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*Original Article*

# Factors associated with survival in patients with spinal metastases from lung cancer

Wenjia Xia*, Ming Li*, Youtao Xu, Lin Xu

*Thoracic Surgery Department, Jiangsu Cancer Hospital and Jiangsu Institute of Cancer Research and The Affiliated Cancer Hospital of Nanjing Medical University, Nanjing 210018, Jiangsu, China. *Equal contributors.*

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**Abstract:** The spine is a common site for metastases in lung cancer. Precise identification of factors associated with survival and reliable prediction of prognosis are essential for clinical decision-making in patients with spinal metastasis from lung cancer. A retrospective analysis was conducted on 148 lung cancer patients with spinal metastases between January 2018 and December 2020 to identify prognostic factors and develop a nomogram for predicting survival outcomes. Another 30 patients with spinal metastases due to lung cancer, treated between January 2021 and February 2022, served as an external validation cohort to assess the nomogram's predictive performance. Multivariate analysis identified Karnofsky Performance Status (KPS) score, carbohydrate antigen 125 (CA125), radiotherapy, chemotherapy, and targeted therapy as independent prognostic factors. The nomogram achieved a concordance index of 0.713. The AUCs for the nomogram in predicting 1-, 2-, and 3-year survival were 0.834, 0.750, and 0.733 in the training set; 0.803, 0.738, and 0.713 in the internal validation set; and 0.749, 0.738, and 0.729 in the external validation set. Calibration curves showed good agreement between predicted and observed outcomes. Compared with the modified Tokuhashi and Tomita scores, the nomogram demonstrated superior predictive accuracy and provided greater net clinical benefit in decision curve analysis, indicating good clinical utility. This model may aid individualized prognosis assessment and treatment planning in lung cancer patients with spinal metastases.

**Keywords:** Lung cancer, spinal metastases, survival analysis, prognostic factors, predictive model

## Introduction

Lung caner is one of the most frequently diagnosed and deadliest malignancy worldwide. In 2022, approximately 2.5 million new lung cancer cases were reported, with 1.8 million death. The incidence of bone metastases ranges from 45% to 55% in these patients during disease progression [1-3]. Among distant metastatic sites in advanced lung cancer, the skeletal system is frequently involved, particularly the spine [4]. Evidence suggests that bone metastases affect 40% to 50% of patients, with spinal involvement observed in 63% of these cases [5, 6]. Research from South Korea indicates that bone metastases typically appear around 18.9 months after the initial diagnosis of malignant solid tumors, and over 64% of lung cancer patients have spinal metastases at presentation [7]. Patients with spinal metastases from lung cancer often experience severe axial, neuropathic, and localized pain. Complications like nerve damage, paralysis, pathological fractures, and hypercalcemia may also occur when the tumor invades the spinal canal and causes significant destruction [8]. With a mean survival time of 6 to 10 months, patients with lung cancer-derived spinal metastases have a lower overall survival rate than those with spinal metastases originating from other primary tumors; only 40% to 50% of patients survive for more than a year following treatment [9].

A comprehensive evaluation of variables such as the tumor's pathological classification, comorbidities, and metastatic burden is essential for effective treatment planning. Patients' potential risks and benefits must be carefully evaluated, as well as their financial and physical burden [10]. When aggressive lung cancer spreads to the spine, it is often associated with

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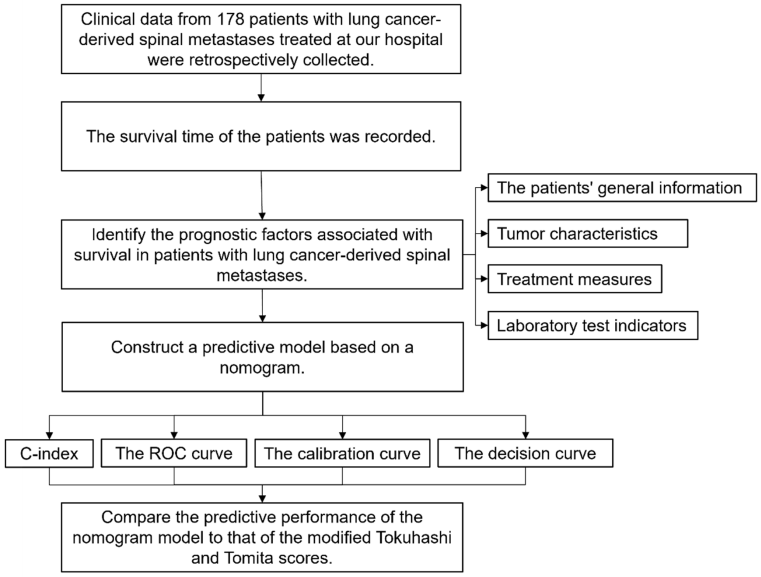


**Figure 1.** The flow chart of this study. Note: ROC: receiver operating characteristic.

a poor prognosis and a brief survival period. As a result, these patients typically derive limited benefit from therapies that require prolonged hospitalization and extensive rehabilitation. Clinical decision-making for these patients depends on accurately identifying prognostic factors and predicting survival outcomes.

The modified Tokuhashi and Tomita scores are two popular prognostic scoring systems for spinal metastases that have been used in clinical practice. However, these models do not account for the unique biological and clinical features of spinal metastases from lung cancer, nor do they incorporate the effects of novel treatments like immunotherapy and targeted therapy [11-13].

Therefore, developing a lung cancer-specific predictive model to estimate survival and support individualized treatment planning is of great significance. In this retrospective study, the clinical data from lung cancer patients with spinal metastases treated between January 2018 and February 2022 were analzyed to establish a prognostic model and guide treatment planning.

## Materials and methods

### *Patient selection*

The required sample size was calculated using the "pmsampsize" package in R software. Based on previous studies [14], assuming a concordance index (C-index) of 0.8 for existing prognostic models, an event rate of 0.5, and the inclusion of 5 candidate predictor variables, a minimum of 135 patients was estimated to be necessary.

This study retrospectively analyzed the clinical data of 148 patients with spinal metastases from lung cancer who were treated at Jiangsu Cancer Hospital between January 2018 to December 2020. The cohort was randomly divided into a training cohort and an internal validation cohort at a ratio of 7:3. In addition, an independent external validation cohort comprising 30 patients treated between January 2021 and February 2022 was collected.

Inclusion criteria: (1) Histopathologically confirmed lung cancer by pulmonary biopsy; (2) Diagnosis of bone metastasis confirmed by radionuclide bone scan; (3) Further confirmation of spinal metastasis by spinal CT or MRI, radionuclide bone scan and spinal CT/MRI were performed within the same clinical evaluation period (interval ≤15 days); (4) Availability of complete clinical records.

Exclusion criteria: (1) Existence of additional primary malignancies or spinal metastases not associated with lung cancer; (2) Mortality resulting from non-tumor-related factors or insufficient follow-up data; (3) Pre-existing severe comorbidities, such as cardiovascular disease, hepatic or renal insufficiency, respiratory failure, or other conditions that could substantially impact survival evaluation.

The Ethics Committee of Jiangsu Cancer Hospital approved this study. The overall research process is illustrated in **Figure 1**.

