

Prognostic factors of survival in patients with non-small cell lung cancer: a competing risk model using the SEER database

Ying Chen[#], Qin Zhang[#], Yantian Lv, Ning Li, Guopeng Xu, Ting Ruan

Department of Respiratory and Critical Care Medicine, The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, Suzhou, China

Contributions: (I) Conception and design: Y Chen, Q Zhang, T Ruan, G Xu; (II) Administrative support: Y Chen, Q Zhang; (III) Provision of study materials or patients: Y Lv, N Li; (IV) Collection and assembly of data: Y Lv, N Li; (V) Data analysis and interpretation: Y Lv, N Li; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

"These authors contributed equally to this work and should be considered as co-first authors.

Correspondence to: Ting Ruan; Guopeng Xu. Department of Respiratory and Critical Care Medicine, The Affiliated Suzhou Hospital of Nanjing Medical University, Suzhou Municipal Hospital, No. 26 Daoqian Street, Suzhou 215006, China. Email: ttruan2021@outlook.com; xuguopeng2046@foxmail.com.

Background: To explore the prognostic factors of survival in non-small cell lung cancer (NSCLC) patients using the competing risk analysis.

Methods: This was a retrospective cohort study. NSCLC patients with complete data were selected from the Surveillance, Epidemiology, and End Results (SEER) database between 2010 and 2015. Outcomes were censored, cancer-specific mortality in NSCLC, and other-cause mortality. Gray's test was used in univariable analysis, and a multivariable Fine-Gray competing risk model with backward elimination was used to explore the prognostic factors of survival. The screened variables were incorporated into a random survival forest (RSF) model for the prediction of 1-, 3-, and 5-year survival in patients with NSCLC. Receiver operator characteristic (ROC) curves, calibration curves, the value of area under the curve (AUC), and decision curve analysis (DCA) were used to evaluate the performance.

Results: Totally 1,251 eligible patients were included, 678 (54.20%) patients were cancer-specific mortality, and 128 (10.23%) patients were other-cause mortality. The median follow-up time was 26 months. Age, primary site, N stage, M stage, surgery type, tumor size, and lymph nodes (LNs) count were included in the multivariable Fine-Gray model for further analysis (P<0.05). The six most important features (surgery type, tumor size, M stage, LNs count, N stage, and primary site) were included in the competing risk analysis using the RSF model. The value of AUC for predicting 1-, 3-, and 5-year survival in the testing set were 0.796, 0.804, and 0.792, respectively. Calibration curves were well-fitted. DCA curves showed that the RSF model had similar or greater clinical net benefits in survival compared with the 8th edition the American Joint Committee on Cancer (AJCC) staging. The good performance of the RSF model under different surgery types, T, N, and M stages.

Conclusions: We conducted a competing risk analysis using the RSF model for predicting the 1-, 3-, and 5-year survival of NSCLC. We generated a web calculator (https://github.com/YingChen19/Prognostic-factors-of-long-term-survival-of-non-small-cell-lung-cancer), which could provide a convenient assessment and could help improve the prognosis and survival of NSCLC.

Keywords: Non-small cell lung cancer (NSCLC); competing risk analysis; survival; random survival forest model

Submitted Sep 29, 2021. Accepted for publication Sep 25, 2022. doi: 10.21037/tcr-21-2114 View this article at: https://dx.doi.org/10.21037/tcr-21-2114

Introduction

Lung cancer is the leading cause of an extremely high mortality rate worldwide, accounting for approximately 27% of cancer deaths in the United States (1). Non-small cell lung cancer (NSCLC) accounts for about 80% of lung cancer cases and the 5-year survival rate is reduced to 5% or less (2,3), which indicated the poor prognosis of NSCLC.

Previous studies have investigated the prognostic factors in NSCLC patients, including age, gender, treatment method, tumor stage, examined lymph node count, etc. (4-8). To our knowledge, little attention has been paid to the existence of competing risks, that is, these patients may also die from other causes in addition to NSCLC. And previous studies tend to mix the two causes of death into one single endpoint event or delete the cases dead from other causes (9,10). The competing risk model developed a new method for regression analysis that corresponds to the hazard model of the cumulative incidence function (11). And it has been widely applied in clinical oncology studies for identifying influencing factors for improving the prognosis of malignant tumors such as lung cancer, breast cancer, and hepatocellular carcinoma (12-14). To date, few studies have used the competing risk model for survival analysis of NSCLC. Lobectomy and lymph node dissection are recognized as standard treatments for earlystage NSCLC (15). A study suggested that lobectomy should be considered the surgery of choice for pleural invasion patients with NSCLC (16). At present, the impact of different surgery types on the survival of patients with NSCLC needs further research.

