

Original Article

Imaging features and clinical markers for predicting postoperative recurrence in early-stage lung cancer

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Abstract: This study aimed to evaluate the predictive value of imaging features and clinical markers for postoperative recurrence in patients with early-stage lung cancer and to establish a nomogram and a neural network model for prediction. A total of 439 patients with early-stage lung cancer who underwent surgical treatment at Changzhou First People's Hospital between January 2020 and January 2023 were retrospectively enrolled. Clinical characteristics, preoperative imaging findings, postoperative pathology, laboratory test results, and recurrence status were collected. By April 1, 2025, 85 of the 439 patients had relapsed, accounting for 19.36% of the cohort. Univariate analysis revealed significant differences between the recurrence and non-recurrence groups in terms of age, tumor density, CYFRA21-1, CA19-9, and CA125 (all $P < 0.05$). Multivariate logistic regression analysis identified solid tumor density (OR=2.132), CYFRA21-1 ≥ 3.3 ng/mL (OR=2.307), CA19-9 ≥ 37 U/mL (OR=2.901), and CA125 ≥ 35 U/mL (OR=5.974) as independent risk factors for postoperative recurrence. In addition, increasing age was associated with higher recurrence risk (OR=1.121) (all $P < 0.05$). The nomogram model based on these predictors demonstrated an area under the receiver operating characteristic curve (AUC) of 0.804 in the training set and 0.760 in the validation set, both exceeding 0.7, indicating good predictive performance. The neural network model yielded AUC values of 0.882 in the training set and 0.734 in the validation set, also showing favorable performance. DeLong test revealed a significant difference in AUC between the two models in the training set ($Z = -3.514$, $P < 0.001$), but no significant difference in the validation set ($Z = 0.374$, $P = 0.709$). External validation showed that the nomogram achieved a sensitivity of 74.36%, specificity of 73.84%, and accuracy of 73.93%, while the neural network model achieved a sensitivity of 79.49%, specificity of 68.60%, and accuracy of 70.62%. In conclusion, this study developed a nomogram and a neural network model incorporating imaging features and clinical markers to predict postoperative recurrence in early lung cancer. These models may serve as valuable tools to identify high-risk patients and guide individualized clinical management.

Keywords: Early lung cancer, imaging, clinical indicators, influencing factors, prediction model

Introduction

With advances in imaging techniques, the detection rate of early-stage lung cancer (stages I and II) has significantly increased [1-3]. Surgery is the primary treatment approach; however, postoperative recurrence remains a major factor influencing long-term survival [4, 5]. Recurrence risk varies among individuals and is influenced by multiple clinical and pathological factors. Despite the availability of diverse treatment options, including adjuvant/neoadjuvant chemotherapy, targeted therapy, and immunotherapy, the necessity of postoperative adjuvant therapy in early-stage disease

remains controversial [6-8]. Current guidelines recommend adjuvant chemotherapy for stage IB patients with high-risk features such as poor differentiation, vascular invasion, or intrapulmonary dissemination, while stage-IA patients are advised to undergo regular follow-up [9-11]. However, some stage-IA patients still experience poor outcomes, indicating that TNM staging alone is insufficient to guide treatment and follow-up. This approach neglects other prognostic factors, potentially delaying intervention in high-risk patients.

High-resolution imaging techniques (e.g., low-dose spiral CT) can detect subtle pulmonary

abnormalities during follow-up, serving as early indicators of recurrence [12-15]. However, relying solely on imaging manifestations is sometimes insufficient for early postoperative recurrence prediction, as some non-specific lesions (such as inflammation or fibrosis) may also present similar characteristics on imaging, leading to misdiagnosis or missed detection. Clinical markers also hold promise for assessing recurrence risk. Blood-based tumor markers and genetic alterations can provide supportive evidence [16-18], but their accuracy is limited by biological variability, and a single marker rarely captures the full complexity of lung cancer pathophysiology [19-22]. Therefore, integrating imaging features with clinical markers is critical to improving the accuracy and reliability of recurrence risk assessment.