### *Data collection*

Clinical data were collected on the following variables: age, sex, history of smoking, Karnofsky Performance Status (KPS) score,

**Table 1.** Comparison of baseline characteristics among groups

| Factor | Training cohort (n=104) | Internal validation cohort (n=44) | External validation cohort (n=30) | $\chi^2$ | P |
|---|---|---|---|---|---|
| Age | | | | 0.539 | 0.764 |
| ≤60 | 55 | 23 | 18 | | |
| >60 | 49 | 21 | 12 | | |
| Sex | | | | 0.048 | 0.976 |
| Male | 61 | 26 | 17 | | |
| Female | 43 | 18 | 13 | | |
| History of smoking | | | | 1.181 | 0.554 |
| No | 44 | 19 | 16 | | |
| Yes | 60 | 25 | 14 | | |
| KPS score | | | | 5.115 | 0.276 |
| 80-100 | 34 | 15 | 7 | | |
| 50-70 | 43 | 18 | 19 | | |
| 10-40 | 27 | 11 | 4 | | |
| Frankel grade | | | | 2.851 | 0.583 |
| E | 33 | 14 | 14 | | |
| C-D | 52 | 22 | 13 | | |
| A-B | 19 | 8 | 3 | | |
| Visceral metastasis | | | | 0.347 | 0.841 |
| No | 78 | 34 | 24 | | |
| Yes | 26 | 10 | 6 | | |
| Extraspinal bone metastasis | | | | 1.312 | 0.519 |
| No | 58 | 24 | 20 | | |
| Yes | 46 | 20 | 10 | | |
| Number of spinal metastases | | | | 3.133 | 0.209 |
| 1 | 41 | 17 | 17 | | |
| ≥2 | 63 | 27 | 13 | | |
| Course of bone metastasis | | | | 0.516 | 0.773 |
| >3 months | 42 | 17 | 14 | | |
| ≤3 months | 62 | 27 | 16 | | |
| Pathological type | | | | 0.068 | 0.966 |
| Adenocarcinoma | 91 | 39 | 26 | | |
| Non-adenocarcinoma | 13 | 5 | 4 | | |
| Radiotherapy | | | | 0.024 | 0.988 |
| Yes | 32 | 13 | 9 | | |
| No | 72 | 31 | 21 | | |
| Chemotherapy | | | | 0.066 | 0.967 |
| Yes | 65 | 27 | 18 | | |
| No | 39 | 17 | 12 | | |
| Targeted therapy | | | | 0.784 | 0.676 |
| Yes | 44 | 18 | 10 | | |
| No | 60 | 26 | 20 | | |
| Immunotherapy | | | | 0.090 | 0.956 |
| Yes | 23 | 9 | 6 | | |
| No | 81 | 35 | 24 | | |
| CEA | | | | 0.018 | 0.991 |
| <5 ng/ml | 30 | 13 | 9 | | |
| ≥5 ng/ml | 74 | 31 | 21 | | |

| | | | | | |
|---|---|---|---|---|---|
| CA125 | | | | 0.077 | 0.962 |
| <35 U/ml | 44 | 19 | 12 | | |
| ≥35 U/ml | 60 | 25 | 18 | | |
| CA19-9 | | | | 0.563 | 0.755 |
| <37 U/ml | 73 | 31 | 19 | | |
| ≥37 U/ml | 31 | 13 | 11 | | |
| $Ca^{2+}$ | | | | 0.199 | 0.905 |
| <2.25 mmol/L | 5 | 2 | 2 | | |
| ≥2.25 mmol/L | 99 | 42 | 28 | | |
| Albumin | | | | 0.040 | 0.980 |
| <35 g/L | 42 | 17 | 12 | | |
| ≥35 g/L | 62 | 27 | 18 | | |

Note: KPS: Karnofsky Performance Status; CEA: Carcinoembryonic antigen; CA125: Carbohydrate antigen 125; CA19-9: Carbohydrate antigen 19-9.

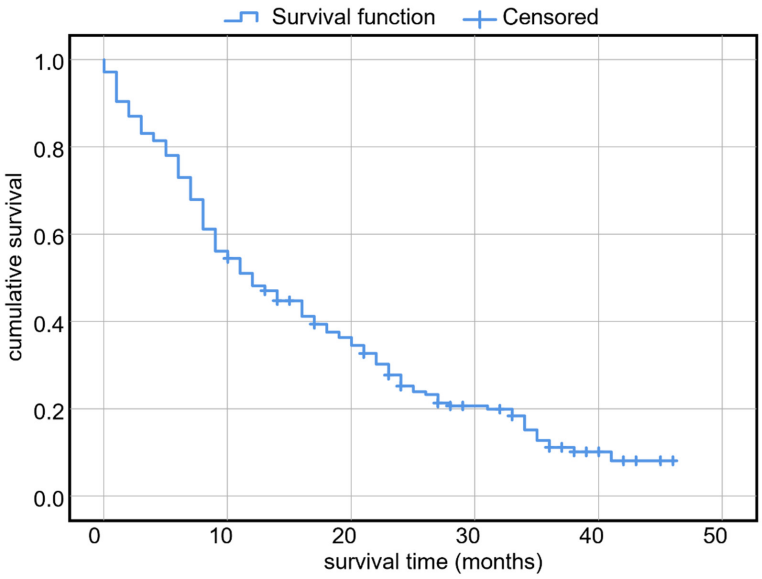


**Figure 2.** The Kaplan-Meier curve (n=178).

Frankel grade, presence of visceral metastases, bone metastases outside the spine, number of spinal metastatic lesions, bone metastasis time, pathological type, and treatment modalities such as radiotherapy, chemotherapy, targeted therapy, and immunotherapy. Laboratory indicators included carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), CA19-9, serum calcium ($Ca^{2+}$), serum albumin, modified Tokuhashi score and Tomita score.

Based on commonly used cutoffs in prior research [15], the KPS score was divided into three groups (10-40, 50-70, and 80-100), representing poor, moderate, and good functional status.

For missing values and outliers, complete-case analysis was applied if missingness was ≤5%; multiple imputation was used if >5%. Cases with >10% of variables missing were excluded.

*Follow-up*

All patients were followed up at 3, 6, 12, 24, and 36 months after discharge through outpatient visits or telephone interviews. The follow-up period ended in February 2025. For survival analysis, the date of initial diagnosis of spinal metastasis from lung cancer was defined as the time zero. Death was considered the event, and the date of the final follow-up served as the censoring time.

*Statistical analysis*

Statistical analyses were conducted using SPSS 26.0 (IBM) and R 4.4.1 software. Categorical variables were presented as frequencies and percentages. Univariate and multivariate Cox proportional hazards regression analyses were used to identify independent prognostic factors associated with patient survival.

