Original Article

Establishment and validation of a long-term prognosis prediction model for patients with non-small cell lung cancer

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Background: The incidence of non-small cell lung cancer ranks second among malignant tumors, while the mortality rate ranks first. We established a prediction model for the long-term prognosis of lung cancer patients to accurately identify patients with a high risk of postoperative death and provide a theoretical basis for improving the prognosis of patients with non-small cell lung cancer.

Methods: The data of 277 non-small cell lung cancer patients who underwent radical lung cancer resection at Shanghai Fengxian District Central Hospital between January 2016 and December 2017 were retrospectively collected. The patients, who were followed up for 5 years, were divided into a deceased group (n=127) and survival group (n=150) according to whether the patients had died 5 years after surgery or not. The clinical characteristics of the two groups were observed, and the risk factors of death within 5 years of surgery in lung cancer patients were analyzed. A nomogram predictive model was then established to analyze the value of the model in predicting the death within 5 years of surgery in patients with non-small cell lung cancer.

Results: Multivariate logistics regression analysis showed that carcinoembryonic antigen (CEA) >193.5 ng/mL, stage III lung cancer, peritumor invasion, and vascular tumor thrombus were independent risk factors of tumor-specific death after surgery in patients with non-small cell lung cancer (P<0.05). R 4.0.3 statistical software was used to randomly divide the dataset into a training set and validation set. The sample size of the training set was 194, and the sample size of the validation set was 83. The area under the receiver operating characteristic (ROC) curve was 0.850 [95% confidence interval (CI): 0.796–0.905] in the training set, and it was 0.779 (95% CI: 0.678–0.880) in the validation set. In the validation set, the model was assessed using the Hosmer-Lemeshow goodness-of-fit test, with a chi-square value of 9.270 and a P value of 0.320.

Conclusions: Our model could accurately identify high risk of death within 5 years of surgery in non-small cell lung cancer patients. Strengthening the management of high-risk patients may help improve the prognosis of these patients.

Keywords: Non-small cell lung cancer; mortality; predictive models; risk factors

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Introduction

The incidence of non-small cell lung cancer ranks second among malignant tumors, and the mortality rate ranks first (1). Surgery is the main method for the radical treatment of non-small cell lung cancer, but even in patients with early-stage lung cancer, the postoperative recurrence rate is still as high as 39%, and postoperative recurrence is also the most important risk factor of death in lung cancer patients (2). To date, studies have confirmed that large tumor diameter, stage III, and surgical method are independent risk factors of mortality in lung cancer patients after surgery (3-7). However, it is still difficult to quantify the risk of postoperative death based on risk factors alone. A nomogram is based on multivariate regression analysis, which integrates multiple indicators, and plots the impact of each index on the patient's prognosis on a graduated line segment so that risk can be assessed more intuitively (8). Studies of patients with small cell lung cancer have shown that a nomogram predictive model could better assess patient prognosis and identify high-risk patients (9,10). The nomogram predictive model has also been shown to be of good value in identifying high-risk patients with poor prognosis among patients with unresectable lung cancer and in patients after total pneumonectomy (11,12). A study based on the Surveillance, Epidemiology, and End Results (SEER) database showed that in patients with stage IA lung cancer, a nomogram also had some predictive value, but the area under the receiver operating characteristic (ROC) curve was only 0.638 [95% confidence interval (CI): 0.629–0.647] (13). There is currently a lack of research on prediction models for long-term prognosis after surgery in patients with non-small cell lung cancer, and thus we designed the present study. We present the following article in accordance with the TRIPOD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-381/rc).

Highlight box

Key findings

- Our model could accurately identify high risk of death within 5 years of surgery in non-small cell lung cancer patients.

What is known and what is new?

- The incidence of non-small cell lung cancer ranks second among malignant tumors, and the mortality rate ranks first.
- Patients with non-small cell lung cancer have a high mortality rate at 5 years after surgery, and our model could accurately identify high risk of death within 5 years of surgery in non-small cell lung cancer patients.

What is the implication, and what should change now?

