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Original Article

Analysis of influencing factors of recurrence after thoracoscopic resection in patients with Stage I a lung adenocarcinoma

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Abstract: This study aimed to investigate the influencing factors of recurrence after thoracoscopic resection in patients with Stage I a lung adenocarcinoma. The derivation cohort consisted of 104 patients admitted between February 2020 and December 2021, categorized into recurrence (n = 39) and non-recurrence (n = 65) groups based on postoperative recurrence status. Internal validation was performed using 10-fold cross-validation. Additionally, a temporally distinct validation cohort of 80 patients admitted between January 2022 and April 2022 was used for external validation, with similar recurrence-based grouping (relapse: n = 30; non-recurrent: n = 50). Univariate analysis revealed significant differences in age, maximum tumor diameter, pleural invasion, tumor differentiation, number of lymph node dissections, comorbidities, family history, and smoking history (P<0.05). Postoperative levels of platelet/lymphocyte count ratio (PLR), carcinoembryonic antigen (CEA), and Cytokeratin 19 Fragment (Cyfra21-1) were significantly lower in the non-recurrence group (P<0.05). Multivariate logistic regression and Cox proportional hazards regression analyses were performed to account for both categorical recurrence outcome and time-to-event data. Both models consistently identified maximum tumor diameter (logistic OR = 2.300, Cox HR = 2.119), tumor differentiation (OR = 2.333, HR = 2.251), number of lymph node dissections (OR = 2.782, HR = 2.581), and pleural invasion (OR = 1.394, HR = 1.411) as independent risk factors for recurrence (all P<0.05). The combined predictive model incorporating these four factors achieved an AUC of 0.924 (P<0.001), with sensitivity of 87.2% and specificity of 86.2%. The model was further validated in an independent external cohort (n = 80), showing an AUC of 0.940. In conclusion, a model integrating maximum tumor diameter, tumor differentiation, number of lymph node dissections, and pleural invasion effectively predicts recurrence risk after thoracoscopic resection in Stage I a lung adenocarcinoma, facilitating individualized treatment planning.

Keywords: Stage I a, lung adenocarcinoma, thoracoscopic resection, postoperative recurrence, influencing factors

Introduction

Lung cancer remains the leading cause of cancer-related mortality worldwide, with an estimated 2.2 million new cases and 1.8 million deaths annually [1, 2]. Non-small cell lung cancer (NSCLC) constitutes the majority of cases, and lung adenocarcinoma is its most prevalent subtype [3]. The prognosis for lung cancer patients is highly dependent on the stage at diagnosis. For those with Stage I disease, surgical resection is the cornerstone of curative treatment, with video-assisted thoracoscopic surgery (VATS) being the preferred minimally invasive approach as recommended by the National Comprehensive Cancer Network (NCCN) guidelines [4].

Despite high overall survival rates for Stage IA lung adenocarcinoma, a significant proportion of patients experience disease recurrence after complete resection [5, 6]. Approximately 20% of these patients face this recurrence [7]. This highlights the clinical heterogeneity within this early stage and the insufficiency of current staging systems alone to precisely identify patients at high risk of recurrence. The TNM classification, specifically the T descriptor ba-

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sed on tumor size, is the primary tool for prognostication in Stage I a disease [8, 9]. However, relying solely on tumor diameter (e.g., T1a/T1b/T1c) provides suboptimal accuracy for predicting relapse-free survival. It is increasingly recognized that other pathological factors, such as tumor differentiation, the extent of lymph node dissection, and the presence of pleural invasion, may significantly influence outcomes, but these are not integrated into the current staging system [10].

The ability to accurately predict recurrence risk is crucial for tailoring postoperative management. While clinicians often rely on experience, this approach is subjective and not standardized. Although several studies have identified various clinical and pathological factors associated with recurrence in early-stage lung cancer [11], a validated, integrated model for routine clinical use in Stage I a adenocarcinoma is lacking. To our knowledge, no previous study has developed a predictive model specifically combining maximum tumor diameter, tumor differentiation grade, number of lymph node dissections, and pleural invasion to estimate recurrence risk following VATS for Stage I a lung adenocarcinoma.

Therefore, this study aimed to investigate the factors influencing recurrence after thoracoscopic resection in this patient population. We sought to identify independent risk factors and to develop and internally validate a novel predictive model based on a combination of readily available clinical and pathological variables. Such a model could potentially assist in stratifying patients for more intensive surveillance or adjuvant therapy, ultimately guiding personalized treatment strategies.

