



A nomogram to predict the recurrence-free survival and analyze the utility of chemotherapy in stage IB non-small cell lung cancer

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Background: Large part of patients of stage IB non-small cell lung cancer (IB NSCLC) may suffer recurrence after surgery. This study is to determine risk factors and establish a nomogram for postoperative recurrence and to provide a reference for adjuvant chemotherapy selection in patients with stage IB NSCLC.

Methods: A total of 394 patients with postoperative stage IB NSCLC who visited Fujian Medical University Union Hospital between January 2010 and June 2016 were selected. Patients were divided into training and validation cohorts based on the time of diagnosis. Independent risk factors were identified using a Cox proportional hazards regression model. A nomogram was created to predict recurrence-free survival (RFS) and was validated with an independent cohort. The predictive ability of the nomogram was evaluated using the concordance index (C-index) and calibration curve. RFS between the high- and low-risk groups was determined using Kaplan-Meier curves, and subgroup analysis of chemotherapy was performed.

Results: Visceral pleura invasion, micropapillary structures, tumor size, preoperative serum carcinoembryonic antigen (CEA) level, preoperative serum cytokeratin-19 fragments (Cyfra21-1) level, and postoperative histology were identified as independent risk factors for stage IB NSCLC recurrence. Discrimination of the nomogram showed good prognostic accuracy and clinical applicability, with a C-index of 0.827 and 0.866 in the training and validation cohorts, respectively. The difference in RFS between the high- and low-risk groups in both cohorts was significant ($P < 0.05$). Finally, a significant difference was observed on whether high-risk group should accept postoperative chemotherapy ($P < 0.05$).

Conclusions: This nomogram can predict postoperative recurrence probability in patients with stage IB NSCLC, and can select patients with risk factors who need adjuvant chemotherapy.

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Introduction

At present, lung cancer has the highest rates of morbidity and mortality among all malignancies worldwide (1). According to the histological morphology of cancer cells, lung cancer can be divided into two major categories: non-small cell lung cancer (NSCLC) and small cell lung cancer, with NSCLC accounting for 80–85% of the cases (2). In recent years, with the development of chest imaging technology, the differentiation of small lung nodules has become increasingly precise, and the detection rate for early-stage lung cancer has been increasing annually (3). Stage I lung cancer patients are generally included in the early-stage lung cancer cohort. Currently, surgery is the main treatment for stage I NSCLC in clinical practice. Previous studies have reported that the recurrence rate of stage I NSCLC patients within 5 years after surgery is 18–29% (4), with age, sex, pathological (p) and clinical (T) stage status, surgical approach, and tumor size being independent risk factors (5). Considering the high rate of recurrence, it is necessary to identify the relevant risk factors of NSCLC and take the necessary precautions to prevent it. Compared to the 7th edition of the TNM staging system, the stage T2 in the 8th edition was changed: the maximum diameter of primary tumor is not greater than 5 cm, or has any of the following: the T stage was determined only by the maximum dimension of the invasive component and excludes the lepidic component and the size range of the T2a was also reduced from 3–5 to 3–4 cm (6). Clearly, patients with stage II and IIIA NSCLC benefit from adjuvant chemotherapy, but this treatment remains controversial for patients with stage IB disease (7,8). According to the National Comprehensive Cancer Network (NCCN) guidelines (version 2, 2021), postoperative adjuvant chemotherapy is recommended for patients with high-risk factors (poorly differentiation, lymphatic-vascular invasion, visceral pleural invasion etc.) (9). Previous studies also show the risk factors of recurrence in IB NSCLC patients are histology, smoking history and LVI (10). In this study, we put more indicators into consideration to predict the recurrence of IB NSCLC, such as elevated preoperative serum carcinoembryonic antigen, which is one of most commonly used marker to

evaluate the prognosis of cancer (11).

To establish a quantitative relationship between risk factors and tumor recurrence, survival and risk models can provide an early warning for recurrence or metastasis. To simplify the complex regression equation model, this study transforms the quantitative model into visualized graphs, a nomogram. Based on the nomogram, risk stratification of patients can aid both patients and physicians in making better evaluations regarding recurrence as well as suitable decisions for adjuvant chemotherapy. We present the following article in accordance with the TRIPOD reporting checklist (available at <https://tlcr.amegroups.com/article/view/10.21037/tlcr-21-1038/rc>).