Given this, we performed a competing risk model to explore the prognostic factors of the 1-, 3-, and 5-year survival of NSCLC, and explored the performance of the model under different surgery types, which may help clinicians to provide precision treatment and improve the quality of life for NSCLC patients. We present the following article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/ view/10.21037/tcr-21-2114/rc).

Methods

Study population and data acquisition

NSCLC patients with complete data we studied in this retrospective cohort study were extracted from the Surveillance, Epidemiology and End Results (SEER) database between 2010 and 2015. The SEER database is representative of the US population, extracting patientlevel data from 18 geographically diverse populations representing rural, urban, and regional populations (17). Patients without lymph node examination and with incomplete information on the variables we studied were excluded. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study used the SEER database and all patient identifiers were removed from the SEER database, which was exempt from institutional review board approval. Individual consent for this retrospective analysis was waived.

Baseline variables including age (<65, 65-74, and \geq 75 years old), gender (male and female), ethnicity (White, Asian, Black and others), primary tumor site (upper lobe, middle lobe, lower lobe, main bronchus and overlapping lesion), TNM staging [T stage (T1-4), N stage (N0-3) and M stage (M0-1)], surgery type (no surgery of primary site, excision or resection of less than one lobe, lobe or bilobectomy extended, resection of at least one lobe or bilobectomy, and pneumonectomy), tumor size, LNs count, follow-up time, and patient outcome were collected in the SEER database. The patients were staged according to the eighth edition of the TNM classification (18). The LNs count was divided into <16 and \geq 16 (17). The outcomes of this study included cancer-specific mortality in NSCLC and other-causes mortality. Patients who were alive at the end of the study were defined as the censored. According to their outcomes, patients were divided into three groups: the censored, cancer-specific mortality, and other-cause mortality. In the present study, other-causes mortality was the competing event.

Statistical analysis

All statistical tests were performed using the two-sided test, and P<0.05 was considered statistically significant. All statistical analyses were completed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA) and R 3.6.0 software. Characteristics of the included patients were described. Gray's test (19) was used in univariable analysis to compare the cumulative incidences among three groups (the censored, cancer-specific mortality, and other-cause mortality). Predictor screening was performed using a multivariable Fine-Gray (19) competing risk model with backward elimination (P<0.05) to explore the prognostic factors of the survival of NSCLC. The screened variables were incorporated into a random survival forest (RSF) model (20) for the prediction of 1-, 3-, and 5-year survival



Figure 1 The flow chart for screening. NSCLC, non-small cell lung cancer

in patients with NSCLC. The population was divided into training and testing sets in a ratio of 7:3. The performance of the RSF model was evaluated using receiver operator characteristic (ROC) curves, calibration curves, and the value of area under the curve (AUC). Decision curve analysis (DCA) was used to compare the performance of the RSF model we developed with the eighth edition of the American Joint Committee on Cancer (AJCC) staging. The performance of the RSF model was also reported under different surgery types, T, N, and M stages.

Results

Baseline description

Initially, a total of 17,923 NSCLC patients were extracted from the SEER database. After excluding patients without lymph node examination (n=14,059), with incomplete data including age, gender and ethnicity (n=2,508), tumor size (n=5), and surgery types (n=62), and patients with T0 or TX staging (n=38), we finally enrolled 1,251 eligible NSCLC patients (*Figure 1*). There were 721 (57.63%) males and 530 (42.37%) females. Among them, there were 997 (79.70%) White patients, 82 (6.55%) Asian patients, 162 (12.95%) Black patients, and 10 (0.80%) patients of other ethnicities. The median number of LNs was 5 [2, 11], where 1,064 (85.05%) patients have <16 LNs and 187 (14.95%) have \geq 16 LNs. The median follow-up time was 26 [8, 55] months with a maximum follow-up of 95 months. Besides, 445 (35.57%) patients were censored, 678 (54.20%) patients were cancer-specific mortality, and 128 (10.23%) patients were other-cause mortality. All baseline characteristics were shown in *Table 1*.