Patients and methods

General information

During February 2020 to April 2022, patients with Stage I a lung adenocarcinoma cured in our hospital were retrospectively enrolled. All the patients went through video-assisted thoracoscopic surgery, which included lobectomy, segmentectomy, or wedge resection, and were pathologically diagnosed as Stage I a lung adenocarcinoma. A total of 104 patients admitted from February 2020 to December 2021 were included in the derivation cohort. According to the recurrence after operation, there were two categories of patients, including recurrences (n = 39) and non-recurrences (n = 65). The general data of all patients are shown in **Table 1**. In addition, this study conducted an internal validation of the prediction model using a 10-fold cross-validation method to ensure the stability and reliability of the model. Moreover, 80 patients admitted from January 2022 to April 2022 who met the same inclusion criteria were selected as the validation cohort. Based on the recurrence after operation, these patients were similarly divided into relapse group (n = 30) and non-recurrent group (n = 50). This temporal split ensures that the validation cohort represents a distinct cohort for external validation.

Inclusion criteria: (1) thoracoscopic resection of lung cancer had been performed; (2) postoperative samples can be used for pathological diagnosis and evaluation; (3) according to the new TNM staging data (9th edition) published by the International Association for Lung Cancer Research (IASLC) [12], T stages in IA can be divided into T1a (maximum diameter of tumor ≤1 cm), T1b (1 cm < maximum diameter of tumor ≤2 cm) and T1c (2 cm < maximum diameter of tumor ≤3 cm).

Exclusion criteria: (1) patients did not have complete clinical data (defined as missing demographic, surgical, pathological, or essential laboratory records); (2) no pathological specimens after operation; (3) anti-tumor therapy such as radiotherapy and chemotherapy before and after operation; (4) history of other types of malignant tumor; (5) patients had died of perioperative complications (defined as mortality directly attributable to any complication occurring within 30 days post-surgery); (6) patients with cognitive impairment (**Figure 1**).

Diagnostic criteria of relapse was shown [13]: (1) according to the postoperative CT images of the lungs, the progress of local lung cancer was indicated, and the metastasis to other parts of the body was excluded; (2) new pulmonary nodules were examined pathologically by lung puncture biopsy; (3) new nodule signs were found to be consistent with the characteristics of primary lung cancer, and the postoperative pathological results of the second pulmonary nodule operation were diagnosed as non-small cell lung cancer (NSCLC).

Data collection

General information: The general data of age, sex, course of disease, body mass index (BMI), tumor diameter, smoking history, drinking history, basic disease history, operation method

Table 1. General information of patients

Group	Relapse group (n = 39)	Non-recurrent group (n = 65)	t/χ^2	P
Age	36.49±4.91	45.93±2.93	10.896	<0.001
Gender (male/female)	19/20	31/34	0.010	0.919
BMI (kg/m^2)	20.98±3.85	20.81±3.31	0.248	0.804
Maximum diameter of tumor (cm)	3.59±0.22	2.48±0.11	30.048	<0.001
Pleural invasion	22 (56.41)	19 (29.23)	7.540	0.006
Degree of tumor differentiation				
High	19 (48.72)	11 (16.92)	12.175	0.002
Medium	13 (33.33)	32 (49.23)		
Low	7 (17.95)	22 (33.85)		
Number of lymph node dissection	16.13±2.84	12.19±1.15	8.259	<0.001
Mode of operation				
Radical resection	23 (58.97)	43 (66.15)	0.542	0.462
Palliative resection	16 (41.03)	22 (33.85)		
Comorbidities				
High blood pressure	17 (43.59)	8 (12.31)	13.063	<0.001
Hyperlipidemia	11 (28.21)	8 (12.31)	4.126	0.042
Diabetes	10 (25.64)	4 (6.15)	7.946	0.005
Family history	6 (15.38)	1 (1.54)	5.402	0.020
Smoking history	34 (87.18)	25 (38.46)	23.568	<0.001

BMI, Body Mass Index.

and operation site of the two groups were collected.

Laboratory index: The following laboratory parameters were detected before and 4 weeks after operation: carcinoembryonic antigen (CEA), platelet/lymphocyte count ratio (PLR), Cytokeratin 19 Fragment (Cyfra21-1).

Data collection procedure: Data were retrospectively extracted from the hospital's electronic medical record (EMR) system. Demographic, clinical, and surgical data were obtained from anesthesia and surgical reports. Pathological data, including tumor diameter, differentiation, and pleural invasion status, were collected from the formal histopathology reports. Laboratory test results (PLR, CEA, Cyfra21-1) were retrieved from the laboratory information system (LIS). All data were anonymized and compiled into a standardized database by two independent researchers, with discrepancies resolved by a third senior investigator.

Statistical analysis

SPSS21.0 statistical software was used for statistical analysis. Shapiro-Wilk test showed that the continuous variables conformed to normal distribution and were expressed as mean ± standard deviation ($\overline{x}\pm s$). An independent samples T-test was employed to compare the two groups. Count data were exemplified and reported as n (%), with the χ^2 test applied for comparisons. To identify the factors influencing recurrence following surgical resection in Stage I a lung adenocarcinoma patients, a logistic regression analysis was conducted. Cox proportional hazards regression was additionally conducted to account for time-to-recurrence and to calculate hazard ratios (HRs). Categorical variables in the regression models were assigned as follows: pleural invasion (0 = no, 1 = yes), tumor differentiation (1 = well, 2 = moderate, 3 = poor), and comorbidities (0 = absent, 1 = present). Analyzing the predictive value with ROC curve, we found that there was a statistically significant difference when P<0.05 was taken into account.

