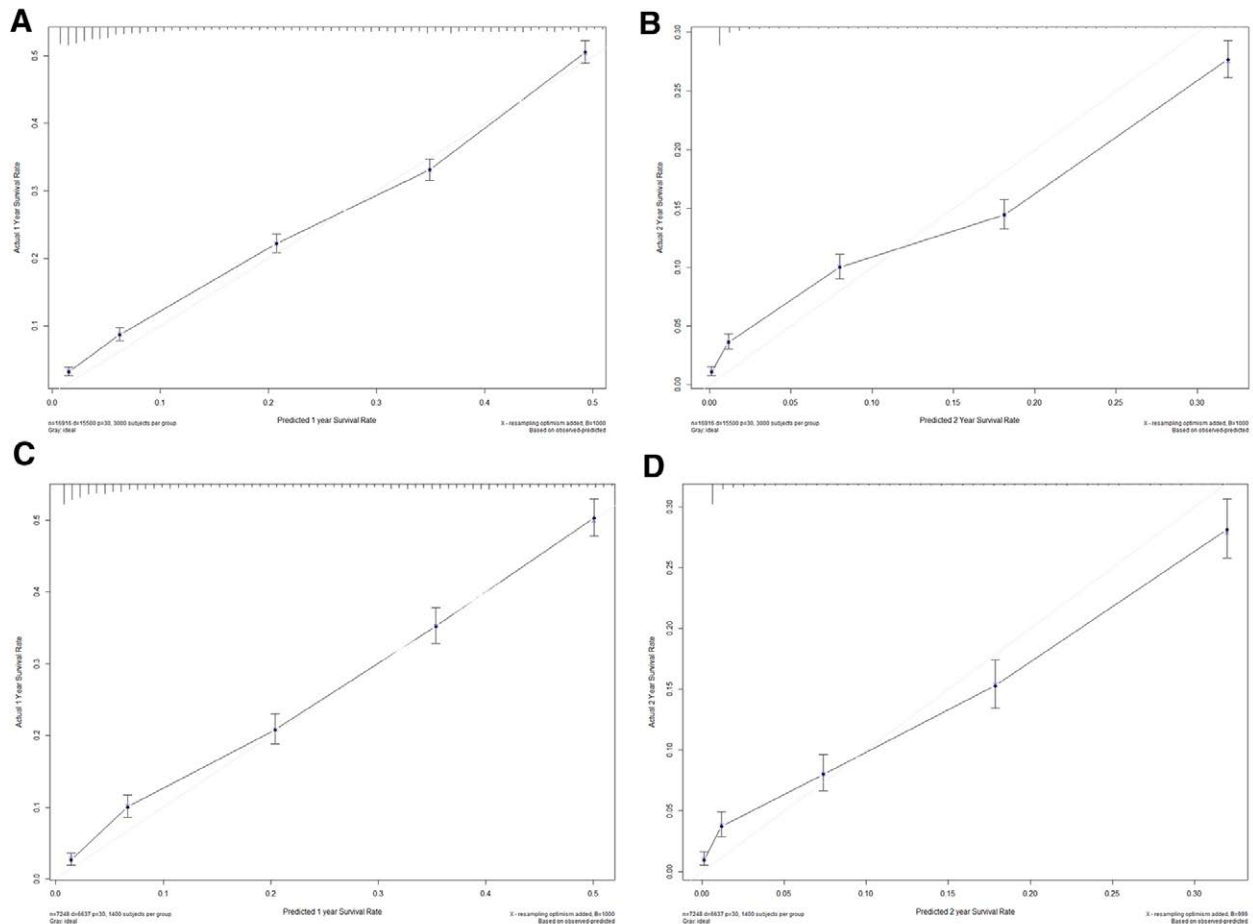
**3.3. The construction and validation of the nomogram**

Age, sex, race, marital status, site, histology, grade, T and N stage, radiation, and chemotherapy were used to construct