Cumulative incidences of cancer-specific mortality in NSCLC

The cumulative incidence of cancer-specific mortality in NSCLC was shown in *Table 2*. The cancer-specific mortality in NSCLC was significantly different in age (P=0.012), gender (P=0.040), primary tumor site (P<0.001), T stage (P<0.001), N stage (P<0.001), M stage (P<0.001), surgery type (P<0.001) and LNs count (P<0.001). The cumulative incidences of cancer-specific mortality in different age ranges were 56.685%, 58.863%, and 65.698%, respectively. The cumulative incidences of cancer-specific mortality in male and female patients were 63.372% and 56.347%, respectively. The cumulative incidences of cancer-specific mortality in patients undergoing different surgery types were 85.792%, 52.442%, 48.841%, 36.923% and 44.055%, respectively. More details were shown in *Table 2* and Figure S1.

Translational Cancer Research, Vol 11, No 11 November 2022

Table 1 Baseline characteristics of all patients

Variables	Description (n=1,251)
Age (years), n (%)	
<65	491 (39.25)
65–74	472 (37.73)
≥75	288 (23.02)
Gender, n (%)	
Male	721 (57.63)
Female	530 (42.37)
Ethnicity, n (%)	
White	997 (79.70)
Asian	82 (6.55)
Black	162 (12.95)
Others	10 (0.80)
Primary site, n (%)	
Upper lobe	810 (64.75)
Middle lobe	78 (6.24)
Lower lobe	316 (25.26)
Main bronchus	30 (2.40)
Overlapping lesion	17 (1.36)
T stage, n (%)	
T1	384 (30.70)
T2	444 (35.49)
Т3	263 (21.02)
T4	160 (12.79)
N stage, n (%)	
NO	587 (46.92)
N1	126 (10.07)
N2	382 (30.54)
N3	156 (12.47)
M stage, n (%)	
M0	967 (77.30)
M1	284 (22.70)
Surgery type, n (%)	
No surgery of primary site	536 (42.85)
Excision or resection of less than one lobe	91 (7.27)

Table 1 (continued)

Variables	Description (n=1,251)
Lobe or bilobectomy extended	41 (3.28)
Resection of at least one lobe or bilobectomy	532 (42.53)
Pneumonectomy	51 (4.08)
Tumor size (mm), M (Q ₁ , Q ₃)	35.00 (21.00, 52.00)
LNs count, n (%)	
<16	1,064 (85.05)
≥16	187(14.95)
LNs count, M (Q1, Q3)	5.00 (2.00, 11.00)
Follow-up time, months, M (Q_1 , Q_3)	26.00 (8.00, 55.00)
Outcome, n (%)	
Censored	445 (35.57)
Dead from NSCLC	678 (54.20)
Dead from other causes	128 (10.23)
1-year outcome, n (%)	
Censored	844 (68.01)
Dead from NSCLC	350 (28.20)
Dead from other causes	47 (3.79)
3-year outcome*, n (%)	
Censored	653 (52.92)
Dead from NSCLC	514 (41.65)
Dead from other causes	67 (5.43)
5-year outcome [#] , n (%)	
Censored	486 (41.65)
Dead from NSCLC	596 (51.07)
Dead from other causes	85 (7.28)

Table 1 (continued)

*, 17 patients were lost to follow-up during 3-year follow-up duration; [#], 84 patients were lost to follow-up during 5-year follow-up duration. M (Q1, Q3), median and interquartile range; LNs, lymph nodes; NSCLC, non-small cell lung cancer.

Multivariable competing risk analysis

Age, primary site, N stage, M stage, surgery type, tumor size, and LNs count were included in the multivariable Fine-Gray model for further analysis (*Table 3*). Patients aged \geq 75 years had a 1.506-fold higher risk of cancer-specific mortality compared to those aged <65 years [hazard ratios

3977

Table 2 Cumulative	e incidence of c	ancer-specific mo	rtality in NSCLC
--------------------	------------------	-------------------	------------------