Results

Comparison of general data

There exhibited no noticeable difference in gender, BMI and operation mode (P>0.05). Noticeable differences were observed in age, maximum diameter of tumor, pleural invasion,

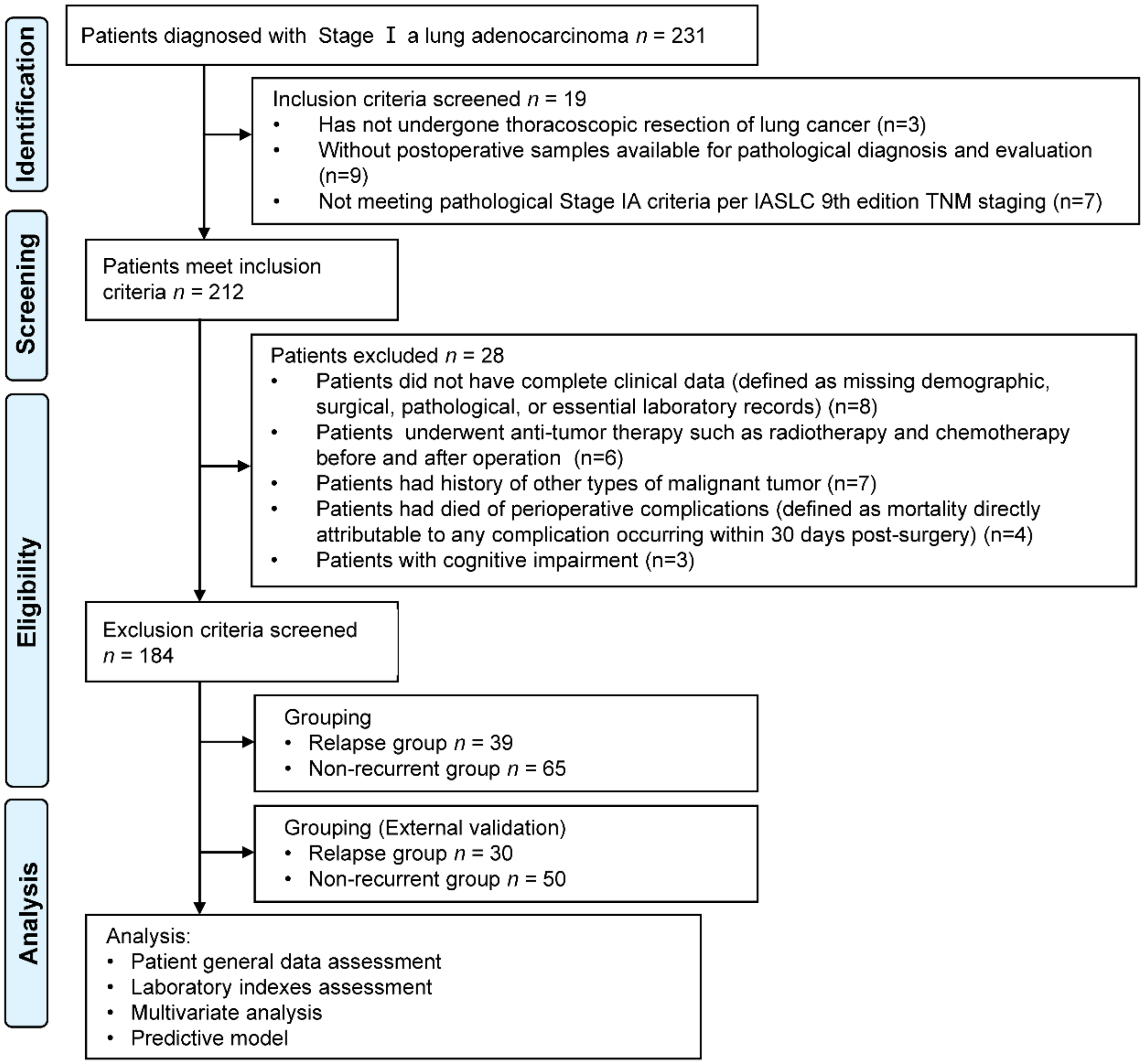

Figure 1. Patient enrollment flow diagram.

degree of tumor differentiation, number of lymph node dissection, comorbidities, family history and smoking history (P<0.05, **Table 1**).

Comparison of laboratory indexes

There exhibited no noticeable difference in laboratory indexes before operation (P>0.05). Following surgery, PLR, CEA, and Cyfra21-1 levels were lessened. Compared between the two groups, the study group had lower levels of PLR, CEA, and Cyfra21-1 (P<0.05, **Table 2**).