In recent years, the rapid development of big data and artificial intelligence technology has enabled predictive modeling based on multi-dimensional indicators, offering new approaches for the diagnosis and prognosis of early-stage lung cancer [23-25]. Building on this, this study aimed to investigate imaging features and clinical markers in early-stage lung cancer, analyze their combined predictive value, and develop two predictive models - a nomogram and a neural network. These models may provide novel strategies for accurate recurrence risk assessment, ultimately enhancing prognosis and quality of life in patients with early-stage lung cancer.

Materials and methods

Patient selection

A total of 439 patients with early-stage lung cancer who underwent surgical treatment in Changzhou First People's Hospital between January 2020 and January 2023 were retrospectively enrolled.

Inclusion criteria: (1) Patients who underwent radical resection with postoperative pathological confirmation of stage IA, IB or IIA NSCLC; (2) Postoperative follow-up and adjuvant therapy performed in our hospital; (3) Aged between 18 and 80 years; (4) Complete clinical data, including preoperative imaging, postoperative pathological reports, and laboratory tests.

Exclusion criteria: (1) Presence of other malignant tumors; (2) Severe cardiopulmonary dys-

function or other major systemic diseases; (3) Severe intraoperative complications (e.g., massive bleeding, infection); (4) Inability to obtain recurrence information through telephone follow-up.

This study was approved by the Ethics Committee of Changzhou First People's Hospital. A total of 511 patients were initially screened. According to the exclusion criteria, 15 patients with other malignancies, 23 patients with severe cardiopulmonary dysfunction or other systemic diseases, and 7 patients with severe intraoperative or postoperative complications (such as massive hemorrhage and infection) were excluded. Additionally, 27 patients were lost to follow-up, as recurrence status could not be confirmed by telephone. Finally, 439 patients with early-stage lung cancer were included in this study. The screening process is illustrated in **Figure 1**.

Data extraction

Clinical information was collected from the electronic medical record system of our hospital, including demographic characteristics, pre-operative imaging, postoperative pathology, laboratory indicators, and recurrence status. (1) General characteristics: sex, age, body mass index (BMI), smoking history, alcohol consumption history, chronic disease (diabetes or hypertension), type of surgery (lobectomy or sublobectomy), and adjuvant therapy (chemotherapy, targeted therapy, or immunotherapy). (2) Imaging features: tumor location (peripheral vs. central), tumor density (solid, part-solid, or pure ground-glass), and margin characteristics (pleural indentation, lobulation, spiculation, cavity sign). (3) Pathological findings: pathological type (adenocarcinoma vs. other) and tumor stage (IA, IB or IIA). (4) Laboratory indicators: neuron-specific enolase (NSE), cytokeratin fragments 21-1 (CYFRA21-1), squamous cell carcinoma antigen (SCC), carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), and carbohydrate antigen 125 (CA125). Each marker was categorized as normal or abnormal according to the cut-off values (NSE: 16.3 ng/mL, CYFRA21-1: 3.3 ng/mL, SCC: 1.5 ng/mL, CEA: 5 ng/mL, CA19-9: 37 U/mL, and CA125: 35 U/mL). (5) Postoperative recurrence: defined as the primary outcome. Recurrence status was determined by telephone follow-up until April 1, 2025. Patients with confirmed recur-