**Table 2.** Univariate Cox regression analysis of factors affecting survival in patients with spinal metastases from lung cancer

| Factor | n | Median survival time (months) | HR | 95% CI | P |
|---|---|---|---|---|---|
| Age | | | | | |
| >60 | 49 | 11 | 1.232 | 0.867-1.750 | 0.245 |
| ≤60 | 55 | 12 | | Reference | |
| Sex | | | | | |
| Female | 43 | 13 | 0.847 | 0.591-1.215 | 0.367 |
| Male | 61 | 10 | | Reference | |
| History of smoking | | | | | |
| Yes | 60 | 11 | 1.205 | 0.844-1.721 | 0.305 |
| No | 44 | 16 | | Reference | |
| KPS score | | | | | 0.048 |
| 10-40 | 27 | 10 | 1.711 | 1.071-2.733 | 0.025 |
| 50-70 | 43 | 11 | 1.039 | 0.687-1.572 | 0.855 |
| 80-100 | 34 | 19 | | Reference | |
| Frankel grade | | | | | 0.387 |
| A-B | 19 | 11 | 1.389 | 0.833-2.317 | 0.208 |
| C-D | 52 | 14 | 1.262 | 0.840-1.896 | 0.263 |
| E | 33 | 16 | | Reference | |
| Visceral metastasis | | | | | |
| Yes | 26 | 9 | 1.219 | 0.818-1.817 | 0.331 |
| No | 78 | 13 | | Reference | |
| Extraspinal bone metastasis | | | | | |
| Yes | 46 | 10 | 1.150 | 0.808-1.637 | 0.437 |
| No | 58 | 13 | | Reference | |
| Number of spinal metastases | | | | | |
| ≥2 | 63 | 11 | 1.384 | 0.956-2.002 | 0.085 |
| 1 | 41 | 14 | | Reference | |
| Course of bone metastasis | | | | | |
| ≤3 months | 62 | 9 | 1.462 | 1.018-2.099 | 0.040 |
| >3 months | 42 | 18 | | Reference | |
| Pathological type | | | | | |
| Non-adenocarcinoma | 13 | 10 | 1.391 | 0.831-2.327 | 0.209 |
| Adenocarcinoma | 91 | 12 | | Reference | |
| Radiotherapy | | | | | |
| No | 72 | 8 | 1.964 | 1.317-2.931 | 0.001 |
| Yes | 32 | 21 | | Reference | |
| Chemotherapy | | | | | |
| No | 39 | 8 | 1.719 | 1.195-2.473 | 0.004 |
| Yes | 65 | 17 | | Reference | |
| Targeted therapy | | | | | |
| No | 60 | 8 | 1.881 | 1.307-2.707 | 0.001 |
| Yes | 44 | 21 | | Reference | |
| Immunotherapy | | | | | |
| No | 81 | 11 | 1.159 | 0.756-1.777 | 0.499 |
| Yes | 23 | 17 | | Reference | |
| CEA | | | | | |
| ≥5 ng/ml | 74 | 10 | 1.416 | 0.957-2.095 | 0.082 |
| <5 ng/ml | 30 | 22 | | Reference | |

| | | | | | |
|---|---|---|---|---|---|
| CA125 | | | | | |
| ≥35 U/ml | 60 | 8 | 1.810 | 1.258-2.605 | 0.001 |
| <35 U/ml | 44 | 18 | | Reference | |
| CA19-9 | | | | | |
| ≥37 U/ml | 73 | 12 | 1.181 | 0.810-1.721 | 0.388 |
| ≥37 U/ml | 31 | 12 | | Reference | |
| $Ca^{2+}$ | | | | | |
| ≥2.25 mmol/L | 99 | 12 | 0.788 | 0.367-1.690 | 0.540 |
| <2.25 mmol/L | 5 | 10 | | Reference | |
| Albumin | | | | | |
| ≥35 g/L | 62 | 14 | 0.985 | 0.687-1.411 | 0.934 |
| <35 g/L | 42 | 11 | | Reference | |

Note: KPS: Karnofsky Performance Status; CEA: Carcinoembryonic antigen; CA125: Carbohydrate antigen 125; CA19-9: Carbohydrate antigen 19-9.

**Table 3.** Multicollinearity results

| Factor | Tolerance | VIF |
|---|---|---|
| KPS score | 0.979 | 1.022 |
| Bone metastasis time | 0.972 | 1.029 |
| Radiotherapy | 0.911 | 1.098 |
| Chemotherapy | 0.982 | 1.019 |
| Targeted therapy | 0.903 | 1.108 |
| CA125 | 0.966 | 1.035 |

Note: VIF: Variance inflation factor; KPS: Karnofsky Performance Status; CA125: Carbohydrate antigen 125.

Using the "rms" and "survival" packages in R, a nomogram was constructed based on the findings of the multivariate analysis to estimate survival probability. The nomogram's predictive ability was assessed using the C-index, receiver operating characteristic (ROC) curve, area under the curve (AUC), calibration curve, and decision curve. Kaplan-Meier survival curves were generated to compare survival between subgroups, and differences were obtained using the log-rank test. The DeLong test was used to compare the differences in the AUC between ROC curves. A C-index of 0.50 to 0.70 implies poor accuracy, 0.71 to 0.90 shows moderate accuracy, and more than 0.90 suggests good accuracy. A two-sided *P* value of <0.05 was considered with statistical significance.

## Results

*Patient overall outcomes*

A total of 178 patients with lung cancer-derived spinal metastases were included in this retrospective study, including 104 patients in the training cohort, 44 in the internal validation cohort, and 30 in the external validation cohort. The baseline characteristics of patients in each cohort are presented in **Table 1**. The median survival time was twelve months. The 1-, 2-, and 3-year survival rates were 48.3%, 27.8%, and 12.8%, respectively. The Kaplan-Meier survival curve is presented in **Figure 2**.

*Prognostic factors for survival*

Univariate Cox regression analysis identified several variables that significantly associated with patient survival, including KPS score, time of bone metastasis, radiotherapy, chemotherapy, targeted therapy, and CA125 levels (**Table 2**). To assess potential collinearity among the candidate variables, we calculated the variance inflation factor (VIF) using a linear regression model. No obvious multicollinearity was observed among these variables (**Table 3**). Further multivariate analysis revealed that KPS score, CA125, radiotherapy, chemotherapy, and targeted therapy were independent prognostic factors for 1-year survival in patients with lung cancer-derived spinal metastasis (**Table 4**). Survival curves for each prognostic factor are presented in **Figure 3**.

*Construction of the nomogram model*

The nomogram (**Figure 4**) was constructed incorporating KPS score, CA125, radiotherapy, chemotherapy, and targeted therapy as predictive factors, considering their respective influence weights.

**Table 4.** Multivariate Cox regression analysis of independent prognostic factors for survival in patients with spinal metastases from lung cancer

| Factor | n | Median survival time (months) | β | HR | 95% CI | P |
|---|---|---|---|---|---|---|
| KPS score | | | | | | 0.044 |
| 10-40 | 27 | 10 | 0.578 | 1.783 | 1.104-2.880 | 0.018 |
| 50-70 | 43 | 11 | 0.083 | 1.086 | 0.705-1.673 | 0.707 |
| 80-100 | 34 | 19 | | Reference | | |
| Course of bone metastasis | | | | | | |
| ≤3 months | 62 | 9 | 0.280 | 1.324 | 0.914-1.918 | 0.138 |
| >3 months | 42 | 18 | | Reference | | |
| Radiotherapy | | | | | | |
| No | 72 | 8 | 0.545 | 1.725 | 1.126-2.641 | 0.012 |
| Yes | 32 | 21 | | Reference | | |
| Chemotherapy | | | | | | |
| No | 39 | 8 | 0.526 | 1.691 | 1.156-2.476 | 0.007 |
| Yes | 65 | 17 | | Reference | | |
| Targeted therapy | | | | | | |
| No | 60 | 8 | 0.380 | 1.462 | 1.002-2.132 | 0.049 |
| Yes | 44 | 21 | | Reference | | |
| CA125 | | | | | | |
| ≥35 U/ml | 60 | 8 | 0.511 | 1.667 | 1.148-2.420 | 0.007 |
| <35 U/ml | 44 | 18 | | Reference | | |

Note: KPS: Karnofsky performance status; CA125: Carbohydrate antigen 125.