Multivariate analysis of influencing factors of postoperative recurrence in patients with Stage I a lung adenocarcinoma after surgical resection

Logistic multivariate analysis indicated that the largest tumor diameter, tumor differentiation, number of lymph nodes dissected, and pleural invasion were independent risk factors for recurrence after surgical resection in Stage I a lung adenocarcinoma patients (P<0.05, **Table 3**).

To account for the time-dependent nature of recurrence, a Cox proportional hazards regression analysis was further conducted. Cox analysis confirmed these findings, with maximum tumor diameter (HR = 2.119, 95% CI: 1.321-3.399, P = 0.002), tumor differentiation (HR = 2.251, 95% CI: 2.064-2.455, P<0.001), number of lymph node dissections (HR = 2.581, 95% CI: 1.161-5.738, P = 0.020), and pleural invasion (HR = 1.411, 95% CI: 1.179-1.688, P<0.001) remaining significant predictors of recurrence (**Table 4**).

Table 2. Comparison of laboratory indexes [$\bar{x}\pm s$]

Group	N	PLR (%)		CEA (ng/ml)		Cyfra21-1 (ng/ml)	
		Before operation	After operation	Before operation	After operation	Before operation	After operation
Non-recurrent group	65	293.91±14.92	72.94±3.11	20.19±2.12	3.55±0.43	23.49±0.92	9.29±1.26
Relapse group	39	298.81±15.72	143.85±13.85	20.32±2.22	12.39±1.91	23.48±0.81	12.84±4.66
t		1.589	31.506	0.301	28.454	0.097	4.650
P		0.115	<0.001	0.764	<0.001	0.923	<0.001

PLR, Platelet to Lymphocyte Ratio; CEA, Carcinoembryonic Antigen; Cyfra21-1, Cytokeratin 19 Fragment.

Table 3. Logistic multivariate analysis of the influencing factors of postoperative recurrence in Stage I a lung adenocarcinoma patients after surgical resection

variable	b	S.E.	Chi-square value	P	OR	95% CI for OR
Age	0.223	0.144	2.398	0.121	1.250	0.942-1.657
Maximum diameter of tumor	0.833	0.244	11.655	0.001	2.300	1.426-3.711
Degree of tumor differentiation	0.847	0.045	354.276	0.000	2.333	2.136-2.548
Number of lymph node dissection	1.023	0.452	5.122	0.024	2.782	1.147-6.746
Pleural invasion	0.332	0.094	12.474	0.000	1.394	1.159-1.676
Comorbidities	0.984	0.532	3.421	0.064	2.675	0.943-7.589
Family history	0.623	0.322	3.743	0.053	1.865	0.992-3.505
Smoking history	0.356	0.284	1.571	0.210	1.428	0.818-2.491
After operation PLR	2.441	1.842	1.756	0.185	11.485	0.311-424.673
After operation CEA	0.983	0.822	1.430	0.232	2.672	0.534-13.385
After operation Cyfra21-1	0.833	0.762	1.195	0.274	2.300	0.517-10.242

S.E., Standard Error; OR, Odds Ratio; CI, Confidence Interval; PLR, Platelet to Lymphocyte Ratio; CEA, Carcinoembryonic Antigen; Cyfra21-1, Cytokeratin 19 Fragment.

Table 4. Cox multivariate analysis of the factors associated with postoperative recurrence in Stage I a lung adenocarcinoma patients

Variable	b	S.E.	Wald χ^2	P	HR	95% CI for HR
Age	0.201	0.139	2.092	0.148	1.223	0.931-1.606
Maximum diameter of tumor	0.751	0.241	9.714	0.002	2.119	1.321-3.399
Degree of tumor differentiation	0.811	0.044	340.091	<0.001	2.251	2.064-2.455
Number of lymph node dissection	0.948	0.408	5.402	0.020	2.581	1.161-5.738
Pleural invasion	0.344	0.092	13.988	<0.001	1.411	1.179-1.688
Comorbidities	0.905	0.501	3.262	0.071	2.473	0.926-6.603
Family history	0.577	0.309	3.488	0.062	1.781	0.972-3.264
Smoking history	0.321	0.270	1.414	0.234	1.379	0.812-2.340

S.E., Standard Error; HR, Hazard Ratio; CI, Confidence Interval.

