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Nomogram to predict cause-specific mortality in extensive-stage small cell lung cancer: A competing risk analysis

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Keywords
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Abstract

Background: Small-cell lung cancer (SCLC) is one of the most aggressive types of lung cancer. The prognosis for SCLC patients depends on many factors. The intent of this study was to construct a nomogram model to predict mortality for extensive-stage SCLC.

Methods: Original data was collected from the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute in the United States. A nomogram prognostic model was constructed to predict death probability for extensive-stage SCLC.

Results: A total of 16 554 extensive-stage SCLC patients from 2004 to 2014 in the SEER database were included in this study. Gender, race, age, TNM staging (including tumor extent, nodal status, and metastasis), and treatment (surgery, chemotherapy, and radiotherapy) were identified as independent predictors for lung cancer-specific death for extensive-stage SCLC patients. A nomogram model was constructed based on multivariate models for lung cancer related death and other cause related death. Performance of the two models was validated by calibration and discrimination, with C-index values of 0.714 and 0.638, respectively.

Conclusion: A prognostic nomogram model was established to predict death probability for extensive-stage SCLC. This validated prognostic model may be beneficial for treatment strategy choice and survival prediction.

Introduction

Small-cell lung cancer (SCLC) is one of the most lethal and aggressive types of lung cancer, with the majority of patients first diagnosed as extensive disease.[1] Platinum-based chemotherapy has remained the first line standard treatment for extensive-stage SCLC for decades.[2,3] However, despite the initial sensitive response to chemotherapy, most patients relapse after three months of treatment, or even show signs of cancer progression during treatment. To date, targeted therapy and immunotherapy have only made modest improvements in SCLC patients' prognosis. The overall survival (OS) for extensive-stage SCLC is poor and the prognosis for these patients is highly variable.

The American Joint Committee on Cancer (AJCC) TNM classification and Veterans Administration Lung Study Group (VALSG) system are commonly used for the prognosis of small cell lung cancer patients. AJCC TNM classification stratifies the disease by primary tumor (T stage), lymph node involvement (N stage), and distant metastasis (M stage)[4], while VALSG divides tumors into limited disease (LD) and extensive disease (ED). However, even for patients at the ED stage, their survival varies dramatically. Previous studies have indicated that clinical pathological characteristics might be related to the survival of SCLC patients.[5–7] However, the predictive value of these clinical factors remains unclear.

A nomogram is a mathematical model to predict certain endpoints, such as disease progression or death[8], based on several parameters. Several studies have constructed nomogram models to stratify the survival probability of SCLC.[9–12] However, the prognosis and treatment strategy for limited and extensive-stage SCLC patients are different. The aims of the current study were to construct and validate a nomogram model utilizing SEER database data involving clinical-pathological characteristics, and to predict survival in extensive-stage SCLC patients using this model. Compared to published models, our nomogram model had the following advantages: (i) the model was developed using a relatively large cohort; (ii) the model was developed to focus uniquely on extensive-stage SCLC; and (iii) the model used the more accurate AJCC TNM staging criteria to classify SCLC patients.

Methods

Study patients

We utilized the SEER program (https://seer.cancer.gov/seerstat, 23 March 2017) of the National Cancer Institute to select the population for this study. Patients diagnosed between 2004 and 2014 with SCLC as a first primary malignancy were selected for the study (SEER datasets opened 2004–2014 period data for researchers are freely available). Patients with the following International Classification of Diseases for Oncology, Third Edition (ICD-O-3), histology codes were included in the study population: 8002/3: malignant tumor, small cell type; 8041/3: small cell carcinoma, NOS; 8042/3: oat cell carcinoma; 8043/3: small cell carcinoma, fusiform cell; 8044/3: small cell carcinoma, intermediate cell; 8045/3: combined small cell carcinoma; the ICD-O-3 site codes: lung and bronchus including main bronchus (C34.0); upper lobe, lung (C34.1); middle lobe, lung (C34.2); lower lobe, lung (C34.3); overlapping lesion of lung (C34.8); and lung, NOS (C34.9).

Extensive-stage SCLC patients (AJCC staging IV) were selected for further analysis. Cancers diagnosed by autopsy or as the result of death certificates only were excluded. Other exclusion criteria for this study included collaborative stage (CS), tumor size code of 990 (microscope), or 996–999 (unknown); CS tumor extent code of 950, 980, or 999 (unknown extent); CS metastasis code 75 (stated as M1, NOS) or 99 (unknown); lymph node involvement (unknown or lymph node involvement, not otherwise specified).

The analysis of the SEER patients used de-identified summary-level data and required no ethical approval.