- Our model could accurately identify high risk of death within 5 years of surgery in non-small cell lung cancer patients. Strengthening the management of high-risk patients may help improve the prognosis of these patients.

Methods

General information

The data of 277 non-small cell lung cancer patients who underwent radical lung cancer resection at Shanghai Fengxian District Central Hospital between January 2016 and December 2017 were retrospectively collected. The patients, who were followed up for 5 years, were divided into a deceased group (n=127) and survival group (n=150) according to whether the patients had died 5 years after surgery or not. The inclusion criteria were: (I) non-small cell lung cancer (intraoperative pathological diagnosis); (II) surgical treatment at our hospital; (III) age ≥18 years old; and (IV) complete clinical data. The exclusion criteria were: (I) combined with other malignant tumors; (II) recurrence of lung cancer after surgery; (III) distant metastases; (IV) small cell lung cancer; (V) did not receive standard treatment; and (VI) loss follow-up. This retrospective study was conducted in accordance with the 2013 edition of the Declaration of Helsinki and approved by the Ethics Committee of Shanghai Fengxian District Central Hospital (No. c202100182). Informed consent was waived in this retrospective study.

Treatment method

In accordance with guidelines for the treatment of lung cancer (14), patients completed preoperative examinations upon admission. All patients underwent radical resection of lung cancer after excluding contraindications to surgery. After surgery, chemotherapy, radiotherapy, or other adjuvant therapy was administered according to the pathological results.

Data collection

Age, gender, body mass index, smoking history, chronic obstructive pulmonary diseases, history of alcoholism, hypertension, diabetes, hyperlipidemia, carcinoembryonic antigen (CEA), tumor site, pathological type, tumor node metastasis (TNM) stage, surgical method, peripheral

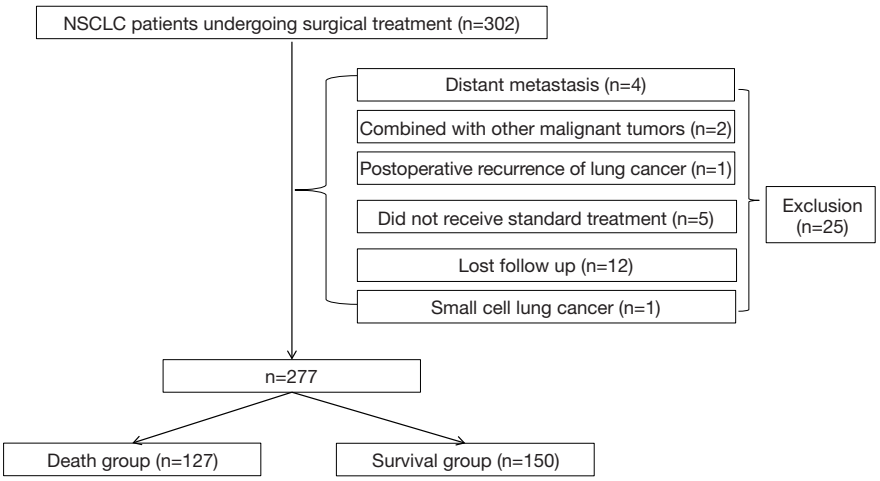

Figure 1 Patients with non-small cell lung cancer who underwent surgery were included. NSCLC, non-small cell lung cancer.

invasion, vascular tumor thrombus, postoperative radiotherapy, postoperative chemotherapy, and tumor-specific mortality at 5 years after surgery were recorded. Postoperative follow-up was conducted via outpatient visits or telephone.

Statistical analysis

SPSS 26.0 (IBM Corp., Armonk, NY, USA) was used to perform data analysis, and P<0.05 indicated that the difference was statistically significant (two-tailed). The measurement data of the two groups are expressed as mean ± standard deviation (SD), and the independent sample *t*-test was used to analyze differences in the measurement data of the two groups. Count data of the two groups are expressed as n (%), and the chi-square test was used to analyze the difference in the count data between the two groups. Multivariate logistics regression analysis was used to explore the risk factors of death at 5 years after surgery in patients with non-small cell lung cancer. ROC curves were used to analyze the value of different indexes in predicting the death of non-small cell lung cancer patients at 5 years after surgery. R 4.0.3 statistical software was used to establish the prediction model.