ROC curve of predictive model for postoperative recurrence in Stage I a lung adenocarcinoma patients

ROC curve of tumor maximum diameter, tumor differentiation, number of lymph node dissection and pleural invasion alone to predict recurrence in patients with I stage lung adenocarcinoma after surgical resection: The largest tumor diameter (A), the degree of tumor differentiation (B), the number of lymph nodes dissected (C), and pleural invasion (D) alone predict the recurrence of Stage I a lung adenocarcinoma patients after surgical resection. The maximum diameter of tumor demonstrated an AUC of 0.812 with a cutoff value of 2.85 cm, achieving a sensitivity of 0.795 and specificity of 0.769 (P<0.001). For the degree of tumor differentiation, when

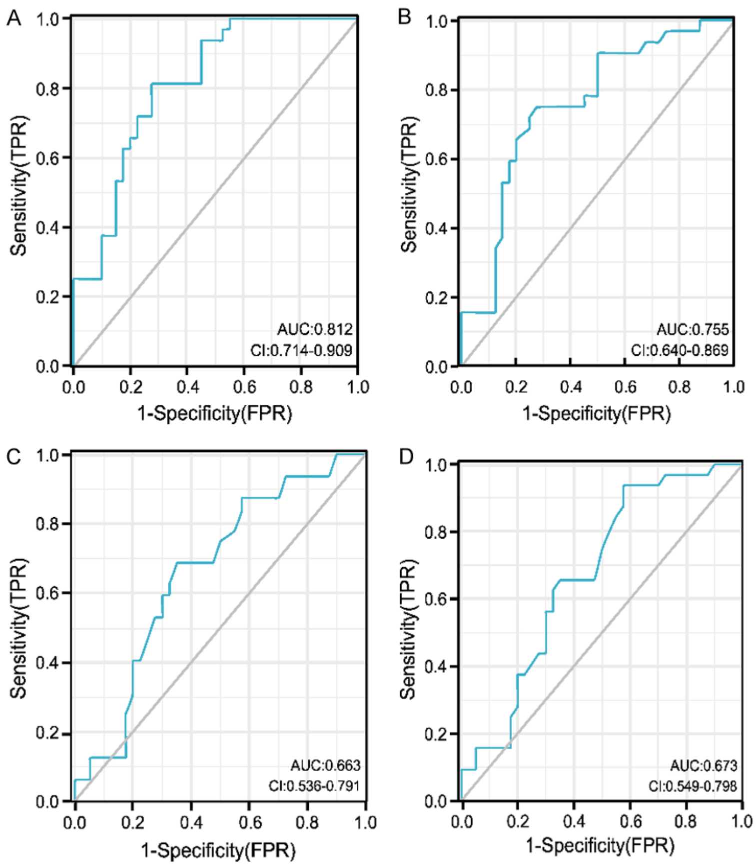

Figure 2. ROC curve analysis of key variables. A: Maximum tumor diameter; B: Tumor differentiation; C: Number of lymph node dissection; D: Pleural invasion. ROC, Receiver Operating Characteristic; AUC, Area Under the Curve.

classified as moderate/poor, the AUC was 0.755, with a sensitivity of 0.744 and specificity of 0.692 (P<0.001). The number of lymph node dissection had an AUC of 0.663 at a threshold of 14.225, resulting in a sensitivity of 0.667 and specificity of 0.631 (P = 0.002). Lastly, the presence of pleural invasion showed an AUC of 0.673, with a sensitivity of 0.564 and specificity of 0.708 (P = 0.001). The results are shown in **Figure 2**.

ROC of tumor maximum diameter, tumor differentiation, number of lymph node dissection combined with pleural invasion as a predictive model for the recurrence following surgical removal of Stage I a lung adenocarcinoma: The largest tumor diameter, tumor differentiation degree, number of lymph node dissections combined with pleural invasion were adopted as prediction models for the recurrence following surgical removal of Stage I a lung adenocarcinoma. The AUC was 0.924 (P<0.05). In **Figure 3**, you will find the results.

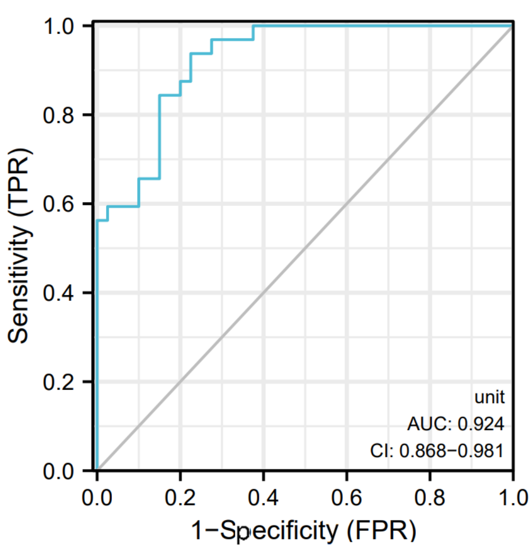

Figure 3. ROC of maximum tumor diameter, tumor differentiation, number of lymph node dissection combined with pleural invasion as a predictive model for postoperative recurrence in patients with Stage I a lung adenocarcinoma. ROC, Receiver Operating Characteristic; AUC, Area Under the Curve.