Statistical analysis

Cause-specific mortality was the primary endpoint. Consistent with the COD code, we classified cause of death as cancer-specific death and death from other causes. Cancer-specific death was defined as those that met the following criteria: (i) Dead = attributable to this cancer dx; and (ii) COD TO SITE RECORD = lung and bronchus; death from other causes defined as cause specific death = dead of other cause. Covariates included in the prediction model were selected based on known clinically prognostic factors and availability in the SEER database and included: age, gender, race (white, black or others/unknown), marriage (married or other status), anatomic sites (upper, middle, lower, bronchus or others), primary tumor location (left or right), tumor size, extent of tumor (local or regional), nodal status (N0, N1, N2 or N3), metastasis (m1a or m1b), grading (well, moderately, poorly, undifferentiated or NOS), surgery (yes or no), chemotherapy (yes or no), and radiotherapy (yes or no). The cumulative incidence function (CIF) was used to describe the probability of death, and the CIF difference between category groups was determined by Gray's test.[13] When CIF was evaluated, the age at diagnosis and tumor size were divided into three groups. The age at diagnosis was regrouped as less than 60, 60 to 75, and above 75 years. Tumor size was regrouped as less than 3 cm, 3–5 cm and above 5 cm.

Fine and Gray proportional hazards regression was performed to predict 3, 6 and 12 month probabilities of two competing mortality outcomes.[14] The continuous variables were fitted and modeled using restricted cubic splines with three knots at the 10%, 50%, and 90% empirical quantiles, and interactions were not evaluated. We used a model selection technique based on Bayesian information criteria when establishing competing risks models to avoid overfitting. Discrimination and calibration were both measured to internally validate the performance of the nomogram. Discrimination was indicated by the Harrell C index, and was defined as the ability of the model to separate subject outcomes.[15] With respect to competing risks, an ordered pair was considered as evaluable if the first patient experienced the event of interest at a time when the second patient was still at risk. The C-index of the model ranged from 0.5 to 1.0 (0.5 represented random chance, while 1.0 represented a perfectly discriminating model). Calibration referred to the agreement between predictions and observed outcomes. Calibration was evaluated at 3, 6, and 12 months with a calibration plot in which we compared the final reduced model-predicted probability of death with the observed cumulative incidence of death. The model-predicted probabilities were averaged within quintiles defined by the magnitude of the predictions. The marginal cumulative incidence of death was calculated within each

quintile of individuals using the method provided by Gray. Finally, a calibration curve was plotted representing the marginal estimate versus model average predictive probability. Predictions in a perfect calibration plot should fall on the 45-degree diagonal line, which indicated the model predicted the actual survival very well. Bootstrapping with 1000 resamples was adopted in internal validation.

All statistical analyses were performed using R software (version 3.3.3; http:// www.r-project.org). The R packages cmprsk, rms, and mstate were used for modeling and developing the nomogram. All reported significance levels were two-sided, with statistical significance set at 0.05.

Results

Patient characteristics

We identified 18 027 eligible extensive-stage SCLC patients from 2004 to 2014 in the SEER database. The flow chart for patient selection is in Figure 1, and the list of the patient demographics and clinical characteristics are displayed in Table 1. The majority of patients were Caucasian (87.1%) and over 60 years old (74.8%). Most received chemotherapy (69.4%) and did not undergo surgical procedures associated with their treatment (99.1%).

The median follow-up time was 5 months (interquartile range 1–10 months). A total of 16 554 (91.8% of 18 027) patients died during the follow-up period: 15683 (94.7% of 16 554) from cancer-specific death and 871 (5.3% of 16 554) from causes other than their cancer. Of those who died of other causes, the most common causes were heart disease (28.0%), chronic obstructive pulmonary disease (COPD). (11.4%), cerebrovascular diseases (3.8%), accidents and adverse effects (3.3%).

Probability of death

The cumulative incidence function curves are plotted in Figure 2. 15 683 patients died from cause-specific death and 871 from causes other than their cancer. The probabilities of cancer-specific death and death from other causes were as follows: 6 months, 51.2% and 3.1%, respectively; one year, 75.7% and 4.0%, respectively; three years, 92.3% % and 5.0%, respectively. Based on univariate analysis, the probability of death increased with age ($P < 0.001$) for patients who died from lung cancer-specific death and other causes. Male and Caucasian patients exhibited higher cumulative incidences of death compared with their counterparts (Table 1) for both groups. For patients who died from lung cancer-specific deaths, anatomic sites, tumor size, nodal status, tumor extension, and metastasis staging and differentiation showed significant associations with the probability of death. Surgery ($P < 0.001$), chemotherapy ($P < 0.001$), and radiotherapy ($P < 0.001$) significantly lowered the cumulative incidence of death among patients who received these treatments. For patients who died from other causes, only metastasis staging was significantly associated with death probability. Chemotherapy ($P = 0.015$) and radiotherapy ($P < 0.001$) also decreased the cumulative incidence of death from other causes. The estimates of the crude cumulative incidence of cause-specific and other causes of death by age at diagnosis, gender, race, marriage, anatomic sites, primary tumor location, tumor size, extent of tumor, nodal status, metastasis, grading, and treatment can be found in Table 1.