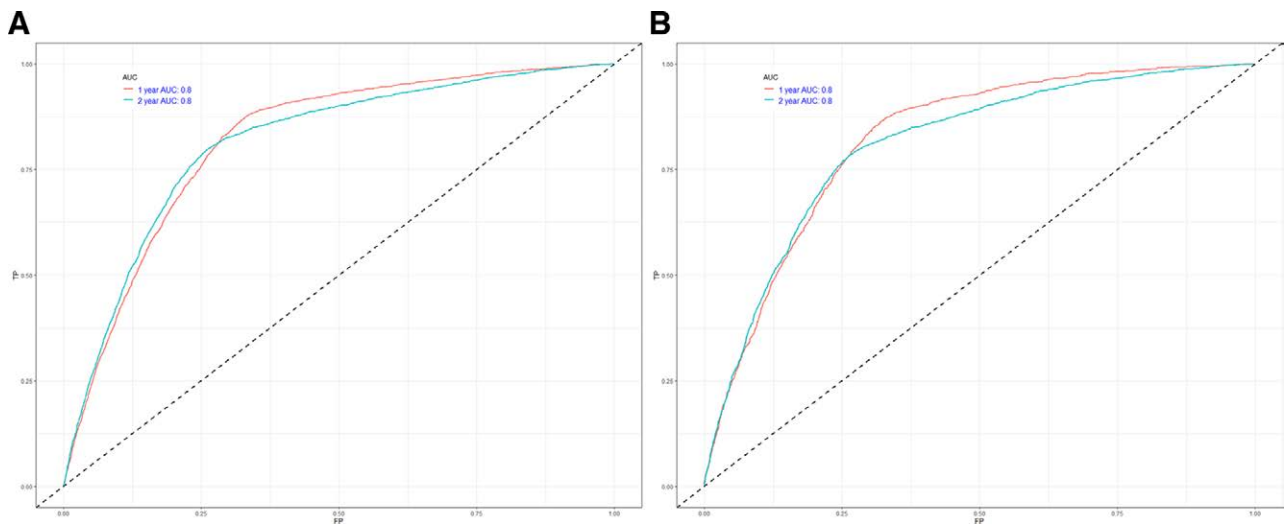
a nomogram for predicting the 1- and 2-year OS of patients with BMNSCLC. The points for each independent prognostic factor were summed to obtain the total score for the predicted individual patient (Fig. 2). A vertical line drawn from the total score row to the bottom timeline can be used to compute the patient’s 1- and 2-year mortality rate, and the corresponding OS can be obtained (Fig. 2). Internal validation showed that the C-index of the nomogram was 0.727 (95% confidence interval: 0.723–0.731) in the training group. The C-index of the external validation was 0.728 (95% confidence interval: 0.722–0.734) in the validation group (Fig. 3). The calibration curves of the nomogram closely corresponded with the 45° ideal curve lines, demonstrating the nomogram’s high prediction accuracy. Figure 4 indicated that the 1- and 2-year OS rates were consistent with the actual survival probabilities within a 10% margin of error represented with respect to the training and validation groups. In addition, all ROC curves of nomogram were 0.8 in the training and validation groups, indicating that the nomogram has strong discriminatory power (Fig. 4). Finally, DCA revealed that the nomogram had an excellent positive net clinical benefit within a specific threshold range, demonstrating the good clinical utility of nomogram. Additionally, nomogram presented a better clinical net benefit than the TNM staging system (Fig. 5).