Results

Comparison of clinical features between the two groups

A total of 277 patients with non-small cell lung cancer who underwent surgical treatment were included. A flow chart of the patient selection process is shown in *Figure 1*. There were significant differences in CEA, TNM stage, peripheral invasion, vascular tumor thrombus, postoperative chemotherapy, and postoperative radiotherapy between the two groups (P<0.05, *Table 1*).

Predictive value of CEA on tumor-specific death at 5 years after surgery in patients with non-small cell lung cancer

CEA was valuable for predicting tumor-specific death in patients with non-small cell lung cancer at 5 years after surgery, with an area under the curve of 0.707 (95% CI: 0.645–0.769, P=0.000). The best diagnostic cut-off was 193.5 ng/mL, and the sensitivity and specificity were 0.630 and 0.713, respectively (*Figure 2*).

Risk factors for postoperative tumor-specific death in patients with non-small cell lung cancer

Multivariate logistics regression analysis showed that CEA >193.5 ng/mL, stage III, peripheral invasion, and vascular tumor thrombus were independent risk factors of tumor-specific death at 5 years after surgery in patients with non-small cell lung cancer (P<0.05, *Table 2*).

Establishment and validation of tumor-specific death prediction model in patients with non-small cell lung cancer 5 years after surgery

R 4.0.3 statistical software was used to randomly divide the

Table 1 Comparison of clinical features between the two groups

Variables	Deceased group (n=127)	Survival group (n=150)	t/χ^2 value	P value
Age (years)	59.04±11.06	59.19±11.87	0.111	0.154
Gender			0.609	0.435
Male	82 (64.57)	90 (60.00)		
Female	45 (35.43)	60 (40.00)		
Body mass index (kg/m^2)	25.72±2.61	25.64±2.64	0.247	0.805
History of smoking	83 (65.35)	100 (66.67)	0.053	0.818
Chronic obstructive pulmonary diseases	12(9.45)	12(8.00)	0.182	0.669
History of alcoholism	21 (16.54)	31 (20.67)	0.770	0.380
Hypertension	12 (9.45)	11 (7.33)	0.404	0.525
Diabetes	6 (4.72)	6 (4.00)	0.087	0.768
Hyperlipidemia	12 (9.45)	18 (12.00)	0.463	0.496
CEA (ng/mL)	226.69±104.60	150.75±80.96	6.805	0.000
CEA >193.5 ng/mL	80 (62.99)	43 (28.67)	32.823	0.000
Tumor location			1.236	0.266
Left lung	72 (56.69)	75 (50.00)		
Right lung	55 (43.31)	75 (50.00)		
Type of pathology			1.889	0.389
Adenocarcinoma	89 (70.08)	116 (77.33)		
Adenosquamous	31 (24.41)	28 (18.67)		
Squamous	7 (5.51)	6 (4.00)		
TNM staging			46.316	0.000
Stage I or II	62 (48.82)	130 (86.67)		
Stage III	65 (51.18)	20 (13.33)		
Surgical methods			0.728	0.394
Minimally invasive surgery	115 (90.55)	140 (93.33)		
Open surgery	12 (9.45)	10 (6.67)		
Peripheral invasion			23.575	0.000
Yes	23 (18.11)	2 (1.33)		
No	104 (81.89)	148 (98.67)		
Vascular tumor thrombus			22.101	0.000
Yes	29 (22.83)	6 (4.00)		
No	98 (77.17)	144 (96.00)		
Postoperative chemotherapy			97.341	0.000
Yes	123 (96.85)	61 (40.67)		
No	4 (3.15)	89 (59.33)		
Postoperative radiotherapy			23.440	0.000
Yes	49 (38.58)	20 (13.33)		
No	78 (61.42)	130 (86.67)		

Data are presented as mean ± SD or n (%). CEA, carcinoembryonic antigen; TNM, tumor node metastasis; SD, standard deviation.

dataset into a training set and validation set. The sample size of the training set was 194 and the sample size of the validation set was 83. The area under the ROC curve was 0.850 (95% CI: 0.796–0.905) in the training set, and it was 0.779 (95% CI: 0.678–0.880) in the validation set. In the validation set, the model was assessed using the Hosmer-Lemeshow goodness-of-fit test, with a chi-square value of 9.270 and a P value of 0.320 (*Figures 3-6*).