Variables	P		0.5	959	95% CI	
variables	P	CIF	0.L	Lower	Upper	
Age (years)						
<65	0.012	56.685	0.097	56.495	56.875	
65–74		58.863	0.069	58.728	58.998	
≥75		65.698	0.123	65.457	65.939	
Gender						
Male	0.040	63.372	0.098	63.180	63.564	
Female		56.347	0.061	56.227	56.467	
Ethnicity						
White	0.660	59.19	0.043	59.106	59.274	
Asian		69.913	0.423	69.084	70.742	
Black		57.701	0.192	57.325	58.077	
Others		63.333	3.456	56.559	70.107	
Primary site						
Main bronchus	<0.001	70.988	0.893	69.238	72.738	
Upper lobe		58.501	0.051	58.401	58.601	
Middle lobe		56.620	0.482	55.675	57.565	
Lower lobe		60.286	0.109	60.072	60.5	
Overlapping lesion		88.235	0.809	86.649	89.821	
T stage						
T1	<0.001	47.721	0.084	47.556	47.886	
Τ2		56.672	0.078	56.519	56.825	
Т3		68.247	0.176	67.902	68.592	
Τ4		79.841	0.132	79.582	80.100	
N stage	<0.001					
NO		42.409	0.066	42.280	42.538	
N1		47.223	0.230	46.772	47.674	
N2		77.780	0.077	77.629	77.931	
N3		88.086	0.079	87.931	88.241	
M stage	< 0.001					
MO		51.051	0.037	50.978	51.124	
M1		88.494	0.108	88.282	88.706	
Surgery type	<0.001					
No surgery of primary site		85.792	0.053	85.688	85.896	
Excision or resection of less than one lobe		52.442	0.368	51.721	53.163	

Table 2 (continued)

Table 2 (continued)

Variables	Р	CIF	S.E -	95% CI	
variables				Lower	Upper
Lobe or bilobectomy extended		48.841	0.723	47.424	50.258
Resection of at least one lobe or bilobectomy		36.923	0.067	36.792	37.054
Pneumonectomy		44.055	0.644	42.793	45.317
LNs count	<0.001				
<16		62.836	0.039	62.760	62.912
≥16		41.812	0.191	41.438	42.186

NSCLC, non-small cell lung cancer; CIF, cumulative incidence function; S.E, standard error; CI, confidence interval; LNs, lymph nodes.

(HR) =1.506, 95% confidence interval (CI): 1.235-1.837]. As compared with patients whose primary tumor site was the upper lobe, patients with the primary site of the lower lobe (HR =1.227, 95% CI: 1.018-1.479) and overlapping lesion (HR =2.057, 95% CI: 1.135-3.728) had higher risks of cancer-specific mortality. Higher T and M stages were associated with higher risks of cancer-specific mortality for tumor staging. Compared to patients with no surgery of the primary site, patients with excision or resection of less than one lobe (HR =2.130, 95% CI: 1.254-3.617) had an increased risk of cancer-specific mortality. Tumor size was associated with the increased risk of cancer-specific mortality (HR =1.007, 95% CI: 1.005-1.008) (Table 3). Patients with ≥16 LNs had a reduced risk of cancer-specific mortality compared with those with <16 LNs (HR =0.980, 95% CI: 0.965-0.995).

Development and validation of the RSF model for the prediction of survival in patients with NSCLC

There was no significant difference in the characteristics between the training set (n=876) and the testing set (n=375), as shown in Table S1. The six most important features (surgery type, tumor size, M stage, LNs count, N stage, and primary site) were shown in *Table 4*. Surgery type (0.1846) was the most crucial survival predictor. The ROC curves and calibration curves in the training and testing sets were in *Figure 2A,2B* and *Figure 3A,3B*, respectively. The value of AUC for predicting 1-year survival, 3-year survival, and 5-year survival in the testing set were 0.796, 0.804, and 0.792, respectively (*Table 5*). The results of DCA showed that the RSF model had a positive net benefit to patients, and compared with the 8th edition AJCC staging, the performance of the RSF model was similar or has greater clinical net benefits in 1-year (*Figure 4A*,4*B*), 3-year (*Figure 4C*,4*D*) and 5-year (*Figure 4E*,4*F*) survival evaluation in the training and testing sets. *Table 5* shows the good performance of the RSF model under different surgery types, T stages, N stages, and M stages.

We generated a web calculator (https://github.com/ YingChen19/Prognostic-factors-of-long-term-survival-ofnon-small-cell-lung-cancer) for calculating the survival of NSCLC patients based on the RSF model, which could provide the convenient assessment.