Methods

Study population

We reviewed our thoracic database and selected patients with stage IB NSCLC from January 2010 to June 2016 at Fujian Union Hospital. A total of 394 patients were included in this retrospective analysis. Patients who received radical treatment between January 2010 and December 2014 were assigned into the training cohort (n=280), while patients from January 2015 to June 2016 were assigned into the validation cohort (n=114) for validation (12,13). The TNM staging system 8th edition was retrospectively used for all of the patients in our study. Patients received adjuvant chemotherapy based on their pathological situation and high-risk factors. The inclusion criteria were as follows: (I) the postoperative pathological type was primary NSCLC with stage IB; (II) patients who did not receive preoperative neoadjuvant treatments such as radiotherapy, immunotherapy, or chemotherapy; and (III) patients who underwent surgical treatment with R0 resection after the first discovery of a lung mass. The exclusion criteria were as follows: (I) patients with incomplete clinical information; (II) patients with past history of cancer; (III) patients with positive surgical margins (R1 or R2). The diagnostic criteria for recurrence were as follows: (I) local progression or distal metastasis was suggested by postoperative computed

tomography (CT) scan or positron emission tomography (PET); (II) local or distant puncture for biopsy or second surgery was performed for pathological examination if necessary and possible. Recurrence means local progression or distant metastasis after surgery, whichever occurs first in patients. The study was approved by the Ethics Committee of Fujian Medical University Union Hospital (No. 2022KY006). Individual consent for this retrospective analysis was waived. All procedures performed in this study were in accordance with the Helsinki Declaration (as revised in 2013).

Clinical characteristic and variables

The basic information of patients included the age, sex, history of smoking, history of hypertension, history of diabetes, pathological variables (including presence of micropapillary component, lymphatic-vascular invasion, etc.), and number of nodes removed. The hematology and laboratory parameters included preoperative platelet to lymphocyte ratio (PLR), preoperative prognostic nutritional index [$\text{PNI} = \text{serum albumin (g/L)} + 5 \times \text{absolute peripheral blood lymphocyte count (}\times 10^9/\text{L)}]$], preoperative peripheral serum tumor marker carcinoembryonic antigen (CEA), and cytokeratin 19 fragment (Cyfra21-1) (14). The platelet count, absolute lymphocyte values, serum albumin levels, CEA, and Cyfra21-1 were obtained from peripheral blood samples taken from patients within 7 days before surgery.

Post-operative follow-ups

Postoperative follow-ups were started from the date of surgery and performed every 3 months in the first year, every 6 months in the second year, and annually thereafter (totally 5 years) by CT scanning or PET-CT. Recurrence-free survival (RFS) was defined as the time from the date of surgery to the date of recurrence, death from any cause, or censored at the time points of last follow-up. Close follow-up can detect recurrence at an earlier time.

Statistical analysis

X-TILE software was used to determine the optimal threshold for PLR, PNI indicators, tumor size, and number of lymph nodes removed. The Kaplan-Meier method was used to analyze the RFS and plot the survival function curves, and the log-rank test was applied to compare the differences in RFS among independent factors. Univariate

analysis was used to analyze all single factors affecting RFS, and each statistically significant single factor was included in the multivariate analysis. Based on the independent risk factors, a nomogram was created using the R software.

The performance of the nomogram was evaluated using discrimination and calibration. The model's discrimination was determined by combining two validation methods: the one validation (bootstrap method with 1,000 resamples) to obtain Harrell's concordance index (C-index), and the validation cohort was used to further validate the prediction model. Calibration curves were plotted to calibrate the model. Finally, the high- and low-risk groups were separated based on the total risk score from the nomogram. The Kaplan-Meier method was used to analyze the RFS between the two risk groups as well as the RFS for chemotherapy in the high- and low-risk groups in both cohorts (subgroup analysis). All statistical test levels were considered statistically significant at $P \leq 0.05$. Statistical analyses were performed using SPSS (version 23.0; SPSS, IBM Corp., Armonk, New York, USA), X-TILE 3.6.1 software (Yale University, New Haven, CT, USA) (15), and R software version 4.0.5 (<http://www.r-project.org>). The packages of R software included rms, rmda, survminer, and survival.

Results

Study cohort and clinical features

A total of 394 patients with stage IB NSCLC were eligible for enrollment. In the training cohort, 173 patients were male and 107 were female, among which 36.8% ($n=103$) of patients received adjuvant chemotherapy. In the validation cohort, there were 76 males and 38 females, among which 59.6% ($n=68$) of patients received adjuvant chemotherapy (the kinds of chemotherapy are shown in [Table S1](#)). The median and mean follow-up times were 60 and 54.7 months, respectively. There were 66/394 (16.7%) patients who experienced recurrence within 5 years. The distribution of demographics and clinicopathologic characteristics of patients in the two cohorts are shown in [Table 1](#).

Assignment of continuous variables to dichotomous variables

Continuous variables such as age, tumor size, PLR, PNI, and number of lymph nodes dissected were converted into dichotomous variables by calculating their optimal cut-off values using the X-TILE software. The optimal cut-off values were obtained for each variable as follows: PLR

Table 1 Demographics and clinicopathologic characteristics of training and validation cohort

Characteristics	Training cohort	Validation cohort	P value
Age (35–80 years)			0.996
≤65 years	172	70	
>65 years	108	44	
Gender			0.362
Male	173	76	
Female	107	38	
Smoking history			0.805
Never smokers	163	66	
Ever smokers	33	16	
Smokers	84	32	
Family history of NSCLC			0.200
No	273	114	
Yes	7	0	
Hypertension			0.954
No	212	86	
Yes	68	28	
Diabetes			0.776
No	258	106	
Yes	22	8	
PLR (=PLT/LY)			0.106
≤114.6	123	40	
>114.6	157	74	
PNI (=ALB+5*LY)			0.004
≤50.9	165	49	
>50.9	115	65	
CEA (ng/mL)			0.834
Normal	214	86	
Abnormal	66	28	
Cyfra21-1			0.004
Normal	214	71	
Abnormal	66	43	
Primary site			0.582
Left upper lobe	75	33	
Left lower lobe	44	20	
Right upper lobe	78	35	