**4. Discussion**

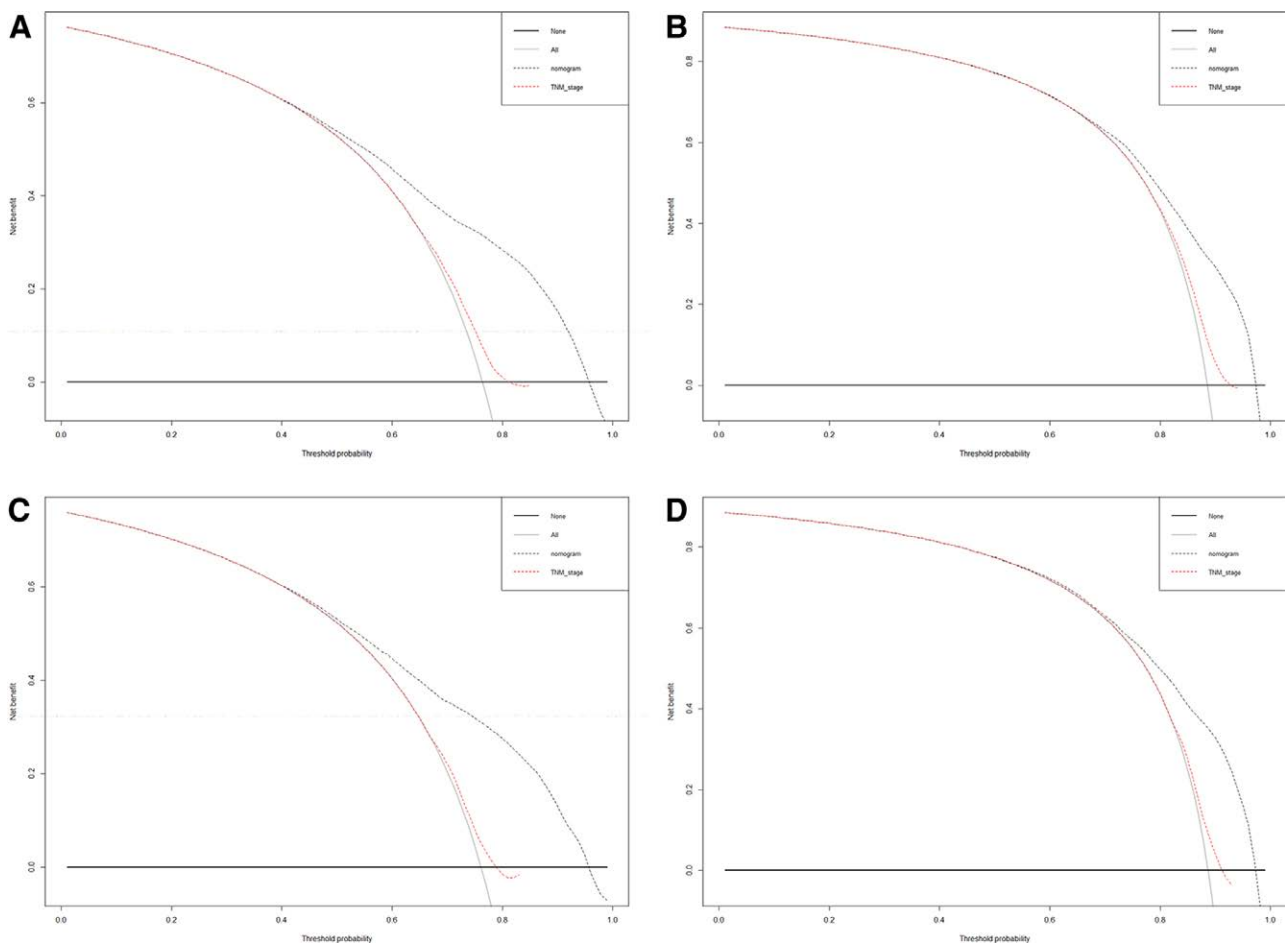
In the current study, we selected several demographic and clinicopathological variables and identified variables associated with the survival of patients with BMNSCLC. Our nomogram,



**Figure 3.** Calibration curves of the 1- and 2- year OS rates nomogram in training and validation groups. A, 1-year OS rate in training group; B, 2-year OS rate in training group; C, 1-year OS rate in validation group; D, 1-year OS rate in validation group.OS = overall survival.



**Figure 4.** The area under the receiver operating characteristics curve (AUC) identified the predictive performance of nomogram. A, AUCs for 1- and 2-year OS rates in training group; B, AUCs for 1- and 2-year OS rates in validation group. OS = overall survival.



**Figure 5.** Decision curve analysis (DCA) based on nomogram, TNM-stage system in different groups. A, DCA for 1-year OS rate in training group; B, DCA for 2-year OS rate in training group; C, DCA for 1-year OS rate in validation group; D, DCA for 2-year OS rate in validation group. OS = overall survival.

constructed by incorporating the abovementioned variables, was used to be the prediction of the 1- and 2-year OS in BMNSCLC patients and proved a good discriminative ability based on the C-index, calibration curves, and AUCs. Moreover, DCA indicated that the constructed nomogram had greater clinical net benefit compared with the TNM staging system at all threshold

probabilities. The nomogram could contribute to the clinical prognostic surveillance and individual treatment strategy for BMNSCLC.