Discussion

In the present study, surgery type, tumor size, M stage, LNs count, N stage, and primary site were included in the competing risk analysis using the RSF model for predicting 1-, 3-, and 5-year survival. The values of AUC in the training and testing sets were good, and calibration curves were well-fitted. DCA curves showed that the RSF model had similar or greater clinical net benefits in survival compared with the 8th edition AJCC staging. We generated a user-friendly web calculator to ease use in clinical practice.

The prognosis and survival of NSCLC are dependent on the stage of the disease, which is associated with the tumor size and nodal metastasis (21). Previous studies have demonstrated that the number of LNs was an independent prognostic factor for the survival of NSCLC patients (7,8). Sun *et al.* (22) established a model to predict the survival of elderly patients with metastatic NSCLC, and found that factors such as primary site and N stage were its prognostic factors. Dong *et al.* (23) found that factors such as primary site, N stage, and surgery were associated with

3980

Madalaa	0		P		95%	% CI
Variables	β	S.E	Р	HR	Lower	Upper
Age (years)						
<65	Ref					
65–74	0.198	0.097	0.040	1.219	1.009	1.473
≥75	0.410	0.101	<0.001	1.506	1.235	1.837
Primary site						
Upper lobe	Ref					
Middle lobe	-0.010	0.165	0.953	0.990	0.717	1.368
Lower lobe	0.205	0.095	0.032	1.227	1.018	1.479
Main bronchus	0.054	0.237	0.819	1.056	0.664	1.680
Overlapping lesion	0.721	0.303	0.018	2.057	1.135	3.728
N stage						
NO	Ref					
N1	0.212	0.163	0.192	1.236	0.899	1.700
N2	0.393	0.107	<0.001	1.482	1.201	1.830
N3	0.593	0.144	<0.001	1.810	1.363	2.402
M stage						
МО	Ref					
M1	0.707	0.096	<0.001	2.029	1.680	2.450
Surgery type						
No surgery of primary site	Ref					
Excision or resection of less than one lobe	0.756	0.270	0.005	2.130	1.254	3.617
Lobe or bilobectomy extended	0.304	0.300	0.311	1.355	0.753	2.440
Resection of at least one lobe or bilobectomy	0.378	0.346	0.274	1.460	0.741	2.876
Pneumonectomy	-0.093	0.265	0.725	0.911	0.542	1.532
Tumor size	0.007	0.001	<0.001	1.007	1.005	1.008
LNs count						
<16	Ref					
≥16	-0.020	0.008	0.008	0.980	0.965	0.995

Table 3 Multivariate Fine-Gray competing risk model

Ref, reference; β , beta coefficient; S.E, standard error; HR, hazard ratios; CI, confidence interval; LNs, lymph nodes.

cancer-specific survival in patients with NSCLC with bone metastases. These studies were consistent with our findings, which were surgery type, tumor size, M stage, LNs count, N stage, and primary site were prognostic factors in the RSF model.

To our knowledge, there are few studies on the long-

term survival of NSCLC patients using competing risk models. In our study, cancer-specific mortality in NSCLC was set as an event of interest and other-causes mortality as a competing event. In the presence of competing risks, the relative risk of a patient dying from NSCLC differs from that when only a single endpoint event is considered. For example, in another database study, David *et al.* reported that the risks of death in NSCLC patients \geq 75 years at stages I, II, and III were 1.29, 1.03, and 0.84 times significantly higher than those <65 years, respectively (21), while through the Fine-Gray model in our study, the risk of death from NSCLC in patients \geq 75 years was only 0.506 times higher compared to those <65 years. Given this, we may propose that the existence of competing risks should be taken into full consideration when analyzing survival issues to avoid biased results. Through the Fine and Gray model, we could provide more direct and accurate estimates of the cumulative incidences of death from NSCLC. The

Table 4 Variable importance of the RSF model

Variables	Variable importance		
Surgery type	0.1846		
Tumor size	0.0762		
M stage	0.0751		
LNs count	0.0364		
N stage	0.0340		
Primary site	0.0265		

RSF, random survival forest; LNs, lymph nodes.

Α

screened prognostic factors were put into the RSF model, which could help clinicians provide precision treatment and improve the quality of life for NSCLC patients.

RSF has emerged as an attractive predictive tool as a machine learning method with less restrictive model assumptions (20,24). We predicted the 1-, 3-, and 5-year survival of NSCLC patients by the RSF model, which performed well by ROC, calibration curves, and DCA analysis. Clinicians should use prediction models in the practice, but machine learning models are difficult to interpret meaningfully. We built a web computing tool to visually demonstrate the clinical application value of our model. The variables in the RSF model are simple and easy to obtain.