Table 1 (continued)**Table 1** (continued)

Characteristics	Training cohort	Validation cohort	P value
Right middle lobe	23	10	
Right lower lobe	60	16	
Surgical approach			0.001
Lung lobectomy	271	100	
Segmentectomy or wedge resection	9	14	
Histology			0.544
Adenocarcinoma	231	89	
Squamous cell carcinoma	31	17	
Others	18	8	
Tumor size			0.256
≤2.4 cm	113	39	
>2.4 cm	167	75	
VPI			0.062
No	81	44	
Yes	199	70	
Micropapillary structure			0.014
No	240	86	
Yes	40	28	
LVI			0.242
No	272	108	
Yes	8	6	
Invasion of bronchus			0.304
No	263	110	
Yes	17	4	
Number of nodes resected			0.040
≤12	42	27	
>12	238	87	
Obstructive pneumonia			0.327
No	275	114	
Yes	5	0	
Adjuvant chemotherapy			<0.001
No	177	46	
Yes	103	68	

NSCLC, non-small cell lung cancer; PLR, platelet to lymphocyte ratio; PLT, platelet; LY, lymphocyte; PNI, prognostic nutritional index; ALB, albumin; CEA, carcinoembryonic antigen; Cyfra21-1, cytokeratin-19 fragments; VPI, visceral pleural invasion; LVI, lymphatic-vascular invasion.

=114.6, PNI =50.9, tumor size =2.4 cm, and number of lymph nodes moved =12. The cut-off values for age, CEA, and Cyfra21-1 are 65 years, 5.0 ng/mL, and 3.3 ng/mL, respectively. According to the rules of clinical laboratory in our hospital, the range of the norm of CEA and Cyfra21-1 is 0–5.0 ng/mL and 0–3.3 ng/mL, separately.

Univariate and multivariate survival analysis and Kaplan–Meier RFS curves

All variables in *Table 1* were calculated using the univariate and multivariate Cox proportional hazards regression model, with each factor ($P < 0.05$) as follows: histology (squamous cell carcinoma: $P = 0.001 < 0.05$ and others: $P = 0.007 < 0.05$), micropapillary component ($P = 0.002 < 0.05$), tumor size ($P < 0.001$), visceral pleura invasion ($P < 0.001$), Cyfra21-1 ($P = 0.008 < 0.05$), and CEA ($P = 0.002 < 0.05$) (*Table 2*). The Kaplan–Meier survival curves for each independent risk factor were plotted separately, as shown in *Figure 1*. The Kaplan–Meier RFS curves for chemotherapy was shown in *Figure S1*.

Nomogram for recurrence-free survival

The six independent risk factors were converted into a nomogram, as shown in *Figure 2*. To verify the degree of discrimination and calibration of the prediction model, validation methods and a calibration curve can be generally adopted. In one validation, the C-index was 0.827 after 1,000 internal self-sampling times (the closer the consistency index was to 1, the better the model was for individualized differentiation). In other validation, a C-index of 0.866 in the validation cohort showed that the nomogram had good accuracy and application. The slope of the calibration curve was close to the reference line, indicating that the model could better predict the RFS rate of patients (*Figure 3*). For instance, a patient with IB NSCLC with tumor size of 2.7 cm (61 points), histology of adenocarcinoma (0 points), involvement of visceral pleura (100 points) and micropapillary structure (37 points) has a sum-point equal to 198, corresponding to predicted 3- and 5-year RFS of 73% and 56%, respectively.

The clinical value of the nomogram for adjuvant chemotherapy in high-risk groups

The score of each patient was calculated (retaining one decimal) from the nomogram, and patients were

divided into high-risk (total scores > 135) and low-risk (total score ≤ 135) groups. A significant difference in RFS between the two groups was observed in the training and validation cohorts ($P < 0.001$ and $P = 0.008$, respectively), as shown in *Figure 4*. Subgroup survival analysis in the training cohort was performed in the high- and low-risk groups, which showed that the RFS was higher in patients who received chemotherapy than in those who did not receive the treatment in the high-risk group ($P = 0.003$). However, this difference was not observed in the low-risk group ($P = 0.220$). In addition, a difference between accepting chemotherapy and not accepting chemotherapy in the high- and low-risk groups was observed in the validation cohort ($P = 0.029$ in the high-risk group and $P = 0.791$ in low-risk group), as shown in *Figure 5*.