We observed that these common demographic and clinicopathological variables were associated with the prognosis of BMNSCLC. Based on univariate and multivariate Cox

regression analyses, patients older than 76 years were more likely to suffer from NSCLC with brain metastases, which was consistent with previous reports.<sup>[14,16]</sup> Our study also indicated that male, White, and unmarried patients were prone to develop BMNSCLC, which was in accordance with previous studies.<sup>[10,14]</sup> In terms of tumor pathology, our study clearly illustrated that patients with the primary site in the lower lung, squamous cell carcinoma, grade IV, and tumor size above 5 cm would have a worse prognosis than other patients. Similarly, previous studies suggested that those factors were associated with a poor prognosis.<sup>[14,8,10,14]</sup> In addition, our nomogram showed that the predicted results of T and N stages were consistent with TNM staging system, which was in line with a previous study.<sup>[14]</sup> Furthermore, the treatment with radiation or chemotherapy was in connection with a higher survival rate compared with patients without treatment.

A previous study developed a nomogram for predicting metastasis to the brain as the first relapse site and the 2- and 5- year OS rates in NSCLC patients.<sup>[9]</sup> Out of 1218 NSCLC patients in the training group, 87 developed brain metastasis. However, the nomogram constructed included only a limit number of demographic and clinicopathological findings, and their C-index was lower than 0.78, indicating that their predictive model was poor discriminative ability than our nomogram. In addition, only internal validation was performed. Compared with their nomogram, there were more complete demographic and clinicopathological risk factors available in our study, and our nomogram achieved better discriminative ability. Not only did we carry out the internal and external validations, but we also compared the nomogram with the TNM staging system in the present study.

In 2016, Zhang et al established an effective nomogram to predict the OS rates of brain metastases of patients with resected NSCLC.<sup>[11]</sup> The nomogram was developed from 4 independent clinicopathological risk factors, such as neuron-specific enolase, histologic type, total number of metastatic lymph nodes, and tumor grade.<sup>[11]</sup> However, these common demographic and clinicopathological variables were not included in their predictive model, which may limit the generalizability of the predictive nomogram. Additionally, DCA revealed that the nomogram had an excellent positive net clinical benefit in our study, demonstrating the good clinical utility of nomogram.

Deng et al constructed and validated a nomogram for predicting the risk of distantly metastatic in NSCLC patients, and the nomogram was developed by numerous identified factors, including race, age, histology, T stage, N stage, marital status, sex, histology, bone metastasis, brain metastasis, liver metastasis, with M1a disease, surgery, and chemotherapy.<sup>[16]</sup> The C-index of 0.704 in the training group and 0.699 in the validation group, showing that our nomogram was better discrimination power for predicting prognosis. In addition, variables of bone and liver metastasis were incorporated to build the nomogram. When bone and liver metastasis were removed, indicating that the predictive nomogram has a worse prognosis.<sup>[16]</sup>

To the best of our knowledge, this is the first effective nomogram completely derived from clinical characteristics and based on the largest population group so far. The C-index of nomogram was 0.727, which demonstrated better predictive ability than the TNM staging system. The AUCs were 0.8, also indicating good predictive power of the nomogram. The calibration curves showed that the predicted 1- and 2-year OS rates were roughly similar to the actual survival probabilities based on the training and validation groups. In addition, DCA clearly indicated that the nomogram had a great clinical net benefit and had a better clinical practicability than the TNM staging system.

Although our nomogram could accurately predict OS rates with BMNSCLC, there were some limitations in our study. First, our study was a retrospective group analysis, which inevitably suffered

from selection bias. Second, in the era of molecular profiling, several studies indicated that certain genes, RNA and other related molecules were prognostic factors, incorporation of these molecules to construct a new model to distinguish the high-risk patients and predict the OS rate would be useful.<sup>[5]</sup> The model derived from the genome-based molecules coupled with clinicopathological factors would be superior to the common clinicopathological variables-based model. In addition, new tumor marker, such as neuron-specific enolase, carcinoembryonic antigen, play a significant role in the treatment responses and survival time.<sup>[1]</sup> Third, we could not collect the immunotherapy information to incorporate in the nomogram. Currently, the wide use of immunotherapy in advanced NSCLC, particularly in distant metastatic NSCLC, has been shown to improve 5-year OS rate. Finally, all eligible patients were randomly assigned into two groups derived from the SEER database. The results of validation showed that the nomogram had a good performance, but it is necessary to externally validate the proposed nomogram in future studies.

## 5. Conclusion

We built a new nomogram to effectively predict the 1- and 2- year OS rates in patients with BMNSCLC and conducted validation for its discrimination and clinical net benefit. The nomogram might be a vital tool to personalize counseling and choose the optimal treatment strategy.

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