However, this study is still subject to some limitations. First, this study is limited by its retrospective nature. Second, the study population in the SEER database was mainly American, which requires more cohorts from different regions for verification. Third, the follow-up time was relatively short, which may affect the estimation of cumulative incidence. Finally, we used the past version of the SEER Cancer Statistics Review that includes statistics from 1975 through 2016, we could not collect the histological type of NSCLC, marital status, rural or urban residence, income, and education level before, these



В

Figure 2 ROC of the RSF model for predicting 1-, 3-, and 5-year survival of NSCLC patients in the training set (A) and the testing set (B). AUC, area under the curve; ROC, receiver operator characteristic; RSF, random survival forest; NSCLC, non-small cell lung cancer.



Figure 3 Calibration curves of the RSF model for predicting 1-, 3-, and 5-year survival of NSCLC patients in the training set (A) and the testing set (B). RSF, random survival forest; NSCLC, non-small cell lung cancer.

Subgroups	AUC for predicting 1-year survival	AUC for predicting 3-year survival	AUC for predicting 5-year survival
Training set	0.871	0.875	0.865
Testing set	0.796	0.804	0.792
Surgery type			
No surgery of primary site	0.880	0.779	0.714
Excision or resection of less than one lobe	0.812	0.799	0.774
Lobe or bilobectomy extended	0.841	0.807	0.756
Resection of at least one lobe or bilobectomy	0.799	0.861	0.820
Pneumonectomy	0.802	0.757	0.765
T stage			
T1	0.825	0.843	0.856
T2	0.852	0.825	0.831
ТЗ	0.810	0.807	0.820
Τ4	0.817	0.889	0.893
N stage			
NO	0.807	0.790	0.781
N1	0.856	0.835	0.856
N2	0.809	0.777	0.781
N3	0.764	0.828	0.769

Table 5 Performance of the RSF model for predicting 1-, 3- and 5-year survival of NSCLC patients

Table 5 (continued)

Translational Cancer Research, Vol 11, No 11 November 2022

Table 5 (continued)

Subgroups	AUC for predicting 1-year survival	AUC for predicting 3-year survival	AUC for predicting 5-year survival
M stage			
MO	0.792	0.791	0.805
M1	0.771	0.862	0.851

RSF, random survival forest; NSCLC, non-small cell lung cancer; AUC, area under the curve.



Figure 4 DCA for comparing the performance of the RSF model with the eighth edition AJCC staging in predicting 1-year (A), 3-year (C), and 5-year survival (E) of NSCLC patients in the training set and 1-year (B), 3-year (D), and 5-year survival (F) of NSCLC patients in the testing set. DCA, decision curve analysis; RSF, random survival forest; AJCC, American Joint Committee on Cancer Staging; NSCLC, non-small cell lung cancer.

variables might be associated with the prognosis of NSCLC. We were also unable to compare the survival of patients undergoing radical treatment and those with disseminated disease due to the lack of data on patients undergoing radical treatment. Herein, long-term, multicenter, and prospective clinical studies are therefore suggested.

Based on the SEER database, we established the RSF model for predicting the 1-, 3- and 5-year survival of NSCLC and generated a web calculator (https://github. com/YingChen19/Prognostic-factors-of-long-term-survival-of-non-small-cell-lung-cancer). The obtained results may provide a reference for survival prediction for NSCLC management, and could help improve the prognosis of NSCLC.

Acknowledgments

Funding: This research was funded by Wu JiePing Medical Foundation (Grant Number: 320.6750.2021-2-70).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tcr. amegroups.com/article/view/10.21037/tcr-21-2114/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-2114/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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study used the SEER database and all patient identifiers were removed from the SEER database, which was exempt from institutional review board approval. Individual consent for this retrospective analysis was waived.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the