Discussion

The tumor nodes metastasis (TNM) staging system for lung cancer is currently used clinically as an important reference for guiding and predicting patient prognosis. However, the prognostic factors incorporated in this system are limited and still cannot accurately predict the prognosis of patients with early-stage NSCLC. In addition, patients with early-stage NSCLC experience local recurrence and distant metastasis due to micrometastasis (16,17). Therefore, there is a need to explore and incorporate more variables to establish an effective model for predicting the prognosis of early-stage NSCLC, in order to improve the prognosis and survival of patients with stage IB NSCLC by early detection, intervention, and scientific treatment plans.

Previous studies have already demonstrated that nomograms can facilitate the stratification of patients into high- and low-risk groups (18). Therefore, we pooled patients into different risk stratification groups to determine the impact of adjuvant chemotherapy in the different risk groups. In our study, the C-index of the training and validation cohorts were better than those reported in previous studies (12,19), indicating a better discrimination of our nomogram. To the best of our knowledge, the postoperative survival and prognosis model in stage IB NSCLC patients in previous studies have mostly reported overall survival (death) as an endpoint, and few laboratory blood tests (albumin, Cyfra21-1, etc.) have been included as variables in these studies (20,21). Compared to other endpoints, RFS may be a better endpoint for the evaluation of adjuvant chemotherapy (22). In our study, we investigated several laboratory variables and histological subtypes for

Table 2 Selected factors in the training cohort for building the nomogram through univariate and multivariate analyses

Characteristics	Univariate analysis			Multivariate analysis		
	HR (95% CI)	P value		HR (95% CI)	P value	
Age (≤ 65 vs. > 65 years)	1.237	0.64–2.205	0.472			
Gender (male vs. female)	0.651	0.349–1.217	0.179			
Smoking history (never smokers vs. ever smokers vs. smokers)	1.299	0.888–1.901	0.178			
Hypertension (no vs. yes)	1.220	0.644–2.312	0.541			
Family history of NSCLC (no vs. yes)	0.789	0.109–5.719	0.814			
Diabetes (no vs. yes)	1.087	0.390–3.029	0.873			
PLR (PLT/LY) (≤ 114.6 vs. > 114.6)	0.663	0.374–1.175	0.159			
PNI (ALB+5*LY) (≤ 50.9 vs. > 50.9)	1.576	0.889–2.792	0.119			
CEA (normal vs. abnormal)	2.466	1.377–4.418	0.002	2.633	1.423–4.873	0.002
Cyfra21-1 (normal vs. abnormal)	2.161	1.200–3.892	0.01	2.342	1.249–4.391	0.008
Primary site (left upper lobe vs. left lower lobe vs. right upper lobe vs. right middle lobe vs. right lower lobe)	0.906	0.744–1.103	0.324			
Histology	1.669	1.125–2.477	0.011			
Adenocarcinoma				Reference		
Squamous cell carcinoma				3.953	1.752–8.920	0.001
Others				3.814	1.445–10.065	0.007
Surgical approach (lung lobectomy vs. segmentectomy or wedge resection)	2.039	0.633–6.567	0.233			
Tumor size (≤ 2.4 vs. > 2.4 cm)	3.676	1.717–7.866	0.001	6.017	2.704–13.099	<0.001
VPI (no vs. yes)	6.587	2.045–21.215	0.002	18.947	5.761–62.306	<0.001
Micropapillary structure (no vs. yes)	3.109	1.663–5.813	<0.001	2.920	1.472–5.791	0.002
Invasion of main bronchus (no vs. yes)	1.901	0.752–4.805	0.175			
LVI (no vs. yes)	0.746	0.103–5.408	0.772			
Number of nodes resected (≤ 12 vs. > 12)	0.536	0.273–1.053	0.07			
Adjuvant chemotherapy (no vs. yes)	0.553	0.287–1.066	0.077			
Obstructive pneumonia (no vs. yes)	0.048	0–479.007	0.519			

HR, hazard ratio; CI, confidence interval; NSCLC, non-small cell lung cancer; PLR, platelet to lymphocyte ratio; PLT, platelet; LY, lymphocyte; PNI, prognostic nutritional index; ALB, albumin; CEA, carcinoembryonic antigen; Cyfra21-1, cytokeratin-19 fragments; VPI, visceral pleural invasion; LVI, lymphatic-vascular invasion.

postoperative recurrence in patients with stage IB NSCLC to establish a postoperative recurrence prediction model. This model can be used to screen suitable patients for adjuvant chemotherapy to improve RFS. Moreover, this risk stratification nomogram was used in the validation cohort to validate the feasibility and replicability of the nomogram.