*Validation of the nomogram model*

The nomogram was tested using the Bootstrap resampling method with 500 resampling iterations. The C-index of the nomogram was 0.713. In ROC curve analysis (**Figure 5**), the AUCs for the nomogram in predicting 1-, 2-, and 3-year survival were 0.834, 0.750, and 0.733 in the training cohort; 0.803, 0.738, and 0.713 in the internal validation cohort; and 0.749, 0.738, and 0.729 in the external validation cohort, respectively, further supporting the model's excellent discriminative ability. The calibration curve demonstrated that the predicted 1-year, 2-year and 3-year survival probabilities closely matched the actual survival rates in patients with lung cancer-derived spinal metastasis, suggesting good calibration of the model (**Figure 6**). The Hosmer–Lemeshow goodness-of-fit tests for 1-, 2-, and 3-year survival were non-significant in the training (P=0.427, 0.361, 0.283), internal validation (P=0.314, 0.277, 0.158), and external validation cohorts (P=0.197, 0.141, 0.099), suggesting good calibration of the model. The decision curve analysis demonstrated that the nomogram provided a higher net benefit across a wide range of threshold probabilities compared with both the 'treat-all' and 'treat-none' strategies (**Figure 7**).

*Comparison between the nomogram model and prognostic scoring systems*

The modified Tokuhashi score and Tomita score were used to predict patient survival. As shown in **Figure 8**, the DeLong test demonstrated that the AUC of the nomogram model in predicting 1-year survival was significantly higher than that of both the modified Tokuhashi score and the Tomita score (P<0.05). The nomogram continuously produced a higher net benefit than the modified Tokuhashi and Tomita scores, suggesting that it may be useful in directing customized clinical decision-making (**Figure 9**).

## Discussion

Over the past decade, lung cancer treatment has undergone significant advancements. The prognosis of advanced lung cancer has improved considerably with the advent of sec-

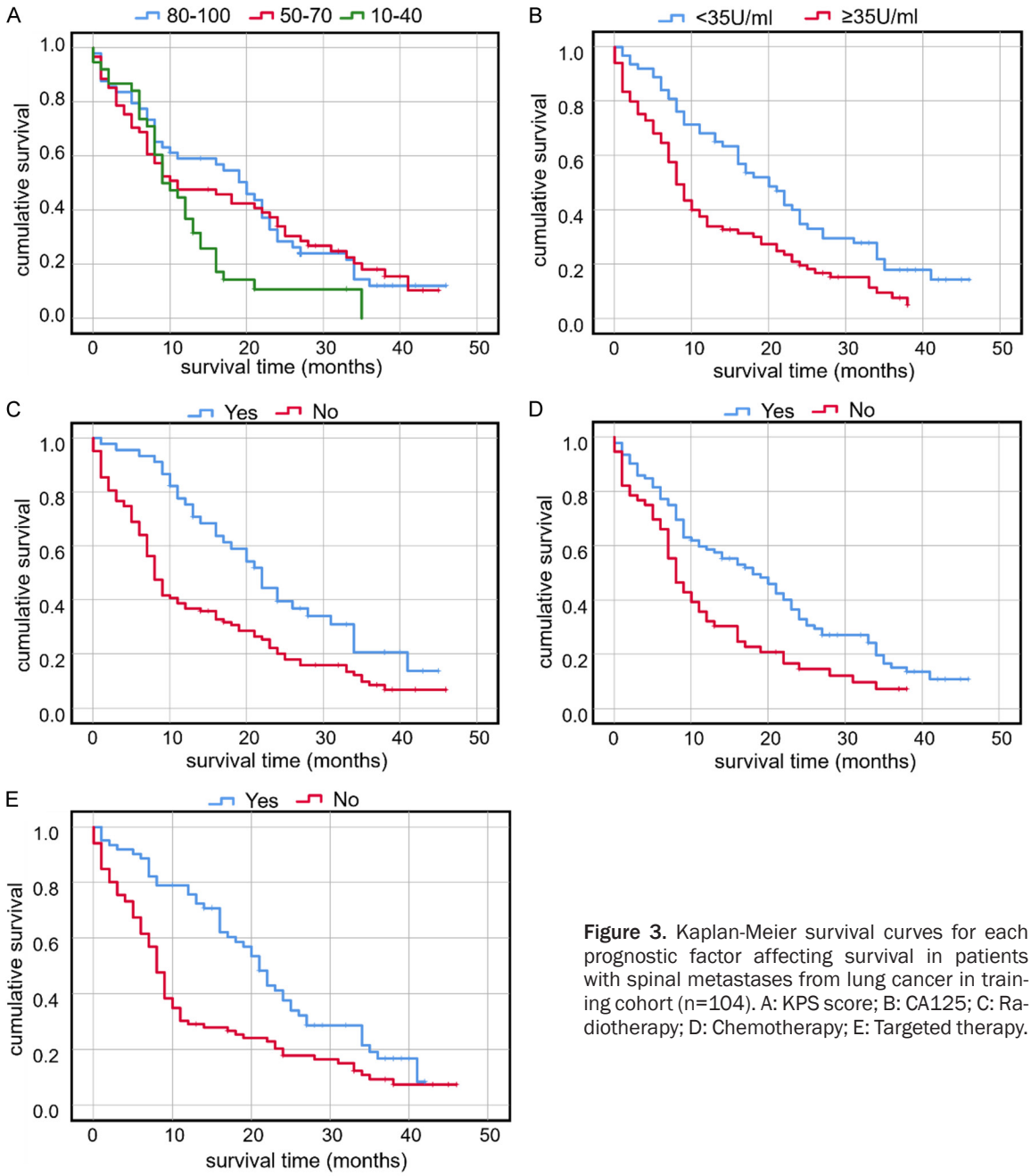


**Figure 3.** Kaplan-Meier survival curves for each prognostic factor affecting survival in patients with spinal metastases from lung cancer in training cohort (n=104). A: KPS score; B: CA125; C: Radiotherapy; D: Chemotherapy; E: Targeted therapy.

ond and third-generation cytotoxic chemotherapeutic agents and the use of anti-angiogenic medications in conjunction with chemotherapy regimens. The development and widespread application of immune checkpoint inhibitors and targeted therapies have contributed to better clinical outcomes. These advances have extended survival for patients with advanced lung cancer. However, this has also led to a rise in the number of individuals with spinal metastases [16]. For symptomatic patients, appropriate interventions must be implemented to alleviate pain, restore neurological function, and stabilize the spine, thereby effectively improving quality of life; However, for patients with a short life expectancy, highly invasive treatments may not yield benefits [17, 18]. Consequently, accurate survival prediction becomes critical.