External validation of the predictive model

In the external validation set, significant differences were observed between the relapse and non-recurrent groups in several parameters. Patients in the relapse group were significantly younger and had a larger maximum tumor diameter. Pleural invasion was more common in the relapse group, as well as higher degree of tumor differentiation. The number of lymph node dissections was also significantly greater in the relapse group. Comorbidities including high blood pressure, hyperlipidemia, diabetes, and family history were more prevalent among those who experienced recurrence. Additionally, smoking history was significantly associated with relapse. Postoperative PLR and CEA levels were significantly elevated in the relapse group compared to the non-recurrent group. Similarly, postoperative Cyfra21-1 levels were higher in

Table 5. Comparison of parameters between relapse and non-recurrent groups in the external validation set

Group	Relapse group (n = 30)	Non-recurrent group (n = 50)	t/χ^2	P
Age	37.41±4.82	45.26±2.85	8.104	<0.001
Gender (male/female)	14/16	24/26	0.013	0.908
BMI (kg/m²)	21.05±3.76	20.88±3.37	0.217	0.828
Maximum diameter of tumor (cm)	3.56±0.23	2.47±0.14	23.444	<0.001
Pleural invasion	17 (56.67)	16 (32.00)	4.708	0.030
Degree of tumor differentiation				
High	14 (46.67)	10 (20.00)	6.375	0.041
Medium	10 (33.33)	24 (48.00)		
Low	6 (20.00)	16 (32.00)		
Number of lymph node dissection	16.22±2.67	12.24±1.36	7.591	<0.001
Mode of operation				
Radical resection	17 (56.67)	32 (64.00)	0.425	0.515
Palliative resection	13 (43.33)	18 (36.00)		
Comorbidities				
High blood pressure	13 (43.33)	7 (14.00)	8.604	0.003
Hyperlipidemia	9 (30.00)	6 (12.00)	3.988	0.046
Diabetes	8 (26.67)	3 (6.00)	5.123	0.024
Family history	5 (16.67)	1 (2.00)	3.892	0.049
Smoking history	26 (86.67)	25 (38.00)	10.908	<0.001
PLR (%)				
Before operation	298.75±15.63	293.87±14.85	1.395	0.167
After operation	143.66±13.73	73.15±3.26	27.657	<0.001
CEA (ng/ml)				
Before operation	20.34±2.23	20.20±2.14	0.284	0.777
After operation	12.34±1.86	3.58±0.45	25.3	<0.001
Cyfra21-1 (ng/ml)				
Before operation	23.45±0.80	23.48±0.90	0.119	0.906
After operation	12.81±4.62	9.33±1.28	4.038	<0.001

BMI, Body Mass Index; cm, centimeter; PLR, Platelet to Lymphocyte Ratio; CEA, Carcinoembryonic Antigen; Cyfra21-1, Cytokeratin 19 Fragment.

the relapse group (all P<0.05). No significant differences were found in gender, BMI, mode of operation, preoperative PLR, preoperative CEA, or preoperative Cyfra21-1 levels (P>0.05) (**Table 5**).

External validation ROC

The external validation ROC curve shows an AUC of 0.940, indicating excellent discriminatory ability of the model in distinguishing between relapse and non-recurrent cases (**Figure 4**). The optimal cutoff value was determined at 0.521, corresponding to a sensitivity of 87.5% and specificity of 89.5%, suggesting high accuracy in predicting recurrence. These results confirm the robustness and generalizability of the model in an independent cohort.

Discussion

Currently, lung cancer holds the world record for the highest incidence of malignant tumors [14]. Lung cancer ranks as the most frequently diagnosed malignancy in men and is the second most prevalent cancer type in women. The incidence of lung cancer remains still high recently, with nearly 700000 new diagnosed cases of lung cancer annually [3]. In China, lung cancer is highly prevalent, with lung cancer accounting for roughly 18% of all cancer fatalities. It is estimated that fewer than 20% of lung cancer patients remain alive for five years fol-