original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

- Howlader N, NA KM, Miller D, et al. SEER cancer statistics factsheets: lung and bronchus cancer. National Cancer Institute, Bethesda, Maryland 2016.
- National Cancer Institute. SEER Cancer Statistics Review (CSR) 1975-2013. Available online: https://seer.cancer. gov/archive/csr/1975_2005/results_merged/sect_33_VA_ adjustment.pdf
- Bittoni MA, Arunachalam A, Li H, et al. Real-World Treatment Patterns, Overall Survival, and Occurrence and Costs of Adverse Events Associated With First-line Therapies for Medicare Patients 65 Years and Older With Advanced Non-small-cell Lung Cancer: A Retrospective Study. Clin Lung Cancer 2018;19:e629-45.
- Thakur MK, Gadgeel SM. Predictive and Prognostic Biomarkers in Non-Small Cell Lung Cancer. Semin Respir Crit Care Med 2016;37:760-70.
- Chansky K, Sculier JP, Crowley JJ, et al. The International Association for the Study of Lung Cancer Staging Project. Prognostic factors and pathologic TNM stage in surgically managed non-small cell lung cancer. Zhongguo Fei Ai Za Zhi 2010;13:9-18.
- Sculier JP, Chansky K, Crowley JJ, et al. The impact of additional prognostic factors on survival and their relationship with the anatomical extent of disease expressed by the 6th Edition of the TNM Classification of Malignant Tumors and the proposals for the 7th Edition. J Thorac Oncol 2008;3:457-66.
- Saji H, Tsuboi M, Yoshida K, et al. Prognostic impact of number of resected and involved lymph nodes at complete resection on survival in non-small cell lung cancer. J Thorac Oncol 2011;6:1865-71.
- Fukui T, Mori S, Yokoi K, et al. Significance of the number of positive lymph nodes in resected non-small cell lung cancer. J Thorac Oncol 2006;1:120-5.
- Martinez-Meehan D, Lutfi W, Dhupar R, et al. Factors Associated With Survival in Complete Pathologic Response Non-Small Cell Lung Cancer. Clin Lung Cancer 2020;21:349-56.
- Wen YS, Xi KX, Xi KX, et al. The number of resected lymph nodes is associated with the long-term survival outcome in patients with T2 N0 non-small cell lung

Translational Cancer Research, Vol 11, No 11 November 2022

cancer. Cancer Manag Res 2018;10:6869-77.

- 11. Kuk D, Varadhan R. Model selection in competing risks regression. Stat Med 2013;32:3077-88.
- Wu X, Wang Y, Lin X, et al. Racial and Ethnic Disparities in Lung Adenocarcinoma Survival: A Competing-Risk Model. Clin Lung Cancer 2020;21:e171-81.
- Li Y, Zhang H, Zhang W, et al. A Competing Risk Analysis Model to Determine the Prognostic Value of Isolated Tumor Cells in Axillary Lymph Nodes for T1N0M0 Breast Cancer Patients Based on the Surveillance, Epidemiology, and End Results Database. Front Oncol 2020;10:572316.
- He C, Zhang Y, Lin X. Increased Overall Survival and Decreased Cancer-Specific Mortality in Patients with Hepatocellular Carcinoma Treated by Transarterial Chemoembolization and Human Adenovirus Type-5 Combination Therapy: a Competing Risk Analysis. J Gastrointest Surg 2018;22:989-97.
- Xu J, Huang L, Wang Y, et al. A Retrospective Study of Effectiveness of Thoracoscopic Lobectomy and Segmentectomy in Patients with Early-Stage Non-Small-Cell Lung Cancer. Dis Markers 2022;2022:6975236.
- Song X, Xie Y, Zhu Y, et al. Is lobectomy superior to sublobectomy in non-small cell lung cancer with pleural invasion? A population-based competing risk analysis. BMC Cancer 2022;22:541.
- 17. Liang W, He J, Shen Y, et al. Impact of Examined Lymph Node Count on Precise Staging and Long-Term Survival of Resected Non-Small-Cell Lung Cancer: A Population Study of the US SEER Database and a Chinese Multi-

Cite this article as: Chen Y, Zhang Q, Lv Y, Li N, Xu G, Ruan T. Prognostic factors of survival in patients with nonsmall cell lung cancer: a competing risk model using the SEER database. Transl Cancer Res 2022;11(11):3974-3985. doi: 10.21037/tcr-21-2114 Institutional Registry. J Clin Oncol 2017;35:1162-70.