Discussion

We designed this study to more accurately identify people at high risk of tumor-specific death at 5 years after surgery in patients with non-small cell lung cancer, and in the present study, we hoped to predict the risk of death for patients at the time of admission, so we did not include factors related to postoperative treatment. In the present study, multivariate logistics regression analysis showed that CEA >193.5 ng/mL, stage III lung cancer, peritumor invasion, and vascular tumor thrombus were independent risk factors of tumor-specific death after surgery in patients with non-small cell lung cancer (P<0.05). R 4.0.3 statistical software was used to randomly divide the dataset into a training set and validation set. The sample size of the training set was 194, and the sample size of the validation set was 83. The area under the ROC curve was 0.850 (95% CI: 0.796–0.905) in the training set, and the area under the curve of the ROC was 0.779 (95% CI: 0.678–0.880) in the validation set. In the validation set, the model was assessed using the Hosmer-Lemeshow goodness-of-fit test, with a chi-square value of 9.270 and a P value of 0.320, indicating that the predictive value and reliability of the model were high.

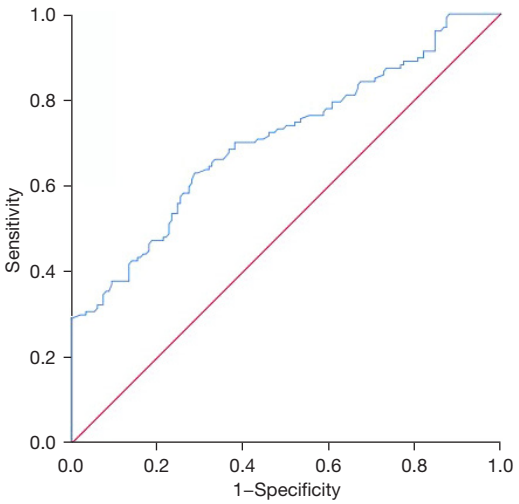

Figure 2 Predictive value of CEA on tumor-specific death at 5 years after surgery in patients with non-small cell lung cancer. CEA, carcinoembryonic antigen.

As a broad-spectrum tumor marker, CEA is not used as a specific indicator for the diagnosis of a malignant tumor. However, in the differential diagnosis and efficacy evaluation of malignant tumors, CEA is still important. Increased CEA in non-small cell lung cancer patients indicates that recurrence and metastasis are more likely to occur, and recent studies have shown that CEA is valuable for predicting prognosis in non-small cell lung cancer patients (15-18). The TNM staging system is used to comprehensively evaluate the stage of lung cancer. As stage III non-small cell lung cancer patients have regional lymph node metastasis, they are more likely to have tumor-specific death (19-21). Lung cancer can invade surrounding tissues, including in the superior vena cava, aorta, pericardium, pleura, and other important tissues of the mediastinum. When peripheral invasion occurs, it indicates that the tumor has potential to spread, leading to postoperative recurrence and metastasis, and eventually death (22). Finally, the formation of vascular tumor thrombus has been confirmed to be closely related to distant metastasis and

Table 2 Risk factors of postoperative tumor-specific death in patients with non-small cell lung cancer

Variables	B value	Standard error	Wald value	P value	Relative risk (95% CI)
CEA >193.5 ng/mL	1.338	0.292	21.045	0.000	3.810 (2.152–6.748)
Stage III	1.664	0.329	25.635	0.000	5.279 (2.772–10.052)
Peripheral invasion	2.042	0.797	6.575	0.010	7.709 (1.618–36.732)
Vascular tumor thrombus	1.294	0.550	5.540	0.019	3.646 (1.242–10.708)
Constant	–11.143	1.890	34.777	0.000	0.000

CI, confidence interval; CEA, carcinoembryonic antigen.