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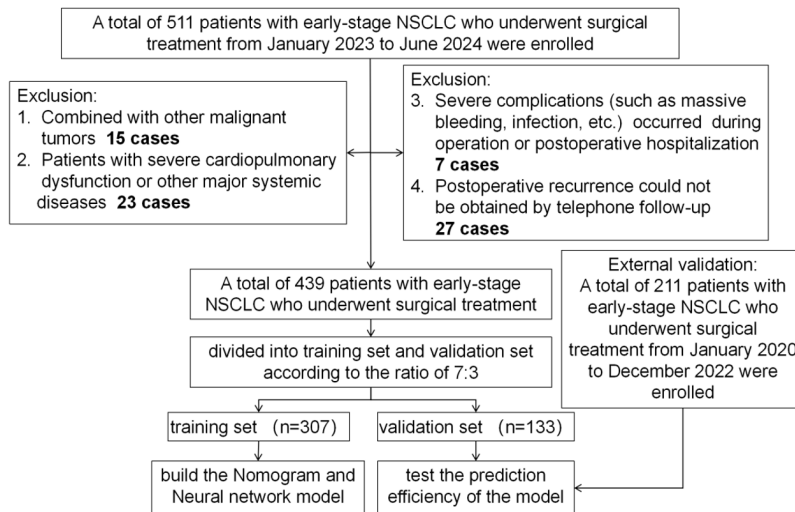


Figure 1. Study flowchart.

rence by this date were classified into the recurrence group, and those without recurrence into the non-recurrence group.

Model construction

(1) Nomogram model: patients were randomly divided into a training set and a validation set in a 7:3 ratio. The training set was used for model development, and the validation set for performance evaluation. First, clinical data were compared between the recurrence and non-recurrence groups, and variables with significant differences were identified. Then, these variables were included as independent variables, with recurrence as the dependent variable, and logistic regression analysis was performed to determine predictors of postoperative recurrence. Finally, the results of logistic regression were visualized to construct the nomogram, and model performance was assessed using the receiver operating characteristic (ROC) curve and calibration curve.

(2) Neural network model: the subjects were randomly divided into a training set and a validation set in the same 7:3 ration. The neural network consisted of an input layer, a hidden layer, and an output layer. Significant variables identified by univariate analysis were included in the input layer, with each node representing one variable. Recurrence was defined as the output variable, and the hidden layer performed automatic feature extraction through a multi-layer perceptron. The model was implemented in R4.5.1 software using the *mlbench* and *neuralnet* packages.

Detailed parameters were as follows: the input layer consists of 5 nodes, corresponding to variables from the multivariate regression analysis; the hidden layer contained 10 nodes; the hidden layer used the ReLU (Rectified Linear Unit) activation function, and the output layer used the Sigmoid activation function to yield recurrence probability. To reduce overfitting, L2 regularization was applied with a penalty parameter of 0.01. The model was trained using the Adam

optimizer with a learning rate of 0.001 for 1000 epochs, with a batch size of 32.

Statistical analysis

SPSS 26.0 and R 4.5.1 software were used for statistical analysis. Continuous variables with normal distribution were expressed as mean $\pm$ standard deviation (SD), and between-group comparison was conducted using independent sample t test; those with non-normal distribution were expressed as median (interquartile range), and the between-group comparison was conducted using the rank-sum test. Categorical variables were expressed as frequency (percentage) and compared using the chi-square test. The DeLong test was applied to compare differences in the areas under the ROC curves (AUCs). A two-tailed $P < 0.05$ was considered statistically significant.

Results

Clinical characteristics of the study population

A total of 439 patients with early-stage lung cancer were included, including 267 males (60.82%) and 172 females (39.18%), with an average age of (56.29 ± 7.19) years. Detailed baseline characteristics are summarized in **Table 1**.

Postoperative recurrence

All 439 patients underwent surgical treatment. Representative imaging before surgery, after

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Table 1. Clinical data of study subjects