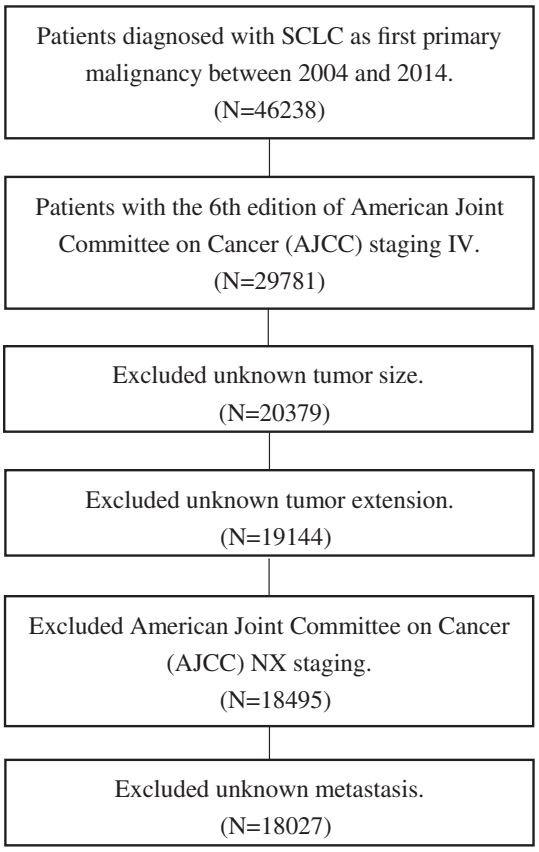

Figure 1 Flow chart of study patients' selection.

The results of competing risk model found that age at diagnosis, tumor size, gender, race, extent of tumor, nodal status, metastasis, surgery, chemotherapy, and radiotherapy could strongly predict cause-specific death (Table 2). Extensive-stage SCLC patients with advanced age, larger tumor size, distant and lymph node metastasis, and those both male and Caucasian had a higher probability of death as a result of lung cancer. Patients who underwent surgery, chemotherapy or radiotherapy had a lower rate of lung cancer-specific mortality. For those patients who died from other causes, the tumor related factors such as tumor size,