- Detterbeck FC, Chansky K, Groome P, et al. The IASLC Lung Cancer Staging Project: Methodology and Validation Used in the Development of Proposals for Revision of the Stage Classification of NSCLC in the Forthcoming (Eighth) Edition of the TNM Classification of Lung Cancer. J Thorac Oncol 2016;11:1433-46.
- Austin PC, Lee DS, Fine JP. Introduction to the Analysis of Survival Data in the Presence of Competing Risks. Circulation 2016;133:601-9.
- Ishwaran H, Kogalur UB, Blackstone EH, et al. Random survival forests. The Annals of Applied Statistics 2008;2:841-60.
- David EA, Cooke DT, Chen Y, et al. Does Lymph Node Count Influence Survival in Surgically Resected Non-Small Cell Lung Cancer? Ann Thorac Surg 2017;103:226-35.
- Sun H, Liu M, Yang X, et al. Construction and validation of prognostic nomograms for elderly patients with metastatic non-small cell lung cancer. Clin Respir J 2022;16:380-93.
- 23. Dong Q, Deng J, Mok TN, et al. Construction and Validation of Two Novel Nomograms for Predicting the Overall Survival and Cancer-Specific Survival of NSCLC Patients with Bone Metastasis. Int J Gen Med 2021;14:9261-72.
- Yang L, Fan X, Qin W, et al. A novel deep learning prognostic system improves survival predictions for stage III non-small cell lung cancer. Cancer Med 2022;11:4246-55.

Supplementary



Figure S1 The cumulative incidences of cancer-specific mortality in NSCLC in age (A), gender (B), ethnicity (C), primary site (D), T stage (E), N stage (F), M stage (G), surgery type (H), LNs count (I). CIF, cumulative incidence function; NSCLC, non-small-cell lung cancer; LNs, lymph nodes.

CD 11 04	O1 · ·		1		1	
Lable SL	(haracteristics	comparison	between	training of	set and	testing set
I HOLE OI	Onaracteristics	companioon	Detween	ci anning .	occ and	cesting see

Variables	Overall (n=1,251)	Training set (n=876)	Testing set (n=375)	Р
Age, years, n (%)				0.635
<65	491 (39.25)	339 (38.70)	152 (40.53)	
65-74	472 (37.73)	338 (38.58)	134 (35.73)	
≥75	288 (23.02)	199 (22.72)	89 (23.73)	
Primary site, n (%)				0.106
Upper lobe	810 (64.75)	577 (65.87)	233 (62.13)	
Middle lobe	78 (6.24)	45 (5.14)	33 (8.80)	
Lower lobe	316 (25.26)	220 (25.11)	96 (25.60)	
Main bronchus	30 (2.40)	20 (2.28)	10 (2.67)	
Overlapping lesion	17 (1.36)	14 (1.60)	3 (0.80)	
N stage, n (%)				0.188
NO	587 (46.92)	428 (48.86)	159 (42.40)	
N1	126 (10.07)	83 (9.47)	43 (11.47)	
N2	382 (30.54)	257 (29.34)	125 (33.33)	
N3	156 (12.47)	108 (12.33)	48 (12.80)	
M stage, n (%)				0.620
M0	967 (77.30)	681 (77.74)	286 (76.27)	
M1	284 (22.70)	195 (22.26)	89 (23.73)	
Surgery type, n (%)				0.481
No surgery of primary site	536 (42.85)	368 (42.01)	168 (44.80)	
Excision or resection of less than one lobe	91 (7.27)	62 (7.08)	29 (7.73)	
Lobe or bilobectomy extended	41 (3.28)	28 (3.20)	13 (3.47)	
Resection of at least one lobe or bilobectomy	532 (42.53)	41 (4.68)	10 (2.67)	
Pneumonectomy	51 (4.08)	377 (43.04)	155 (41.33)	
Tumor size, mm, M (Q1, Q3)	35.00 (21.00, 52.00)	35.00 (22.00, 54.25)	33.00 (20.50, 50.00)	0.167
LNs count, n (%)				1.000
<16	1,064 (85.05)	745 (85.05)	319 (85.07)	
≥16	187(14.95)	131 (14.95)	56 (14.93)	
Follow-up time, months, M (Q_1 , Q_3)	26.00 (8.00, 55.00)	26.00 (9.00, 55.00)	25.00 (8.00, 55.00)	0.567
Outcome, n (%)				0.632
Censored	445 (35.57)	319 (36.42)	126 (33.60)	
Dead from NSCLC	678 (54.20)	469 (53.54)	209 (55.73)	
Dead from other causes	128 (10.23)	88 (10.05)	40 (10.67)	

M (Q1, Q3), median and interquartile range; LNs, lymph nodes; NSCLC, non-small-cell lung cancer.