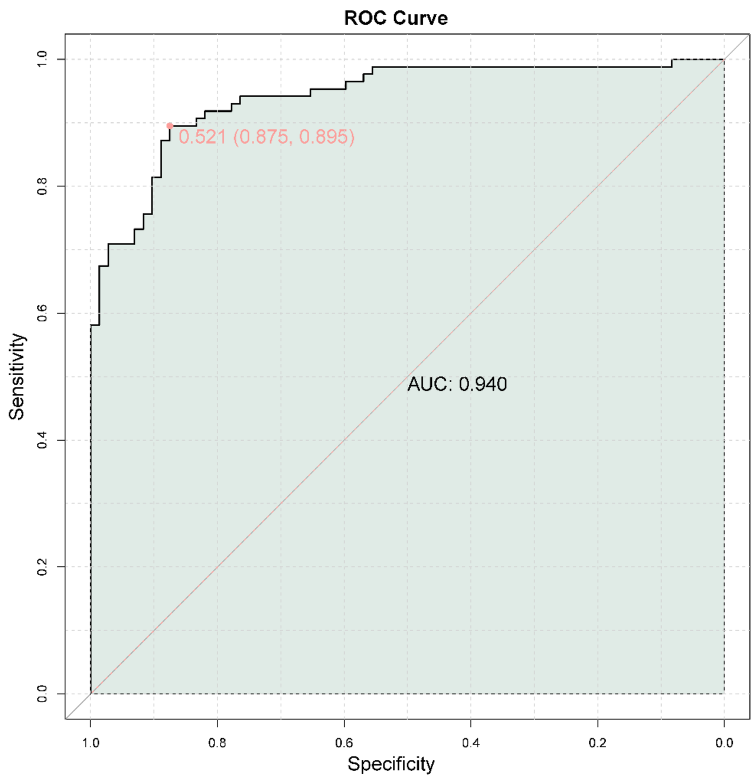

Figure 4. External validation ROC curve. ROC, Receiver Operating Characteristic; AUC, Area Under the Curve.

lowing diagnosis. The 5-year survival rate of patients with Stage I a lung adenocarcinoma can be as high as more than 80%. Consequently, lung cancer patients' clinical stage at the time of diagnosis influences their therapeutic response and long-term outcome. The eighth edition of TNM staging of lung cancer released in 2017 to assist clinical diagnosis and treatment [15, 16].

According to the morphological characteristics of cancer cells under microscope, lung cancer is mainly divided into two categories, such as NSCLC and SCLC [17]. NSCLC most commonly occurs as lung adenocarcinomas and squamous cell carcinomas. Recently, the incidence of squamous cell carcinoma has lessened greatly. As of now, lung adenocarcinoma is the most frequently diagnosed subtype of cancer, and its proportion increases over time. To prevent the metastasis of lung cancer from spreading, early detection and prompt treatment are particularly crucial [18-20]. In 1995, the American Lung Cancer Research Group indicated that lobectomy had a lower local recurrence rate and higher long-term survival rate than sub-lobectomy for early NSCLC patients with diameter <3 cm without lymph node metastasis. Since lobectomy is the optimal treatment option for Stage I a NSCLC, it has become the standard of care for many years [21-23]. The sub-lobectomy has been used as a compromise for patients who cannot tolerate lobectomy because of its high postoperative recurrence rate for patients with Stage I a lung adenocarcinoma, if sub-lobectomy can achieve the same effect as lobectomy. Then this operation can undoubtedly benefit more patients [24-26]. This still needs to be confirmed by relevant randomized controlled trials. Although the prognosis of early-stage NSCLC, especially Stage I a patients is generally good, local recurrence occurs in 4% of patients after surgery [27, 28].

In this study, three kinds of markers, including PLR, CEA, Cyfra21-1, were included to assess the long-term prognosis of patients. Previous studies have shown that PLR, CEA, Cyfra21-1 have a noticeable effect on the prognosis of patients. CEA is an acidic glycoprotein extracted from colon cancer by foreign scholars in 1965, which has the characteristics of human embryonic antigen. Cyfra21-1 is a soluble 40 kDa epithelial protein in blood [29, 30]. The results indicated that there were noticeable differences in postoperative PLR, CEA and Cyfra21-1 between the recurrence group and the non-recurrence group. In previous studies, for several common tumor markers currently used for lung cancer screening [31]. The ROC curve and logistic regression analysis were adopted to determine the best marker combination for the diagnosis of lung cancer. The findings revealed that CEA and Cyfra21-1 were two biomarkers. To a certain extent, CEA and Cyfra21-1 are strongly associated with the whole course of lung cancer development [32]. Although CEA has been shown to lack sensitivity and specificity by many studies, it has noticeable significance as a predictor of recurrence risk and mortality risk in lung cancer patients. Early study by other scholars has found that circulating tumor cells combined with carcinoembryonic antigen can effectively diagnose lung cancer and evaluate the prognosis of lung cancer [33]. Compared with CEA, PLR, CEA, and Cyfra21-1 have better sensitivity and specificity, and patients with high Cyfra21-1 levels have a later clinical stage, a lower degree of differentiation and a lower overall survival rate. In general, serum tumor markers are still an indispensable biomarker in the diagnosis and prognostic evaluation of patients with early-stage adenocarcinoma of the lung, and the development of new tumor markers and the improvement of the accuracy of the collection of tumor markers that have been discovered. degree will also be the focus of further research [34]. However, the results of this study indicated that PLR, CEA, and Cyfra21-1 were not independent predictors for individuals with Stage I a lung adenocarcinoma according to the logistic multivariate analysis outcomes, which could be influenced by the TNM stage of the participants and the restricted sample size in this study.