Table 1 Cumulative incidence of death among patients with extensive-stage SCLC

					Cancer-specific death				Death from other causes			
Characteristics	*N*	%	Event	%	Six months	One year	Three years	*P*-value	Six months	One year	Three years	*P*-value
Total	18 027		16 554		51.2	75.7	92.3		3.1	4.0	5.0	
Demographic characteristics												
Age at diagnosis, years								<0.001				<0.001
<60 years	4551	25.2	4102	24.8	41.1	70.6	92.5		1.8	2.8	3.7	
60–75 years	9785	54.3	8953	54.1	50.0	75.4	92.1		3.0	4.0	5.0	
>75 years	3691	20.5	3499	21.1	67.2	82.8	92.4		4.7	5.6	6.2	
Gender								<0.001				0.014
Female	8453	46.9	7690	46.5	49.1	73.4	92.0		2.7	3.6	4.5	
Male	9574	53.1	8864	53.5	53.2	77.7	92.5		3.4	4.5	5.3	
Race								<0.001				<0.001
White	15 709	87.1	14 465	87.4	51.7	76.3	92.7		2.9	3.9	4.7	
Black	1604	8.9	1459	8.8	48.6	72.9	90.7		3.6	4.4	6.1	
Others	714	4.0	630	3.8	47.7	67.8	86.3		5.2	6.1	8.4	
Marriage								<0.001				0.010
Married	9134	50.7	8378	50.6	48.2	74.3	92.4		2.8	3.7	4.6	
Others	8893	49.3	8176	49.4	54.3	77.2	92.1		3.3	4.4	5.4	
Disease characteristics												
Anatomic sites								0.009				0.203
Upper	9369	52.0	8563	51.7	50.4	74.9	92.3		3.0	3.8	4.7	
Middle	746	4.1	695	4.2	50.3	73.2	92.2		2.9	4.1	5.1	
Lower	4011	22.2	3695	22.3	51.4	76.2	92.0		3.3	4.7	5.6	
Bronchus/others	3901	21.6	3601	21.8	53.3	77.6	92.5		3.0	3.9	4.8	
Primary tumor location								0.702				0.720
Left-sided	7764	43.1	7131	43.1	51.2	75.9	92.4		3.1	4.1	4.9	
Right-sided	10 263	56.9	9423	56.9	51.3	75.5	92.2		3.1	4.0	5.0	
Tumor size (cm)								<0.001				0.319
≤3 cm	4747	26.3	4351	26.3	48.2	72.4	91.1		3.3	4.2	5.3	
3–5 cm	5016	27.8	4634	28.0	51.8	76.3	92.3		3.1	4.2	5.0	
>5 cm	8264	45.8	7569	45.7	52.6	77.2	92.9		2.9	3.8	4.7	
Tumor extension								<0.001				0.487
Local	7741	42.9	7023	42.4	48.6	73.9	91.5		3.1	4.1	5.1	
Regional	7304	40.5	6599	39.9	51.1	75.7	92.4		3.0	3.9	4.8	
Distant	2982	16.5	2932	17.7	58.4	80.2	93.7		3.3	4.2	4.8	
Nodal status								0.002				0.366
N0	2338	13.0	2136	12.9	52.1	72.2	90.4		3.2	3.8	4.9	
N1	1246	6.9	1148	6.9	50.1	73.7	90.7		3.3	4.5	5.8	
N2	10 695	59.3	9899	59.8	52.0	76.5	92.7		3.0	4.1	4.9	
N3	3748	20.8	3371	20.4	48.9	76.4	92.8		3.2	3.8	4.8	
Metastasis								<0.001				<0.001
M1a	1514	8.4	1326	8.0	38.6	60.6	83.7		4.7	5.9	7.4	
M1b	16 513	91.6	15 228	92.0	52.4	77.1	93.1		2.9	3.9	4.7	

Table 1 Continued

Characteristics	*N*	%	Event	%	Cancer-specific death			*P*-value	Death from other causes			*P*-value
					Six months	One year	Three years		Six months	One year	Three years	
Grading								0.024				0.846
Well or moderately	82	0.5	74	0.4	37.0	65.1	89.3		3.7	3.7	3.7	
Poorly	1464	8.1	1342	8.1	50.2	74.5	91.9		2.9	4.1	4.9	
Undifferentiated	3399	18.9	3193	19.3	50.2	74.7	91.8		3.0	4.4	5.3	
NOS	13 082	72.6	11 945	72.2	51.7	76.2	92.4		3.1	3.9	4.9	
Treatment characteristics												
Surgery								<0.001				0.566
Yes	171	0.9	141	0.9	35.8	57.8	81.1		2.4	3.7	5.2	
No	17 856	99.1	16 413	99.1	51.4	75.9	92.4		3.1	4.0	5.0	
Chemotherapy								<0.001				0.015
Yes	12 513	69.4	11 199	67.7	37.1	69.4	91.6		2.2	3.5	4.7	
No	5514	30.6	5355	32.3	83.4	90.0	93.9		4.9	5.3	5.4	
Radiotherapy								<0.001				<0.001
Yes	7587	42.1	6752	40.8	40.3	68.4	91.1		2.0	3.0	4.3	
No	10 440	57.9	9802	59.2	59.2	81.0	93.1		3.9	4.8	5.5	

tumor extension, nodal status, and treatment (chemotherapy and surgery) were no longer associated with death from other causes.

Nomogram

A nomogram was constructed in order to produce a user-friendly model that would allow users to estimate the risk for lung cancer specific death and death from other causes by entering a patient's clinicopathologic characteristics and treatment information. The nomogram based on Fine and Gray's model can be found in Figure 3. For example, consider a 60 year-old Chinese man classified using the American Joint Committee on Cancer (AJCC) stage IV (T3N2M1a) SCLC, who only received chemotherapy. The probabilities of death from lung cancer in 3, 6, and 12 months predicted by the nomogram model were 0.14, 0.24 and 0.42, respectively.

Model performance was internally validated for discrimination and calibration. Discrimination, as measured by the 1000 resample bootstrap-corrected C-index, was 0.714 (95% CI, 0.712–0.716) for the cancer-specific death and 0.638 (95% CI, 0.628–0.649) for death from other causes. The calibration plot (Figure 4) showed good agreement between predicted and observed outcomes.