Visceral pleural invasion was an independent risk factor

for recurrence in patients with stage IB NSCLC in our series and is now included in the T2 staging criteria of the 8th edition of the international TNM staging system for lung cancer (23). It has been found that there are abundant lymphatic connections between the lung parenchyma and visceral pleura, with drainage converging to the hilar lymph nodes (24). Therefore, patients with NSCLC involving

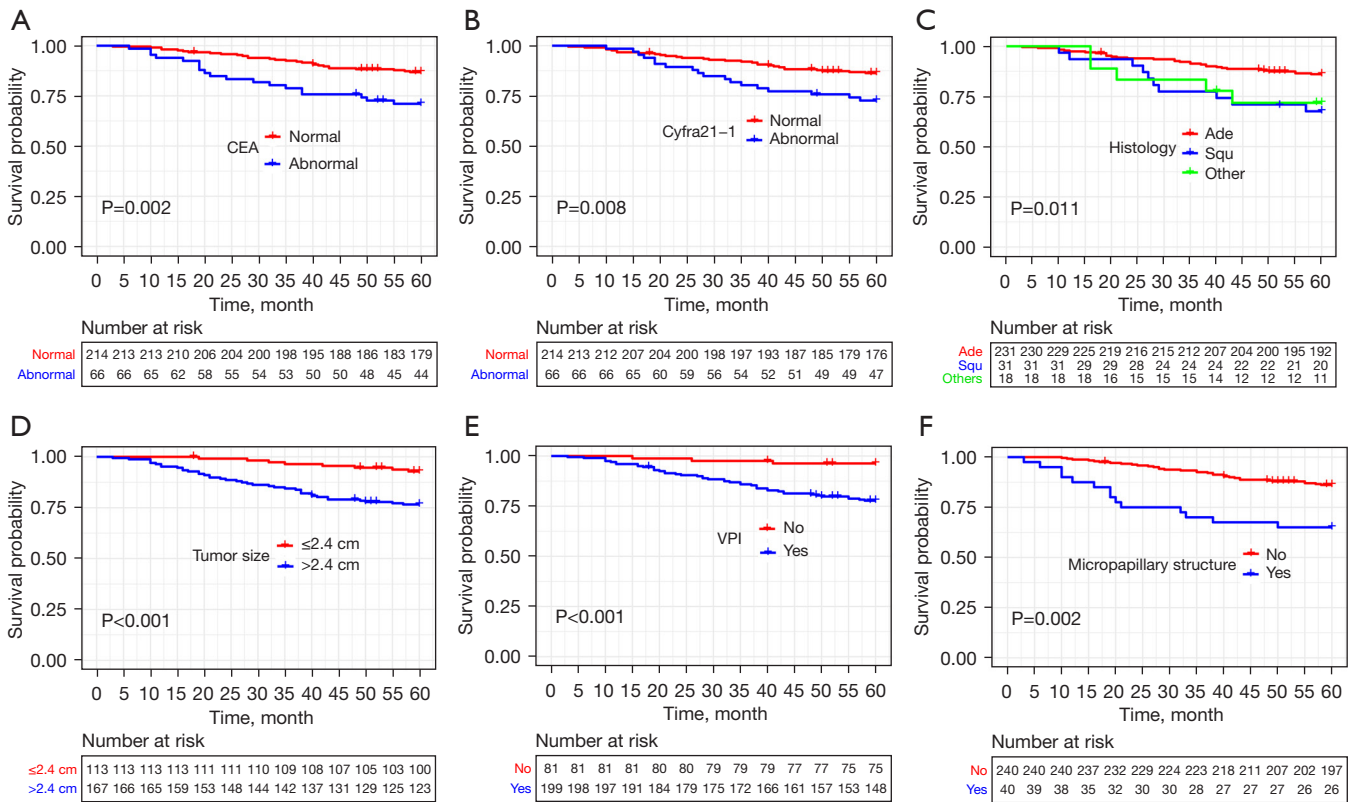


Figure 1 Kaplan-Meier curves of RFS. Stratified by CEA, Cyfra21-1, histology, tumor size, visceral pleura involvement, micropapillary structure, respectively. RFS, recurrence-free survival; CEA, carcinoembryonic antigen; Cyfra21-1, cytokeratin-19 fragments.

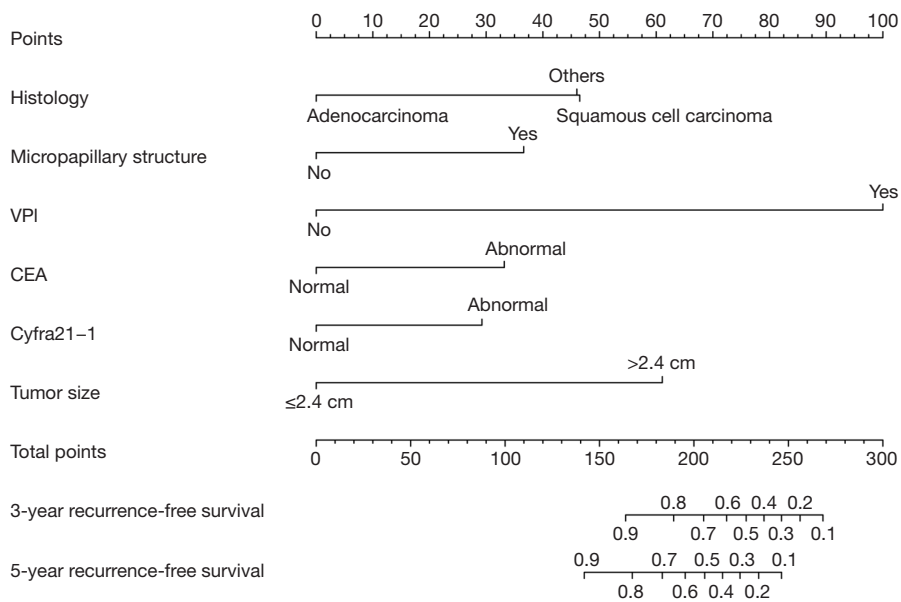


Figure 2 Prognostic nomogram for the 3- and 5-year recurrence-free survival. CEA, carcinoembryonic antigen; Cyfra21-1, cytokeratin-19 fragments; VPI, visceral pleura involvement.