Index	Circumstance
Gender	
Male	267 (60.82)
Female	172 (39.18)
Age (years)	56.29±7.19
BMI (kg/m ²)	24.16±1.23
Smoking	
Yes	211 (48.06)
No	228 (51.94)
Alcohol consumption	
Yes	237 (53.99)
No	202 (46.01)
Chronic disease	
With	134 (30.52)
Without	305 (69.48)
Type of surgery	
Lobectomy	301 (68.56)
Sublobectomy	138 (31.44)
Adjuvant therapy	
With	102 (23.23)
Without	337 (76.77)
Tumor type	
Peripheral	279 (63.55)
Central	160 (36.45)
Solid density	
Yes	228 (51.94)
No	211 (48.06)
Pleural indentation	
With	146 (33.26)
Without	293 (66.74)
Lobulation	
With	289 (65.83)
Without	150 (34.17)
Spiculation	
With	198 (45.10)
Without	241 (54.90)
Cavity sign	
With	76 (17.31)
Without	363 (82.69)
Pathological classification	
Adenocarcinoma	362 (82.46)
other	77 (17.54)
Tumor stage	
IA and IB	351 (79.95)
IIA	88 (20.05)
NSE (ng/mL)	
≥16.3	208 (47.38)
<16.3	231 (52.62)

CYFRA21-1 (ng/mL)	
≥3.3	170 (38.72)
<3.3	269 (61.28)
SCC (ng/mL)	
≥1.5	82 (18.68)
<1.5	357 (81.32)
CEA (ng/mL)	
≥5	251 (57.18)
<5	188 (42.82)
CA19-9 (U/mL)	
≥37	152 (34.62)
<37	287 (65.38)
CA125 (U/mL)	
≥35	60 (13.67)
<35	379 (86.33)

surgery, and at 1 month postoperatively are shown in **Figure 2**. Among the 439 patients, 85 patients (19.36%) experienced recurrence. The cohort was randomly divided into a training set (n=307) and a validation set (n=133) at a 7:3 ratio. Group comparison, univariate and multivariate Logistic regression analysis were performed in the training set to construct the predictive model for post-operative recurrence. Model performance was further verified in the validation dataset. As shown in **Figure 3**, recurrence occurred in 52 of 307 patients (16.94%) in the training set and in 33 of 133 patients (24.81%) in the validation set.

Comparison of clinical data between recurrence and non-recurrence groups

Clinical variables were compared between the recurrence and non-recurrence groups. As shown in **Table 2**, significant differences were observed in age, tumor density, CYFRA21-1, CA19-9, and CA125 levels (all $P<0.05$), whereas other indicators were comparable between groups (all $P>0.05$).

Univariate and multivariate logistic regression analysis

Univariate logistic regression was performed in the training set. Variables that differed between the two groups (age, tumor density, CYFRA21-1, CA19-9 and CA125; see **Table 3** for variable assignments) were included as independent variables, with postoperative

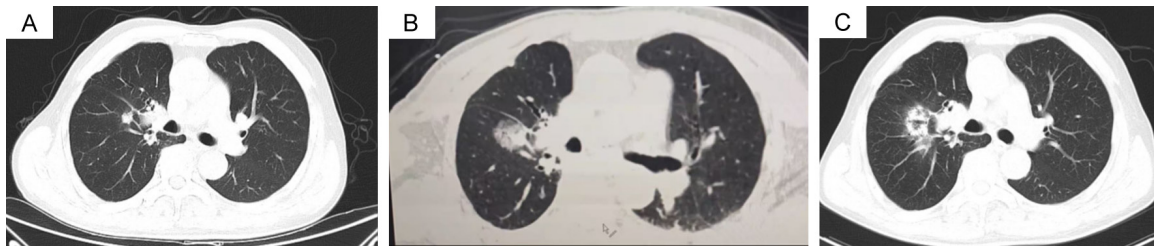


Figure 2. Typical imaging data of a patient. (A) Before surgery, (B) after surgery, (C) 1 month after surgery.