Discussion

The treatment of extensive-stage SCLC is relatively uniform. However, the prognosis for most patients is highly variable. Veterans Administration and AJCC TNM staging are currently used for the prognosis of SCLC; however, more accurate prognostic models integrating additional demographic and clinical parameters are needed. Several prognostic scoring systems have been developed for SCLC, including the Manchester Score[16] and the Spain prognostic index.[17] However, patients in both studies received treatment nearly 40 years ago (1979–1993). The intensive treatment regimens involved in both studies, including cyclophosphamide, etoposide, and methotrexate, are no longer used.

The nomogram has been considered a more accurate model to predict patient prognosis.[15,18] Our study developed a prognostic model for the prediction of lung cancer related death for extensive-stage SCLC. Although several studies have identified clinical-pathologic and treatment predictors for survival of SCLC.[9–12] to our knowledge, the current study is the first to develop a nomogram prediction model for extensive-stage SCLC. Additionally, our study was based on a relatively large cohort of patients and involved various treatment strategies. This is the first nomogram model for SCLC based on the SEER database,

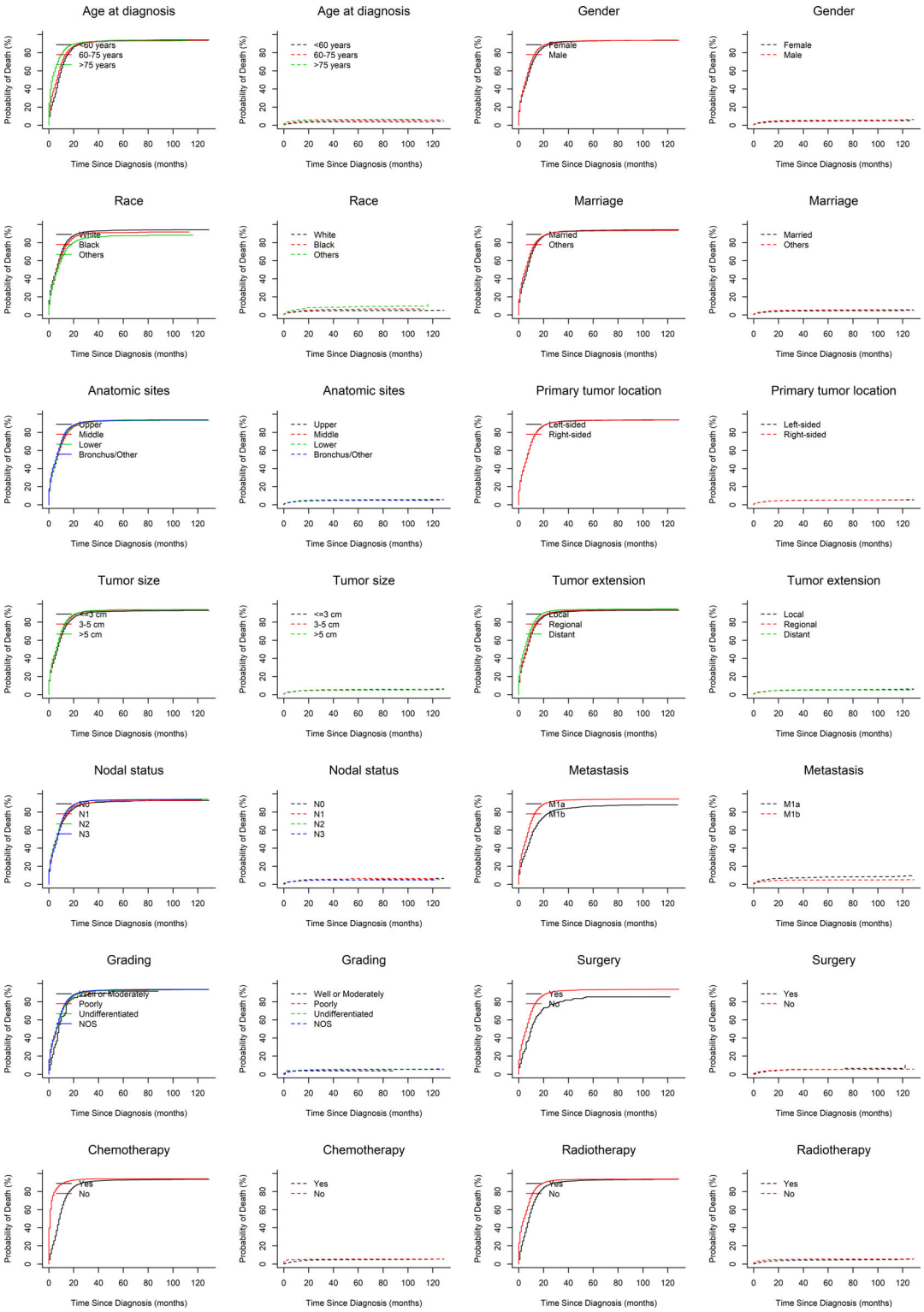

Figure 2 Cumulative incidence estimates of death according to patient characteristics (solid line indicates cause-specific death; dotted lineindicates other causes of death).