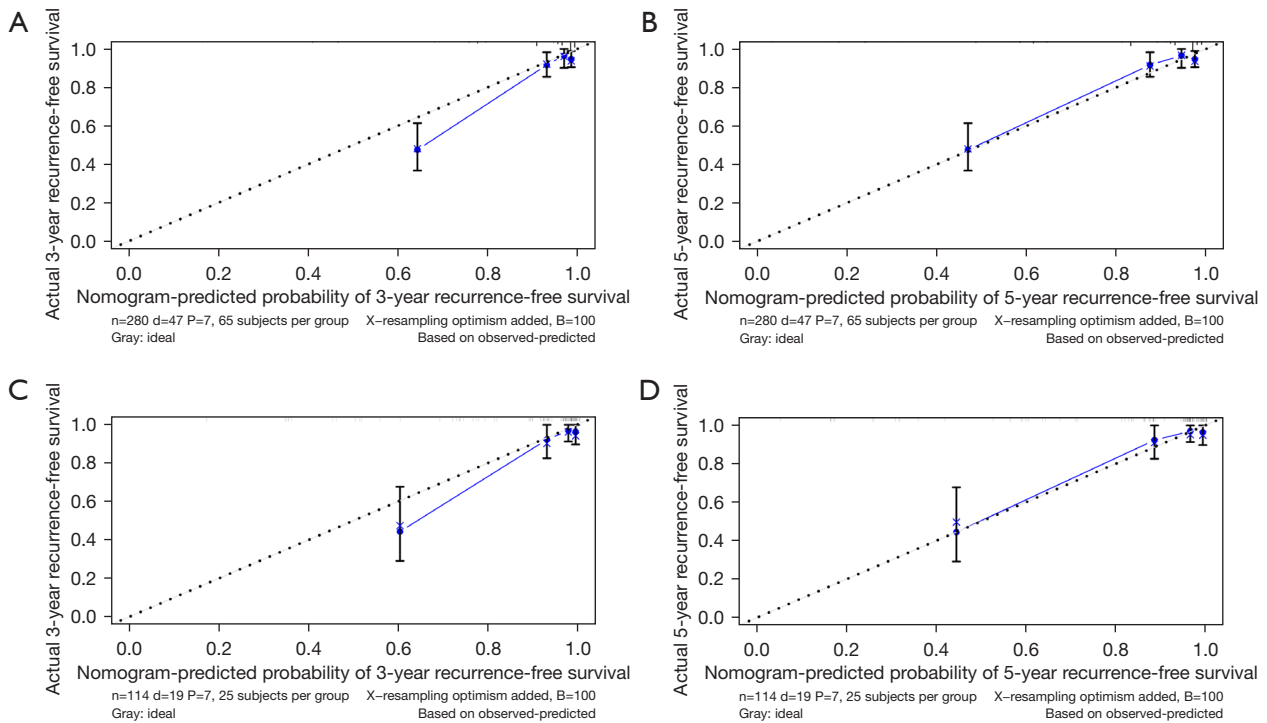


Figure 3 Calibration curves predicting the 3- and 5-year RFS of patients in the training (A,B) and validation (C,D) cohorts. The x-axis indicates the predicted survival probability, and the y-axis indicates the actual survival probability. The 45-degree line indicates that the prediction agrees with actuality. RFS, recurrence-free survival.

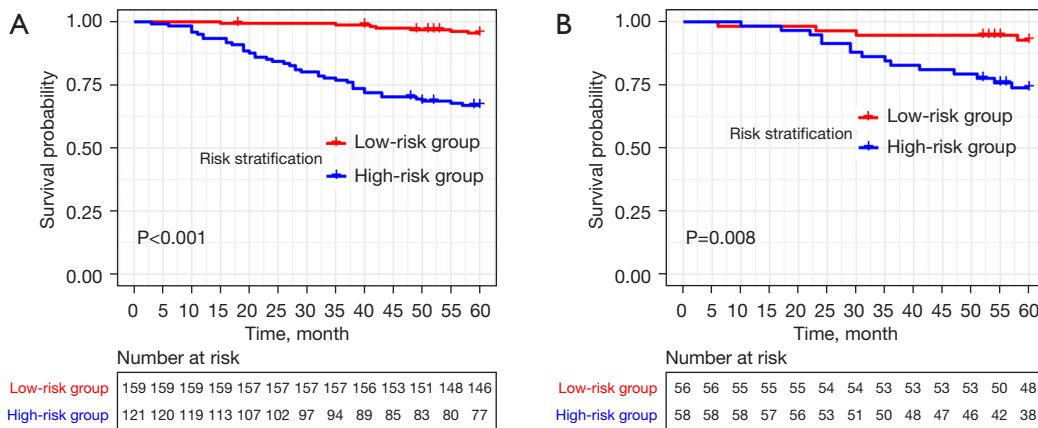


Figure 4 Kaplan-Meier curves of RFS for risk stratification in the training (A) and validation (B) cohorts. RFS, recurrence-free survival.