Lung cancer stage and prognosis are affected by tumor diameter, according to recent research [35]. Further research by foreign scholars found that compared with tumor diameter >2 cm, tumor diameter ≤2 cm had higher 5-year disease-free survival (DFS) and 5-year overall survival rate after anatomic segmentectomy. Ovexrall survival (OS). Other scholars have also believed that the largest tumor diameter, tumor differentiation, the number of lymph node dissections, and pleural invasion are high-risk factors for postoperative recurrence in patients with Stage I a lung cancer [36]. A retrospective study found that for patients with Stage I a NSCLC, tumor diameter was a factor influencing postoperative recurrence, but not recurrence pattern. As the tumor grows in diameter, the method of surgery and treatment also changes. At present, there are limited reports indicating that the maximal tumor diameter, tumor differentiation level, number of lymph nodes dissected, and pleural invasion act are independent risk factors for patients with Stage I a lung adenocarcinoma. However, it is agreed that the maximum diameter of tumor and the degree of tumor differentiation are the risk factors of postoperative recurrence of I lung adenocarcinoma. Combined with this study, logistic multivariate analysis indicated that the largest tumor diameter, tumor differentiation, the number of lymph nodes dissected, and pleural invasion were independent predictors for postoperative recurrence in individuals with Stage I a lung adenocarcinoma, aligning with the findings of the above scholars.

However, the association between a higher number of lymph node dissections and increased recurrence risk may reflect more aggressive tumor biology or occult nodal involvement not captured by conventional staging. While this finding may initially seem counterintuitive, as more extensive dissection is traditionally associated with better staging accuracy and potentially curative intent, it likely reflects underlying tumor biology rather than procedural bias [37]. Mechanistically, tumors with more aggressive biological behavior may induce a more pronounced desmoplastic or immunomodulatory response within the regional lymphatic basin, prompting a more extensive reactive lymphadenopathy that leads surgeons to perform a wider dissection [38, 39]. Furthermore, a higher count of resected lymph nodes could indicate the presence of occult micrometastases or isolated tumor cells that evade detection by standard histopathological examination (pN0), yet contribute to subsequent systemic recurrence. This underscores the potential limitation of conventional nodal staging (pN0) and highlights the need for more sensitive molecular staging techniques [40, 41]. Therefore, the number of lymph nodes dissected may serve as an indirect surrogate marker for a tumor's invasive potential and the likelihood of undetected regional spread.

In this investigation, the AUC values for the largest tumor diameter, tumor differentiation degree, number of lymph node dissections, and pleural invasion in predicting postoperative recurrence among individuals with Stage I a lung adenocarcinoma were 0.821, 0.755, 0.663, 0.673, respectively. The largest tumor diameter, tumor differentiation degree, the number of lymph node dissection in conjunction with pleural invasion were used as a prediction model for postoperative recurrence in individuals with Stage I a lung adenocarcinoma, and the AUC was 0.924. All of these important prognostic factors for patients with lung adenocarcinoma take into account tumor diameter, differentiation status, lymph node count, and pleural invasion. For example, an intuitive way to determine tumor size is to measure its size.

The smaller the largest tumor diameter, the better the prognosis may be. In terms of the number of lymph nodes, the most suitable lymph node dissection strategy will be enrolled according to the patients' different preoperative conditions and intraoperative findings. In terms of pleural invasion, if the tumor is small (≤3 cm) but invades the visceral pleura, it will lead to the increase of tumor stage, converting from T1 stage to T2 stage. Through the prediction and analysis of the above four indicators, it can effectively help us to predict the long-term prognosis. Several scholars believe that lung cancer patients' prognoses can be predicted by the tumor diameter, level of differentiation, number of lymph nodes, and pleural invasion. Many studies have proved that the above indexes are strongly associated with the prognosis of cancer patients. Moreover, the relevant computation indicators are simple, fast, cheap, and highly reproducible. There is little discomfort to the patient, so patient compliance is also improved. It has great potential to judge the prognosis of malignant tumors in clinical life, which is worthy of our further research and discussion. It is suggested that patients can achieve a better prognosis by establishing stricter evaluation criteria or taking more effective intervention measures before operation [42-44].

Our study has several limitations. Firstly, its retrospective nature introduces potential for selection bias, as notably observed in the association between the number of lymph node dissections and recurrence risk. Secondly, the extent of lymph node dissection was not standardized, which may have confounded the results. Finally, the sample size, particularly in the recurrence group, is relatively small, and our model requires external validation in larger, prospective cohorts.

To sum up, tumor size measured by its largest diameter, along with the extent of tumor differentiation, the count of excised lymph nodes and pleural invasion were independent risk factors for recurrence in patients with Stage I a lung adenocarcinoma after thoracoscopic resection. The maximum tumor diameter, tumor differentiation degree, and the number of lymph node dissection combined with pleural invasion can predict the recurrence risk after thoracoscopic resection in patients with Stage I a lung adenocarcinoma. The model may help identify high-risk patients who could benefit from adjuvant chemotherapy or closer follow-up imaging [45, 46].

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Informed consent was obtained from all individual participants included in the study.

Disclosure of conflict of interest

None.

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