Table 2 Proportional subdistribution hazard models of probabilities of cancer-specific death and death from other causes for patients with extensive-stage SCLC

	Cancer-specific death						Death from other causes					
	Full model			Reduced model			Full model			Reduced model		
Characteristics	β	$_{sd}$HR (95%CI)	*P*	β	$_{sd}$HR (95%CI)	*P*	β	$_{sd}$HR (95%CI)	*P*	β	$_{sd}$HR (95%CI)	*P*
Age	0.004	1.004 (1.001–1.008)	0.014	0.004	1.004 (1.000–1.007)	0.024	0.026	1.026 (1.009–1.044)	0.003	0.027	1.027 (1.01–1.044)	0.002
Age'	0.005	1.005 (1.001–1.010)	0.029	0.005	1.005 (1.001–1.010)	0.021	−0.013	0.987 (0.969–1.006)	0.180	−0.012	0.988 (0.97–1.007)	0.210
Tumor size	0.034	1.034 (1.021–1.048)	<0.001	0.035	1.036 (1.022–1.049)	<0.001	−0.020	0.981 (0.928–1.036)	0.490	—	—	—
Tumor size'	−0.025	0.975 (0.964–0.988)	<0.001	−0.026	0.975 (0.963–0.987)	<0.001	−0.001	0.999 (0.944–1.059)	0.980	—	—	—
Male	0.078	1.081 (1.045–1.118)	<0.001	0.071	1.074 (1.039–1.110)	<0.001	0.229	1.257 (1.092–1.447)	0.002	0.219	1.245 (1.083–1.432)	0.002
Race												
Black	−0.111	0.895 (0.844–0.949)	<0.001	−0.105	0.900 (0.849–0.955)	<0.001	0.249	1.283 (1.031–1.596)	0.026	0.236	1.266 (1.018–1.574)	0.034
Others	−0.258	0.772 (0.703–0.849)	<0.001	−0.260	0.771 (0.702–0.847)	<0.001	0.605	1.832 (1.408–2.383)	<0.001	0.590	1.804 (1.388–2.344)	<0.001
Married	−0.035	0.965 (0.933–0.999)	0.046	—	—	—	−0.201	0.818 (0.711–0.940)	0.005	−0.197	0.821 (0.715–0.943)	0.005
Anatomic sites												
Middle	−0.019	0.981 (0.898–1.071)	0.670	—	—	—	0.042	1.043 (0.745–1.459)	0.810	—	—	—
Lower	−0.033	0.967 (0.926–1.010)	0.130	—	—	—	0.133	1.142 (0.970–1.346)	0.110	—	—	—
Bronchus/others	0.032	1.033 (0.989–1.079)	0.140	—	—	—	0.015	1.015 (0.852–1.209)	0.870	—	—	—
Right-sided	−0.006	0.994 (0.961–1.029)	0.750	—	—	—	0.010	1.010 (0.880–1.159)	0.890	—	—	—
Tumor extension												
Regional	0.050	1.051 (1.011–1.093)	0.012	0.056	1.058 (1.018–1.099)	0.004	−0.020	0.981 (0.840–1.144)	0.800	—	—	—
Distant	0.140	1.150 (1.093–1.210)	<0.001	0.143	1.153 (1.096–1.214)	<0.001	−0.018	0.982 (0.808–1.193)	0.850	—	—	—
Nodal status												
N1	0.037	1.038 (0.959–1.123)	0.360	0.036	1.036 (0.958–1.121)	0.380	0.190	1.210 (0.903–1.621)	0.200	—	—	—
N2	0.126	1.135 (1.076–1.197)	<0.001	0.126	1.134 (1.076–1.196)	<0.001	0.011	1.011 (0.825–1.240)	0.910	—	—	—
N3	0.118	1.125 (1.058–1.196)	<0.001	0.119	1.126 (1.059–1.198)	<0.001	−0.027	0.973 (0.766–1.237)	0.820	—	—	—
Metastasis M1b	0.414	1.513 (1.424–1.608)	<0.001	0.413	1.511 (1.423–1.606)	<0.001	−0.487	0.614 (0.505–0.748)	<0.001	−0.479	0.619 (0.509–0.753)	<0.001
Grading												
Poorly	0.243	1.275 (1.008–1.612)	0.043	—	—	—	0.342	1.407 (0.442–4.479)	0.560	—	—	—
Undifferentiated	0.246	1.279 (1.015–1.612)	0.037	—	—	—	0.441	1.555 (0.495–4.881)	0.450	—	—	—
NOS	0.270	1.310 (1.042–1.648)	0.021	—	—	—	0.341	1.407 (0.450–4.392)	0.560	—	—	—
Surgery	−0.307	0.736 (0.626–0.864)	<0.001	−0.329	0.720 (0.612–0.846)	<0.001	0.189	1.208 (0.651–2.244)	0.550	—	—	—
Chemotherapy	−0.801	0.449 (0.429–0.470)	<0.001	−0.802	0.448 (0.428–0.469)	<0.001	−0.066	0.936 (0.807–1.085)	0.380	—	—	—
Radiotherapy	−0.162	0.850 (0.824–0.877)	<0.001	−0.164	0.848 (0.822–0.876)	<0.001	−0.158	0.854 (0.742–0.983)	0.028	−0.170	0.844 (0.734–0.97)	0.017