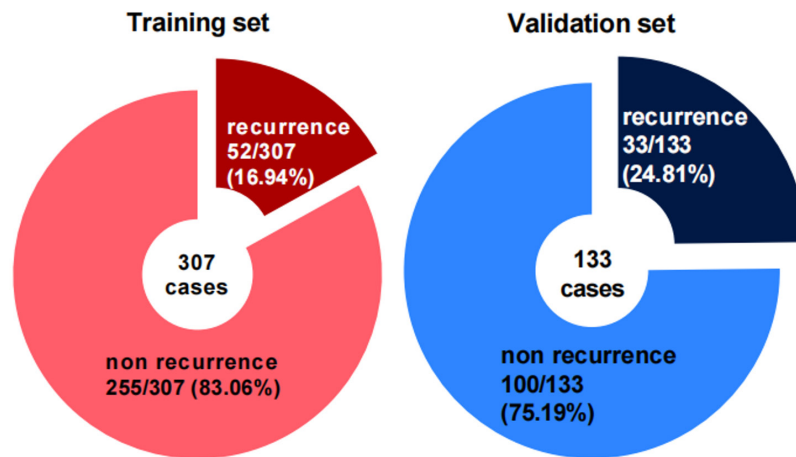


Figure 3. Proportion of subjects with recurrence in the two data sets.

recurrence as the dependent variable. As shown in **Table 4**, all five variables were significantly associated with postoperative recurrence (all $P < 0.05$).

Multivariate logistic regression analysis was then conducted using the variables identified above. As presented in **Table 5**, older age (OR=1.121), solid tumor density (OR=2.132), CYFRA21-1 ≥ 3.3 ng/mL (OR=2.307), CA19-9 ≥ 37 U/mL (OR=2.901), and CA125 ≥ 35 U/mL (OR=5.974) were independent risk factors for postoperative recurrence (all $P < 0.05$).

Construction of the nomogram

Significant predictors identified in the multivariate analysis were incorporated into a logistic regression model, and the results were visualized as a nomogram (**Figure 4**). The nomogram assigns each predictor a weighted score according to its contribution to recurrence risk. By summing the scores of individual predictors for a given patient, a total score is obtained, which can be projected onto the risk scale to

estimate the probability of postoperative recurrence.

Validation of the nomogram model

The ROC curve was used to test the discrimination of the nomogram model. As shown in **Figure 5A**, **5B**, the AUC was 0.804 (95% CI=0.736-0.871) in the training set and 0.760 (95% CI=0.673-0.847) in the validation set, both exceeding 0.7, indicating good discrimination. Calibration curves (**Figure 6A**,

6B) demonstrated that predicted recurrence risk closely matched the observed outcomes in both datasets.

Comparison of predictive efficacy between the model and individual factors

The ROC curves of the nomogram and individual predictors are presented in **Figure 7**. DeLong's test showed that the AUC of the nomogram was significantly higher than that of age, tumor density, CYFRA21-1, CA19-9, and CA125 ($Z=3.862, 4.297, 4.795, 4.831$ and 5.348 , respectively; all $P < 0.05$). The AUCs and the cut-off values of each factor are summarized in **Table 6** (cut-off values of binary variables correspond to their respective risk thresholds).

Neural network model

The neural network architecture is shown in **Figure 8**, with five input nodes corresponding to the variables identified in the multivariate regression analysis. Importance analysis

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Table 2. Differences in clinical data between two groups