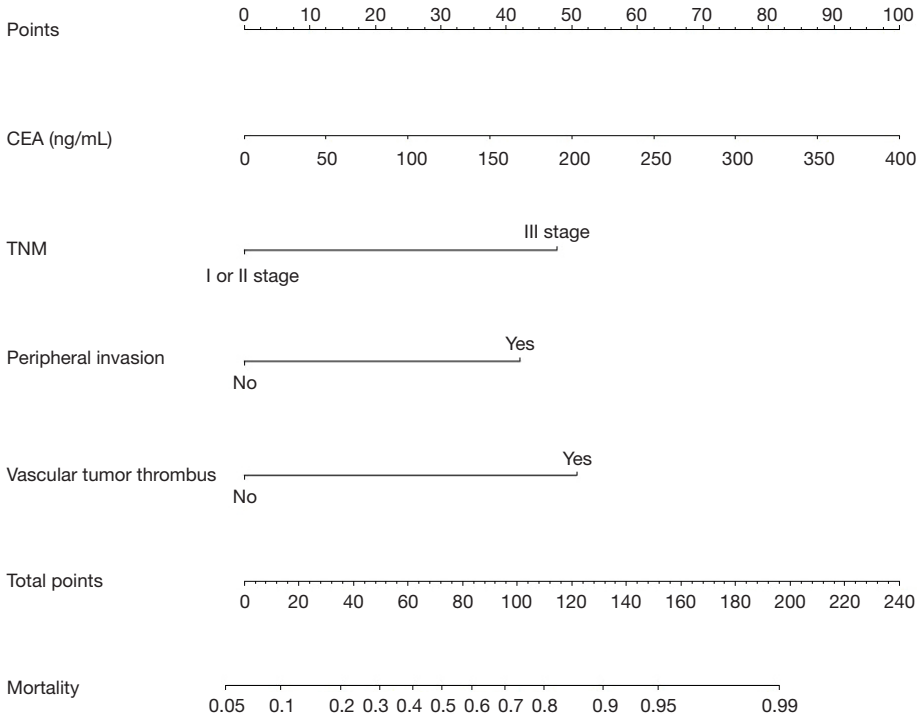

Figure 3 Nomogram of a tumor-specific death prediction model at 5 years after surgery in patients with non-small cell lung cancer. CEA, carcinoembryonic antigen; TNM, tumor node metastasis.

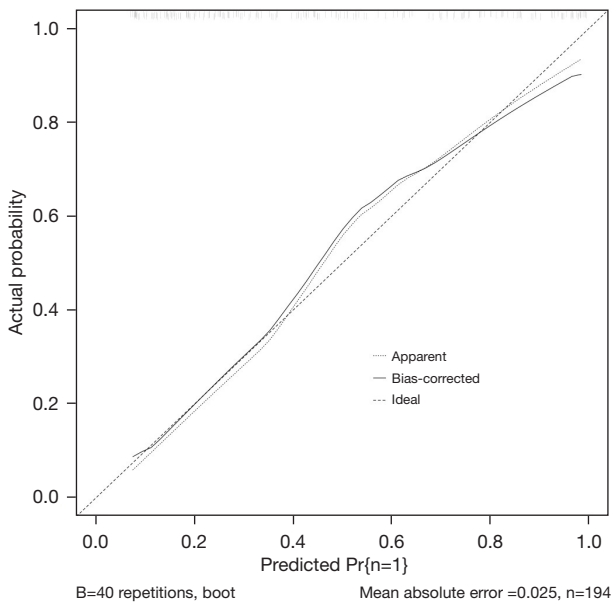

Figure 4 Calibration curve of tumor-specific death prediction model in patients with non-small cell lung cancer at 5 years after surgery.

lymph node metastasis (23,24). Up to now, previous studies have confirmed that increased CEA, high TNM staging, peripheral invasion and vascular tumor thrombus were independent risk factors of death in non-small cell lung cancer, supporting our study (18,19,22,23).