Age' and Tumor size' are constructed spline variables (when k = 3). A model selection technique based on the Bayesian information criteria was used.

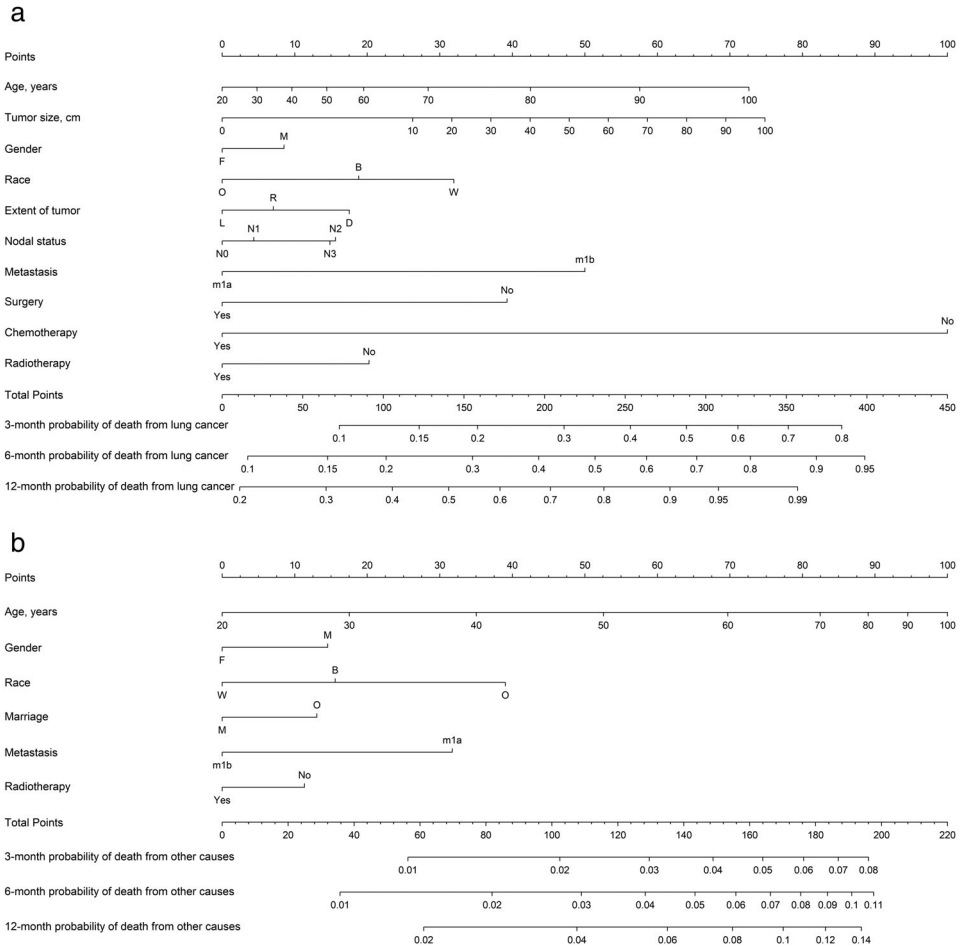

Figure 3 Nomogram for predicting 3, 6, and 12 month probabilities of (a) lung cancer death and (b) other causes death in Extensive-stage patients.

which is one of the largest cancer-related databases worldwide.