KPS score, CA125, radiation, chemotherapy, and targeted treatment were established as

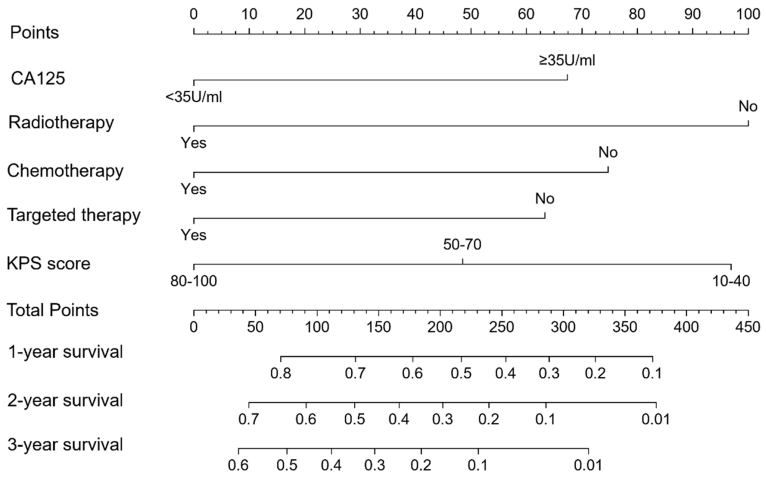


**Figure 4.** The constructed nomogram.

independent prognostic factors in lung cancer patients with spinal metastases. KPS score is a useful indicator for evaluating the overall condition of patients [19]. A low KPS score often suggests poor tolerance to treatments such as surgery, chemotherapy, and high-dose radiotherapy, and is associated with a higher risk of complications [20].

In addition to disease monitoring, tumor serum markers are known for their prognostic and predictive significance, reflecting the biological behavior of malignancies [21]. CA125, commonly expressed on the epithelial cells of the respiratory tract, can bind to mesothelin and galectin-1, thereby promotimg tumor growth. Since mesothelium covers the pleural surface, the interaction between CA125 and mesothelin may further enhance tumor cell adhesion and migration. Elevated CA125 levels may indicate increased biological activity and progression risk of spinal metastases, reflecting not only heightened tumor invasiveness but also potentially adverse effects on patient survival rates [22, 23]. The prognostic value of CA125 has been validated in prior research. For example, Zhai et al. [24] reported that lung cancer patients with normal CA125 levels (<35 ng/mL) had significantly better survival metrics compared to those with elevated CA125 levels. In a cohort of 176 NSCLC patients with spinal metastases, Zang et al. [25] measured serum markers including CEA, CA125, CA19-9, $Ca^{2+}$, and albumin, finding elevated CA125 levels correlated with poor prognosis. These findings align with the results of the present study. However, it should be noted that elevated CA125 levels can also result from non-cancerous conditions like pleural effusion, peritoneal irritation, or hepatic dysfunction [26]. Patients with known gynecological cancers were excluded from our study, thereby reducing the likelihood of confounding factors, though it cannot be entirely ruled out. Furthermore, this study did not analyze pleural involvement. Future studies should investigate the potential impact of pleural involvement on CA125 levels.

Radiotherapy plays a crucial role in treating spinal metastases by minimizing bone loss, alleviating pain, and suppressing local tumor growth. On CT imaging, osteolytic lesions may undergo osteoblastic transformation following radiation therapy, indicating suppressed tumor activity [27]. Previous studies have shown that radiotherapy significantly relieves pain in most patients with bone metastases, with complete pain relief achieved in some cases [28]. However, due to the lower positioning accuracy of conventional radiotherapy, there is a higher risk of damaging the cauda equina or spinal cord. The emergence of new technologies such as stereotactic body radiation therapy (SBRT) has significantly improved the safety and efficacy of radiotherapy for spinal tumors [29]. For example, Kelly et al. [30] found in a large study of 29,144 patients with spinal metastases from lung cancer that radiotherapy was an important prognostic predictor; patients who received SBRT had a median survival time of 9.3 months, significantly higher than 6.2 months in those who received external beam radiation. Li et al. [31] also demonstrated that radiotherapy was linked to better survival in lung cancer patients with bone metastases. Patients who received radiotherapy exhibited significantly longer survival than untreated patients. This study analyzed radiotherapy as a single factor without distinguishing treatment

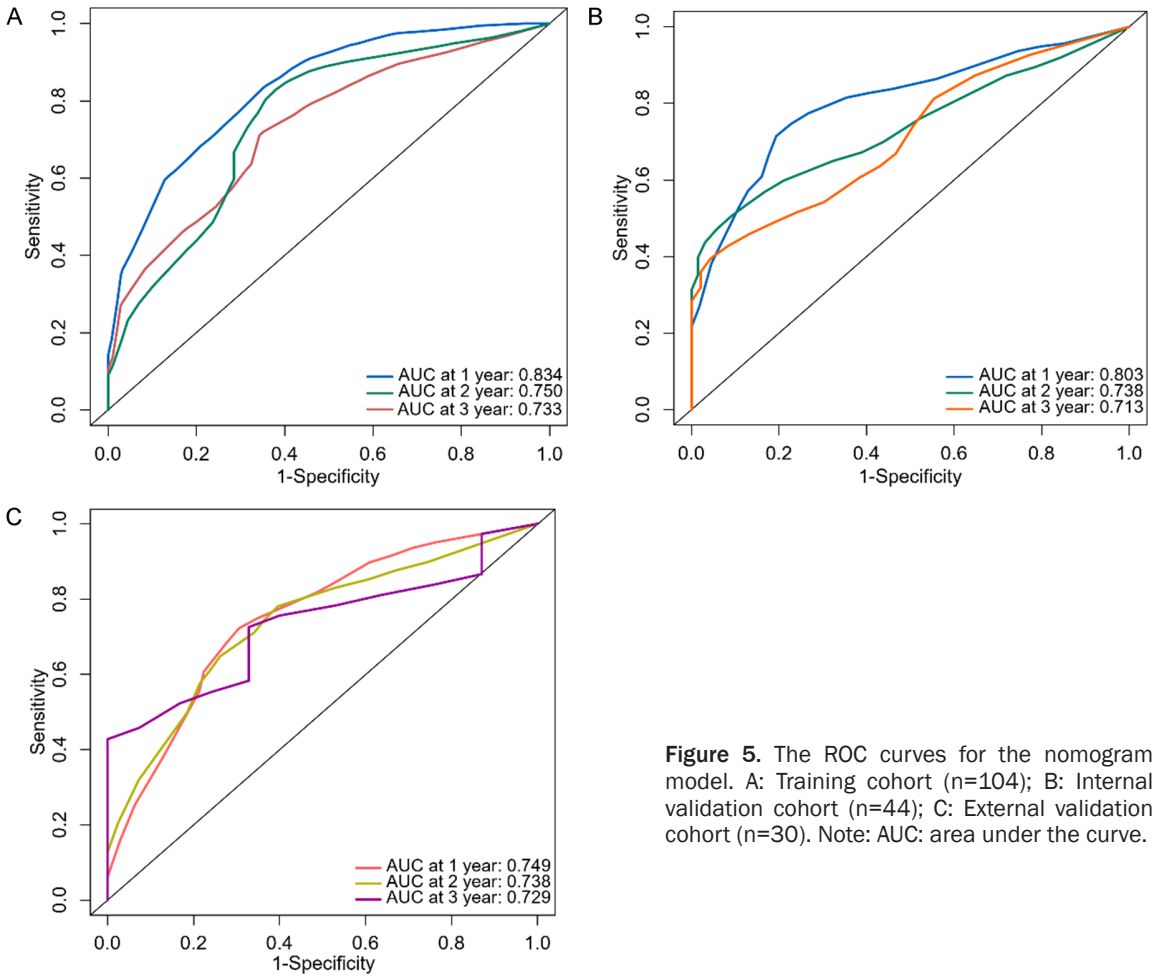


**Figure 5.** The ROC curves for the nomogram model. A: Training cohort (n=104); B: Internal validation cohort (n=44); C: External validation cohort (n=30). Note: AUC: area under the curve.