Index	Recurrence group (n=85)	Non-recurrence group (n=354)	χ^2/t	P
Gender			0.668	0.414
Male	55 (20.60)	212 (79.40)		
Female	30 (17.44)	142 (82.56)		
Age (years)	59.82±6.40	55.45±7.11	5.190	0.000
BMI (kg/m ²)	24.01±1.19	24.20±1.23	1.297	0.197
Smoking			2.984	0.084
Yes	48 (22.75)	163 (77.25)		
No	37 (16.23)	191 (83.77)		
Alcohol consumption			0.569	0.451
Yes	49 (20.68)	188 (79.32)		
No	36 (17.82)	166 (82.18)		
Chronic disease			1.758	0.185
With	31 (23.13)	103 (76.87)		
Without	54 (17.70)	251 (82.30)		
Type of surgery			0.501	0.479
Lobectomy	61 (20.27)	240 (79.73)		
Sublobectomy	24 (17.39)	114 (82.61)		
Adjuvant therapy			3.726	0.054
With	13 (12.75)	89 (87.25)		
Without	72 (21.36)	265 (78.64)		
Tumor type			0.247	0.619
Peripheral	56 (20.07)	223 (79.93)		
Central	29 (18.13)	131 (81.88)		
Solid density			16.602	0.000
Yes	61 (26.75)	167 (73.25)		
No	24 (11.37)	187 (88.63)		
Pleural indentation			0.319	0.572
With	33 (22.60)	113 (77.40)		
Without	52 (17.75)	241 (82.25)		
Lobulation			0.071	0.790
With	57 (19.72)	232 (80.28)		
Without	28 (18.67)	122 (81.33)		
Spiculation			1.281	0.258
With	43 (21.72)	155 (78.28)		
Without	42 (17.43)	199 (82.57)		
Cavity sign			1.871	0.171
With	19 (25.00)	57 (75.00)		
Without	66 (18.18)	297 (81.82)		
Pathological classification			0.964	0.326
Adenocarcinoma	67 (18.51)	295 (81.49)		
other	18 (23.38)	59 (76.62)		
Tumor stage			3.235	0.072
IA and IB	62 (17.66)	289 (82.34)		
IIA	23 (26.14)	65 (73.86)		
NSE (ng/mL)			3.494	0.062
≥16.3	48 (23.08)	160 (76.92)		
<16.3	37 (16.02)	194 (83.98)		

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CYFRA21-1 (ng/mL)			8.979	0.003
≥3.3	45 (26.47)	125 (73.53)		
<3.3	40 (14.87)	229 (85.13)		
SCC (ng/mL)			3.601	0.058
≥1.5	22 (26.83)	60 (73.17)		
<1.5	63 (17.65)	294 (82.35)		
CEA (ng/mL)			3.441	0.064
≥5	41 (16.33)	210 (83.67)		
<5	44 (23.40)	144 (76.60)		
CA19-9 (U/mL)			11.868	0.001
≥37	43 (28.29)	109 (71.71)		
<37	42 (14.63)	245 (85.37)		
CA125 (U/mL)			33.186	0.000
≥35	28 (46.67)	32 (53.33)		
<35	57 (15.04)	322 (84.96)		

Table 3. Variable assignment

Variable	Variable assignment
Dependent variable	
Recurrence situation	1= Recurrence, 0= Non-recurrence
Independent variable	
Age	Enter actual value
Tumor density	1= "solid", 0= "partial solid/pure ground glass density"
CYFRA21-1	1= "≥3.3 ng/mL", 0= "<3.3 ng/mL"
CA19-9	1= "≥37 U/mL", 0= "<37 U/mL"
CA125	1= "≥35 U/mL", 0= "<35 U/mL"

Table 4. Univariate analysis

Variable	β	SE	Wald χ^2	P	OR	95% CI
Age	0.088	0.022	15.324	0.000	1.091	1.045-1.140
Tumor density is solid	0.824	0.321	6.587	0.010	2.280	1.215-4.278
CYFRA21-1≥3.3 ng/mL	0.855	0.309	7.680	0.006	2.352	1.284-4.306
CA19-9≥37 U/mL	0.801	0.309	6.736	0.009	2.228	1.217-4.079
CA125≥35 U/mL	1.742	0.376	21.416	0.000	5.707	2.729-11.934

Table 5. Multivariate logistic regression analysis

Variable	β	SE	Wald χ^2	P	OR	95% CI
Age	0.115	0.026	18.699	0.000	1.121	1.065-1.181
Tumor density is solid	0.757	0.358	4.468	0.035	2.132	1.057-4.300
CYFRA21-1≥3.3 ng/mL	0.836	0.346	5.824	0.016	2.307	1.170-4.550
CA19-9≥37 U/mL	1.065	0.355	8.986	0.003	2.901	1.446-5.820
CA125≥35 U/mL	1.787	0.429	17.344	0.000	5.974	2.576-13.854
Constant	-9.767	1.705	32.819	-	-	-