We identified age, gender, race, TNM staging (including tumor extent, nodal status, and metastasis), and treatment (surgery, chemotherapy and radiotherapy) as independent predictors for lung cancer-specific death. Advanced age, male, and Caucasian ethnicity[9–12] have been reported as risk factors of SCLC survival. Chemotherapy also reduced the risk of death in previously published SCLC nomogram models.[9–12] Notably, our model demonstrated that radiotherapy and surgery also reduced the risk of death in our extensive-stage SCLC cohort. Although previous clinical trials[19] have found extensive-stage SCLC patients do not benefit from radiotherapy and surgery, recent studies reported that thoracic radiotherapy improved survival and local control for extensive-stage SCLC patients who responded to chemotherapy.[20–22] Similarly, certain subgroups of extensive-stage SCLC patients might still benefit from surgery, and this possibility requires further study.

We assessed the performance of a nomogram by calibration and discrimination. The C-index indicated the predictive value of our nomogram. In this study, internal validation provided good discrimination power, and the unadjusted C-index was 0.714. This nomogram performed similarly to, or better than, the published SCLC nomograms of Pan *et al.* (C-index 0.68, 95% CI, 0.64–0.72)[12], Wang *et al.* (C-index 0.722 ± 0.004)[11], Xiao *et al.* (C-index 0.60; 95%CI, 0.55–0.65)[9] and Xie *et al.* (C-index 0.73).[10] Therefore, the nomogram developed in our study possesses great potential to estimate death risk for extensive-stage SCLC patients. This nomogram can be used in clinical practice to avoid over treatment. In randomized clinical trials, prognostic variables in this model can also be used for stratification.

There are several limitations of this study. Firstly, these models were validated by 1000 resamplings, and the use of an independent external cohort may be a better validation method. Secondly, we did not include certain known prognostic variables, such as weight loss, the level of neuron-specific enolase (NSE), and level of lactate dehydrogenase (LDH). Thirdly, the TNM staging in this study utilized the sixth edition, rather than the currently used eighth edition TNM staging guildelines. Additionally, SCLC has a unique

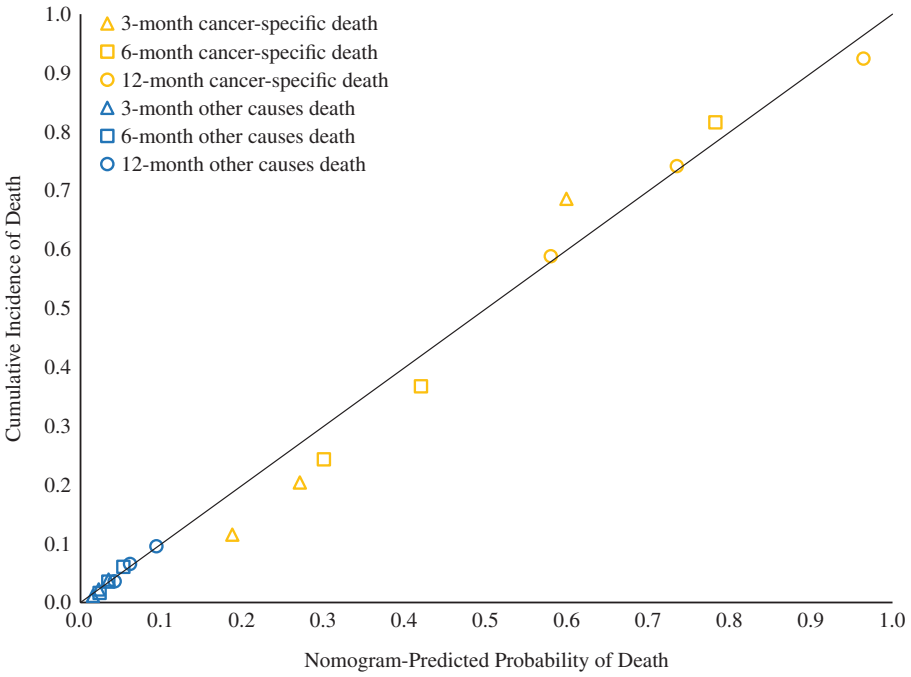

Figure 4 Calibration plot of the nomogram in the original cohort. The x-axis represents the mean predicted probability of the conditional cumulative incidence model. The y-axis represents observed cumulative incidence of death. The solid line represents equality between the predicted and observed probability.

genome map,[23] as demonstrated by next generation sequencing, and parameters such as gene mutation may be used to predict survival in future studies.

In conclusion, a novel predictive nomogram model based on a large database was constructed for prognosis of patients with extensive-stage SCLC. This validated prognostic model may be beneficial for treatment strategy choice and survival prediction.

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