objectives (e.g., prophylactic vs. palliative radiotherapy for pain relief or nerve compression). Since the primary goals of radiotherapy for spinal metastases range from relieving symptoms to controlling the disease, differences in treatment purpose could influence survival outcomes. This limitation may partially explain observed discrepancies in our study; future research should differentiate radiotherapy types by treatment intent to clarify its survival impact.

Furthermore, chemotherapy has been extensively demonstrated to improve the prognosis of patients with lung cancer-derived spinal metastasis [32, 33]. Chemotherapy has elevated the one-year survival rate for patients with advanced metastatic lung cancer from about 10%-20% to 30%-50% [34]. In case of spinal metastases from lung cancer, Truong et al. [13] discovered that postoperative chemotherapy significantly improved patient survival.

With the advancement of targeted therapies and the introduction of gene sequencing technology, lung cancer treatment has gradually shifted toward the combination of multiple targeted drugs. Regardless of patient's history of chemotherapy or other treatments, epidermal growth factor receptor (EGFR) antagonists hold the potential in lung cancer therapy, especially for those harboring EGFR-sensitive mutations [35]. Multiple studies have demonstrated that targeted treatments can considerably prolong the survival in patients with spinal metastases from lung cancer [36, 37]. In a mouse model of bone metastasis from EGFR-mutant lung adenocarcinoma, Osimertinib treatment achieved significant tumor regression of bone lesions, prolonged survival, and demonstrated signs of

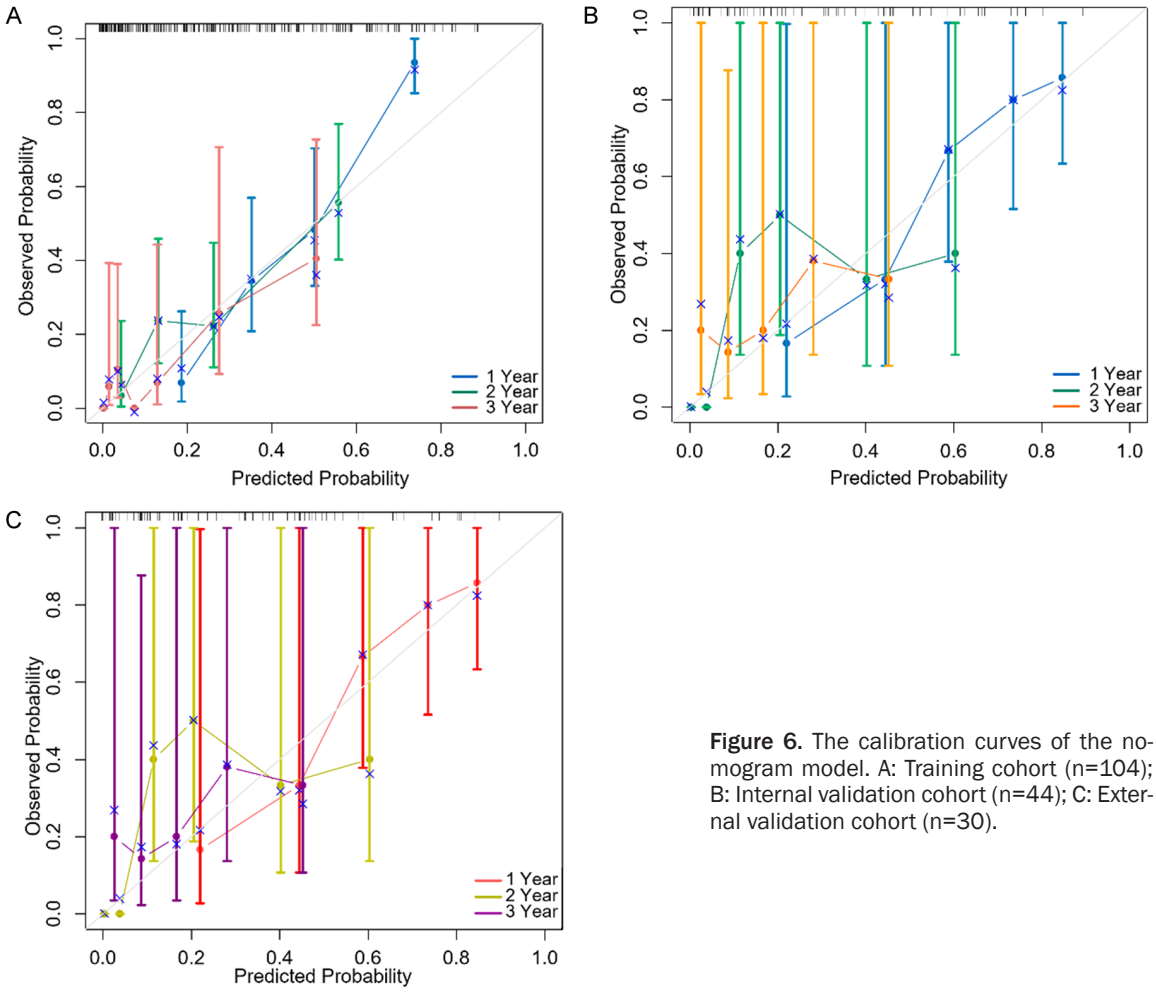


**Figure 6.** The calibration curves of the nomogram model. A: Training cohort (n=104); B: Internal validation cohort (n=44); C: External validation cohort (n=30).

bone remodeling [38]. Additionally, a clinical report on three osimertinib-treated patients showed extended disease stabilization periods, ranging from 12 to 22.7 months [39]. The results of this study are consistent with previous research, indicating that targeted therapy considerably prolongs survival and could serve as a significant predictor of treatment outcome. Despite being a well-established treatment for advanced lung cancer, immunotherapy did not significantly affect survival rates in this study and was therefore excluded from multivariate analysis. This observation may be attributed to the limited number of patients undergoing immunotherapy. However, immunotherapy possesses clear prognostic value and warrants further investigation in subsequent studies.