However, the prognosis of patients with non-small cell lung cancer is affected by many factors, so the predictive value of a single biological indicator on prognosis is limited. Therefore, the nomogram predictive model was developed. A study of non-small cell lung cancer patients with stage N3 showed that the nomogram predictive model could predict patient outcomes better than a single biological marker (25). The present study also showed that the established nomogram prediction model had more value than a single biological indicator such as CEA in predicting tumor-specific death at 5 years after surgery in patients with non-small cell lung cancer. Thus, the prediction model may be valuable in identifying the patients as high risk of death.

Limitations

The present study had the limitations characteristic of a retrospective study. Furthermore, the degree of malignancy

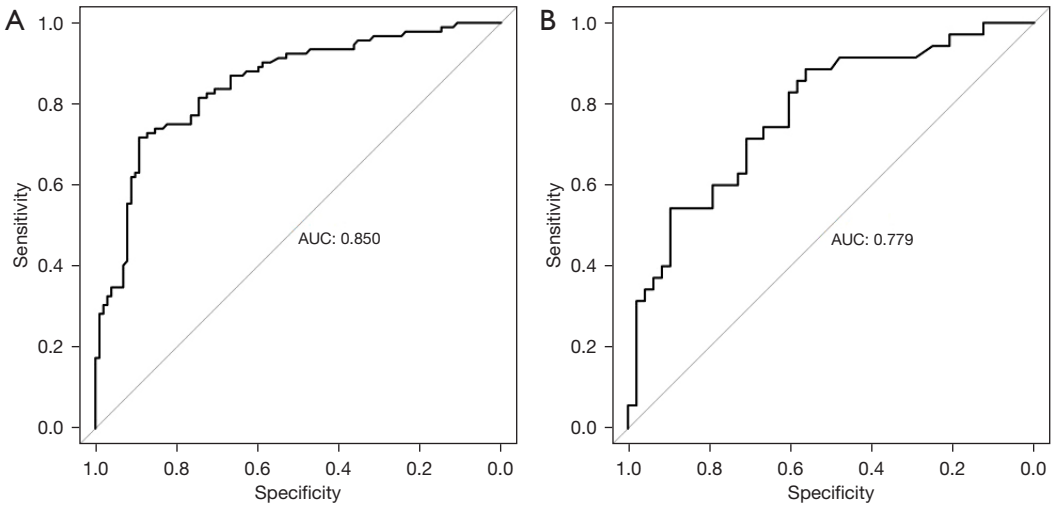

Figure 5 The value of the nomogram for predicting the tumor-specific death at 5 years after surgery in patients with non-small cell lung cancer. (A) Training set; (B) validation set. AUC, area under the curve.

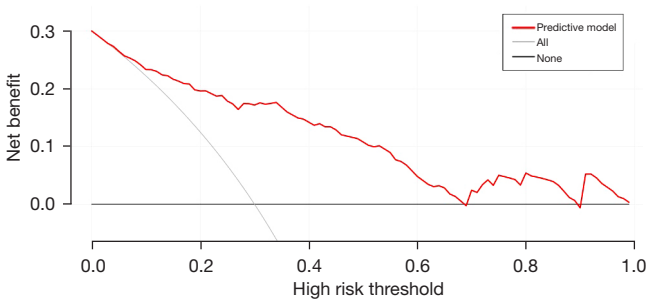

Figure 6 Clinical decision curve of tumor-specific death prediction model at 5 years after surgery in patients with non-small cell lung cancer.

in lung cancer patients is affected by genes and other factors (such as epidermal growth factor receptor mutations), and the present study failed to explore genes and other related indicators. Finally, the diagnostic model in the present study lacks external validation.

Conclusions

Prognosis and related indicators of different diseases are the focus of current research (26-29). Our model could accurately identify high risk of death within 5 years of surgery in non-small cell lung cancer patients. Enhanced management of these high-risk populations may help improve patient outcomes, but further clinical studies are needed.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-381/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-381/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-381/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-381/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This retrospective study was conducted in accordance with the 2013 edition of the Declaration of Helsinki and approved by the Ethics Committee of Shanghai Fengxian District Central Hospital

(No. c202100182). Informed consent was waived in this retrospective study.

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