the visceral pleura have a worse prognosis and are at an increased risk of local recurrence and distant metastasis.

Patients with relatively high preoperative CEA levels have a poorer postoperative prognosis, which is consistent with the results of our study (25). Although CEA levels of patients with long-term smoking habits, cardiovascular

disease, gynecological disease, and other diseases are frequently elevated, but the serum CEA level is one of the most commonly used serum tests to evaluate the prognosis of lung cancer (26,27). In addition, studies have shown a better sensitivity of Cyfra21-1 compared to CEA for early stage of lung cancer diagnosis, especially in squamous cell

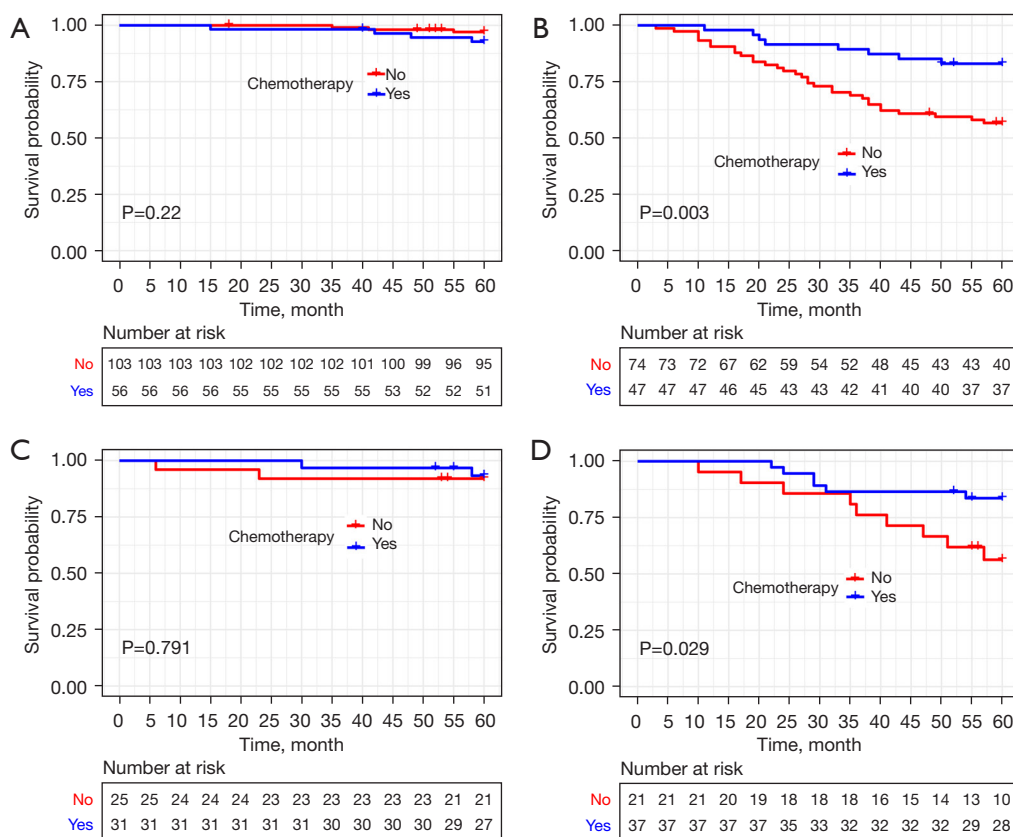


Figure 5 Kaplan-Meier curves of RFS for chemotherapy of the low-risk group in the training cohort (A), high-risk group in the training cohort (B), low-risk group in the validation cohort (C), and high-risk group in the validation cohort (D). RFS, recurrence-free survival.

carcinoma, where the true positive detection rate is much higher than that of CEA and squamous cell carcinoma antigen (SCCA), and is currently considered the most sensitive tumor marker for the diagnosis of NSCLC (28). In 2017, the correlation between Cyfra21-1 levels in the peripheral blood of NSCLC patients and tumor metastasis/survival status was reported to be stronger than that of CEA and neurospecific enolase (NSE), and showing an independent prognostic effect on patients with different stages of lung cancer (29). The results of this study revealed that these two indicators have sufficient predictive strength in the multivariate analysis of the nomogram.