Models for predicting survival of patients with spinal metastases from a variety of cancer types have been proposed in earlier research. Nevertheless, these models are typically nonspecific and fail to focus exclusively on spinal metastases from lung cancer. With the rapid advancement of novel therapies, especially targeted therapies and immunotherapies, the practicality and accuracy of these general models in predicting prognosis have been significantly diminished [40, 41]. The nomogram developed in this study incorporates five independent prognostic factors: KPS score, CA125, radiotherapy, chemotherapy, and targeted therapy, specifically tailored for patients with spinal metastases from lung cancer. This model demonstrates superior performance in survival prediction, with its high predictive accuracy validated through calibration curves. The nomogram outperformed the modified Tokuhashi score and Tomita score, offering clinicians a more accurate and customized tool for predicting prognosis and guiding treatment selection.

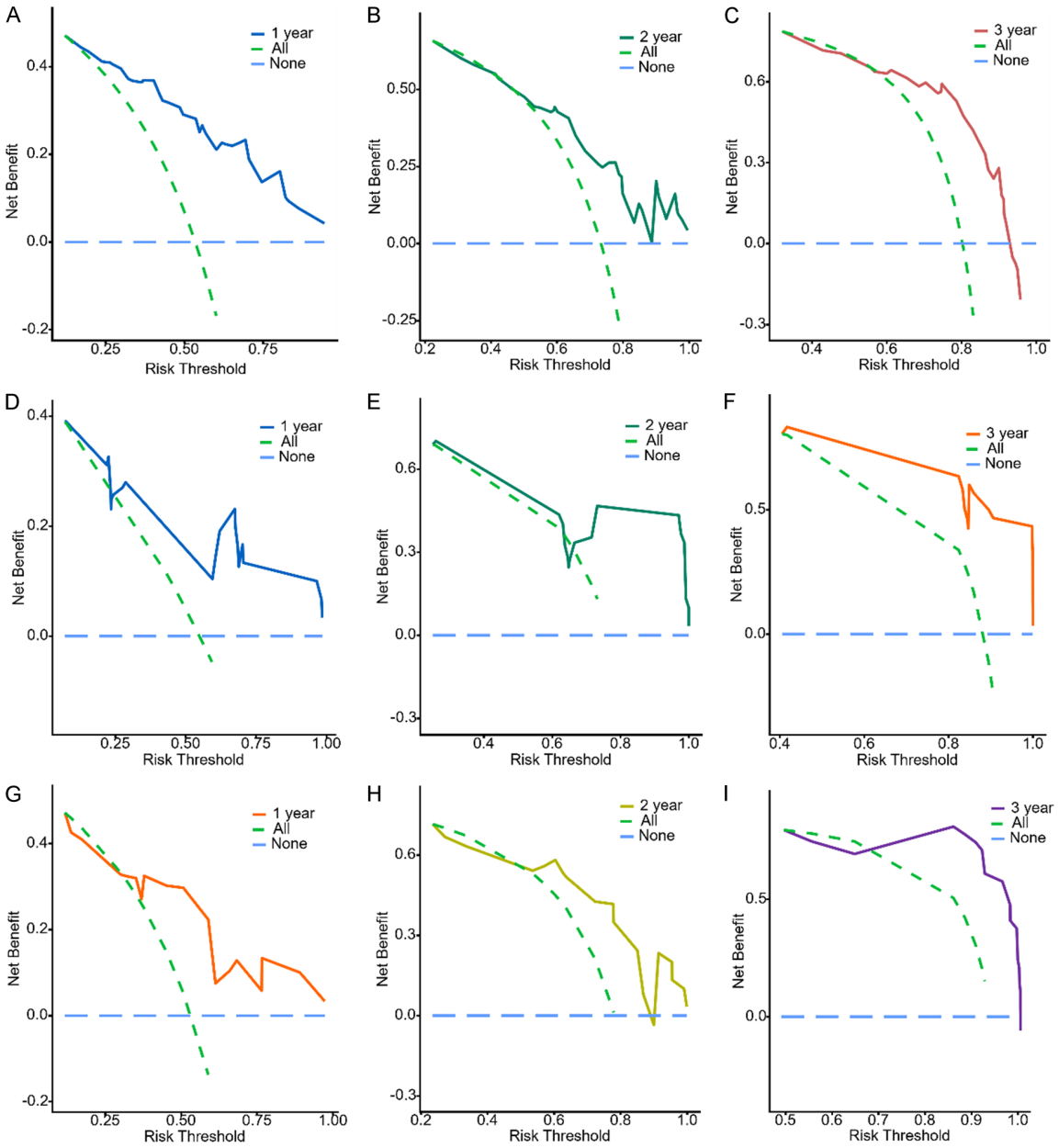


**Figure 7.** The decision curve of the nomogram model. A-C: Training cohort (n=104); D-F: Internal validation cohort (n=44); G-I: External validation cohort (n=30).

Gao et al. [20] constructed a nomogram to predict 3-, 6-, 12-, and 18-month survival rates, with a C-index of 0.732. In this study, the overall C-index was 0.713, demonstrating strong discriminatory power for distingushing different prognostic outcomes, particularly in predicting 2- and 3-year survival rates. Notably, our model incorporates CA125 and contemporary systemic therapies (such as targeted therapy and chemotherapy), improving clinical applicability while accurately reflecting the actual efficacy of current treatments.

This study still has several limitations. First, as a single-center retrospective study with a small sample size, it may have limited generalizability and statistical power, making it difficult to identify subtle prognostic differences. Second, some potentially important prognostic variables were missing or inadequately strati-

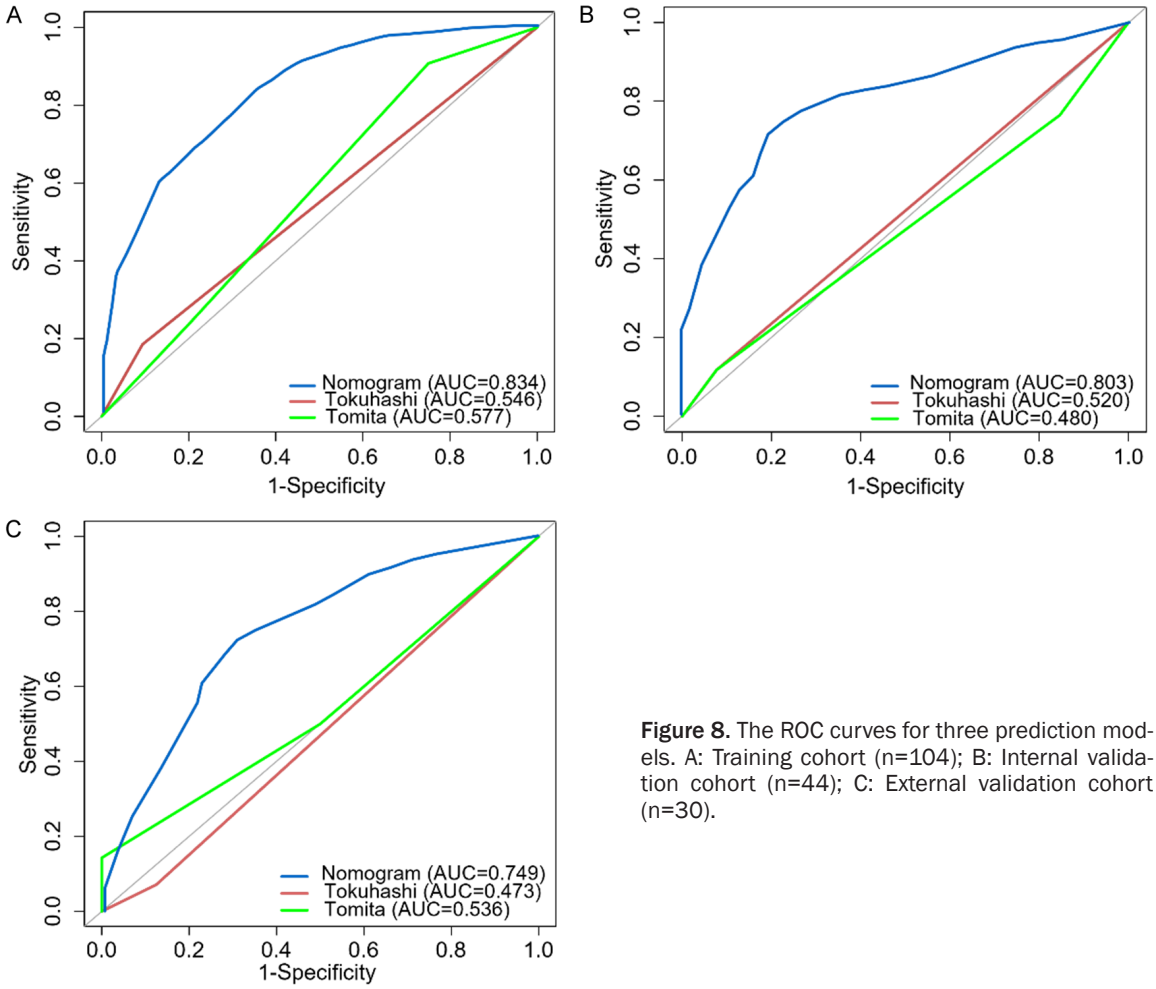


**Figure 8.** The ROC curves for three prediction models. A: Training cohort (n=104); B: Internal validation cohort (n=44); C: External validation cohort (n=30).

fied in the dataset. For example, pathological subtypes were overly simplified, treatment modalities were not differentiated by technique or drug type, and data on primary tumor control status and anatomical location of spinal metastases were not collected, all of which may affect model precision. Third, although external validation was performed, the validation cohort was small and drawn from single center during a subsequent period, constituting temporal validation rather than strict external validation. Therefore, large-scale, multicenter prospective studies are warranted to validate and refine this model.

## Conclusion

KPS score, CA125, radiotherapy, chemotherapy, and targeted therapy are independent prognostic factors influencing survival rate in patients with spinal metastasis from lung cancer. The predictive nomogram model established in this study demonstrated good accuracy in survival prediction and can serve as an effective tool to assist clinical decision-making and prognosis assessment. Future research with larger sample size and randomized controlled trials are warranted to further validate the predictive efficacy of this model.

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## Disclosure of conflict of interest

None.

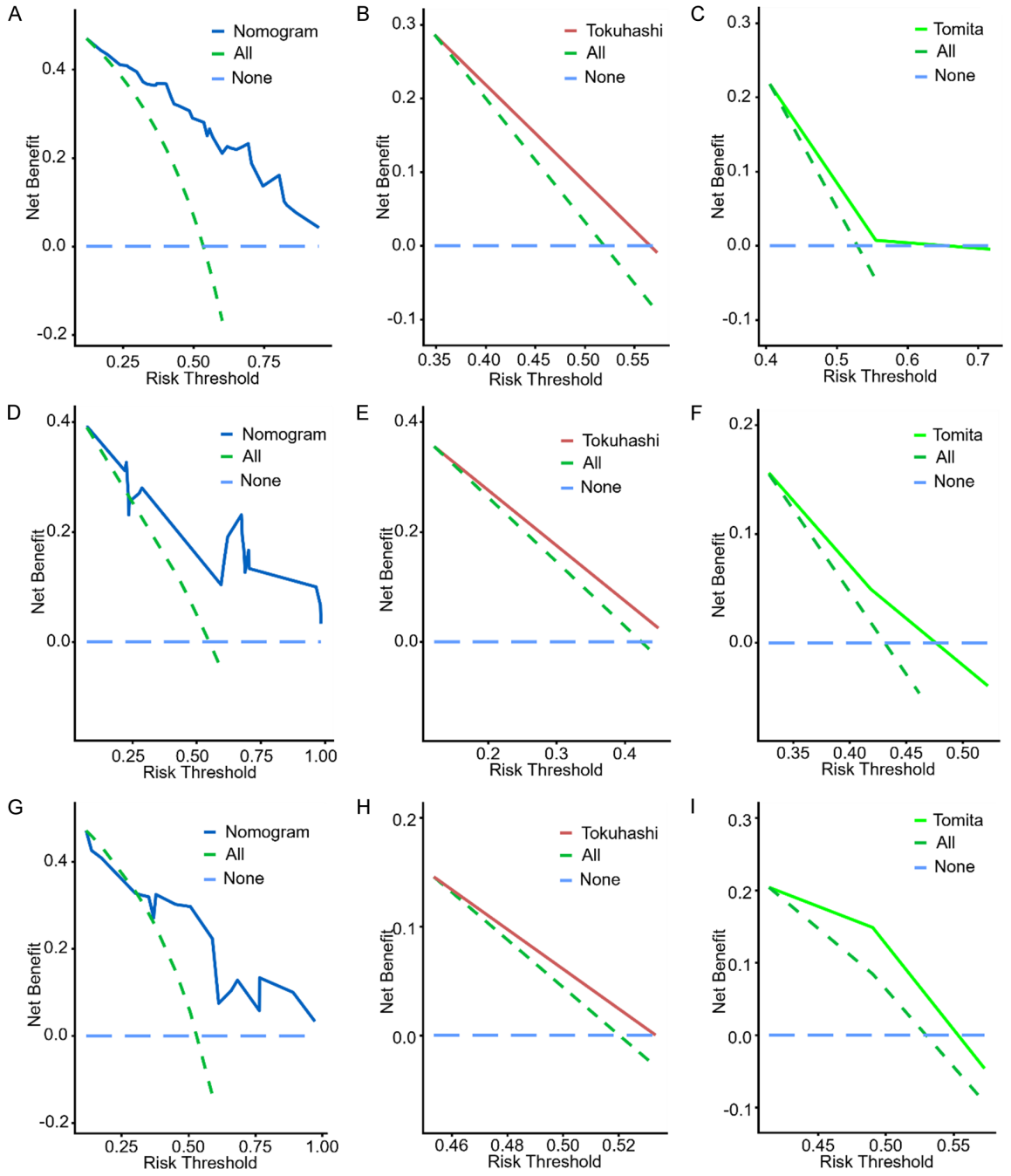


**Figure 9.** The decision curves for three prediction models. A-C: Training cohort (n=104); D-F: Internal validation cohort (n=44); G-I: External validation cohort (n=30).

**Address correspondence to:** Lin Xu, Thoracic Surgery Department, Jiangsu Cancer Hospital and Jiangsu Institute of Cancer Research and The Affiliated Cancer Hospital of Nanjing Medical University, No. 42 Baiziting, Nanjing 210018, Jiangsu, China. Tel: +86-025-83283651; E-mail: xwj09010810@163.com

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