There is a consensus that adjuvant chemotherapy is not required for patients with stage IA NSCLC resected at R0; however, it is still controversial whether chemotherapy is required for patients with stage IB NSCLC, especially if the tumor involves the visceral pleura (30). According to the National Comprehensive Cancer Network, patients with high-risk factors are recommended to receive adjuvant chemotherapy, but it only determined the possible high-

risk factors (8). A previous study also revealed that high-risk patients may benefit from adjuvant chemotherapy (31). In addition, in the subgroup analysis, patients in the low-risk group could choose to refuse chemotherapy after surgery, which does not influence their RFS. However, the subgroup analysis of the high-risk group in the training and validation cohorts suggested that patients in the high-risk group receiving adjuvant chemotherapy had a more significant RFS benefit than those who refused chemotherapy. For local recurrence, salvage surgery can be a good choice, but surgery may be limited or may not be performed owing to poor lung function after the first surgery (32). In addition, although the postoperative pathological reports excluded lymph node metastasis and the postoperative TNM staging was IB stage, micrometastasis may have already occurred, which is difficult to discover and report (33). We recommend that patients with high-risk factors receive chemotherapy after surgery to achieve higher RFS, avoid second surgery for recurrence, and prevent potential metastasis.

A previous study showed that different pathological

subtypes of lung adenocarcinoma have a significant impact on the prognosis of stage I adenocarcinoma based on the 2015 World Health Organization (WHO) classification (34). In this study, the pathologic type is an independent factor for recurrence, especially the micropapillary structure in lung cancer. It has been shown that patients with NSCLC whose pathological subtype is predominantly micropapillary have a higher risk of recurrence and a worse prognosis (35,36). In particular, for patients with stage I NSCLC, micropapillary structures can be an important prognostic predictor (37). Through Kaplan-Meier and Cox analyses were performed in our study, micropapillary structures were strongly associated with RFS rates. From the nomogram, we can also conclude that the micropapillary structure was one of the most weighted among all the included independent risk factors. Numerous scholars have gradually explored the tumor cell microenvironment and suggested that tumor-associated inflammation contributes to the development of tumor networks (38). However, the results of our study failed to show a connection between inflammation contribution and RFS. A possible explanation for this is that the contribution of inflammation may be more common and obvious in advanced cancers than early-stage cancers.

There are some limitations to our study that should be noted. All cases in this study were from our hospital and represent only a single center and only Asian patients. In the future, it is necessary to further collect data from large samples in different centers, in order to gradually improve the prediction model and provide more accurate postoperative intervention plans for patients with stage IB NSCLC. Besides, there are bias on numbers on chemotherapy between training and validation and the number of use of PET-CT was limited. And it is not clear whether these data and prognostic factors can be used for other ethical groups as well.

Conclusions

In this study, we found that visceral pleura invasion, micropapillary structures, tumor size, preoperative serum CEA level, preoperative serum CYFRA21-1 level, and histology were independent risk factors for the recurrence of stage IB NSCLC. Our nomogram can aid clinicians in deciding whether patients need adjuvant chemotherapy, which could greatly improve the postoperative RFS of patients. Patients with high-risk factors receiving adjuvant chemotherapy have a more significant RFS benefit. This nomogram can individually predict the probability of

postoperative recurrence and guide clinical treatment in patients with stage IB NSCLC.

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Footnote

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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. All procedures performed in this study were in accordance with the Helsinki Declaration (as revised in 2013). The study was approved by the Ethics Committee of Fujian Medical University Union Hospital (No. 2022KY006). Individual consent for this retrospective analysis was waived.

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Supplementary

Table S1 Different regimens of chemotherapy in training cohort and validation

Regimen of chemotherapy	Training cohort	Validation cohort
Docetaxel + platinum-based drugs	16	5
Gemcitabine + platinum-based drugs	24	5
Gemcitabine	0	2
Pemetrexed	2	3
Pemetrexed+ platinum-based drugs	17	43
Etoposide + platinum-based drugs	0	1
Vinorelbine + platinum-based drugs	5	0
Paclitaxel + platinum-based drugs	39	9

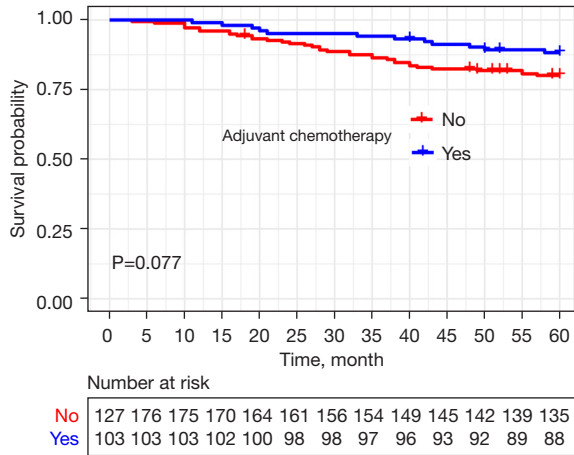


Figure S1 Kaplan-Meier curves for recurrence-free survival (RFS) in regard to the use of adjuvant chemotherapy in the training cohort.