(Figure 9) indicated that the most influential predictors of recurrence were age, tumor den-

sity, CA125, CYFRA21-1, and CA19-9. As shown in Figure 10, the neural network demonstrated

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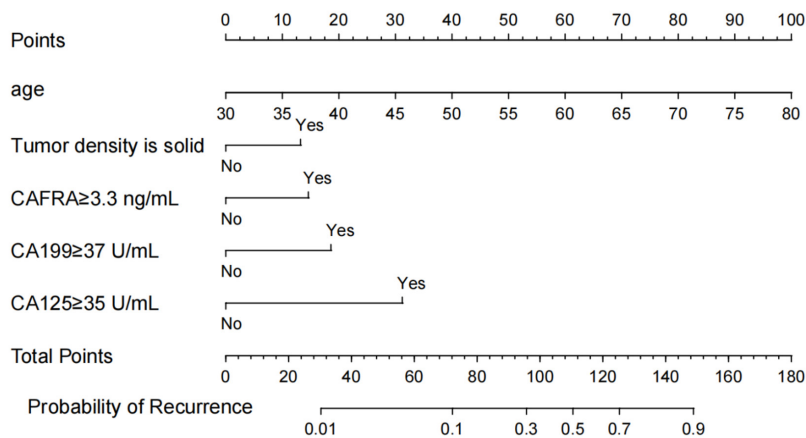


Figure 4. Nomogram model.

good predictive accuracy for both recurrent and non-recurrent cases. ROC analysis (**Figure 11**) showed an AUC of 0.882 (95% CI=0.838-0.926) in the training set and 0.734 (95% CI=0.632-0.836) in the validation set. DeLong's test indicated a significant difference between the neural network and nomogram in the training set ($Z=-3.514$, $P<0.001$), but no significant difference in the validation set ($Z=0.374$, $P=0.709$).

External model verification

According to the same inclusion and selection criteria, an independent cohort of 211 patients with early-stage lung cancer who underwent surgery between February 2023 and July 2024 was used for external validation. This cohort included 139 males and 72 females, with a mean age of (57.68 ± 7.18) years. As of April 1, 2025, 39 patients (16.67%) had experienced recurrence. Using a cut-off value of 0.264, patients were stratified into high- and low-risk groups. For predicting postoperative recurrence, the nomogram achieved a sensitivity of 74.36% (29/39), specificity of 73.84% (127/172), and accuracy of 73.93% (156/211). The neural network model achieved a sensitivity of 79.49% (31/39), specificity of 68.60% (118/172), and accuracy of 70.62% (149/211). Detailed data are shown in **Table 7**.

Discussion

Lung cancer is a highly prevalent malignant tumor worldwide. In 2022, approximately 2.5 million new cases were reported, accounting for 12.4% of all cancers, with 1.8

million deaths, representing 18.7% of cancer-related mortality [26]. Non-small cell lung cancer (NSCLC), the most common subtype, is primarily managed through surgery, chemotherapy, and radiotherapy, which can alleviate symptoms and prolong survival. However, the 5-year survival rate remains below 20% [27-29]. In recent years, targeted therapy and immunotherapy have brought new hope, but the

treatment of advanced lung cancer still faces challenges such as distant metastasis, low chemotherapy sensitivity, and drug resistance [30-33]. Therefore, early detection, timely intervention, and effective control are crucial for improving prognosis and survival rates.

In the present study, among 439 patients with early-stage lung cancer, 85 cases experienced postoperative recurrence (19.36%), consistent with 15.6% reported by Zhao et al. [34]. Multivariate analysis identified solid tumors (OR=2.132), CYFRA21-1 ≥ 3.3 ng/mL (OR=2.307), CA19-9 ≥ 37 U/mL (OR=2.901), and CA125 ≥ 35 U/mL (OR=5.974) as risk factors for postoperative recurrence in NSCLC patients. In addition, recurrence risk increased with the age (OR=1.121). Advanced age is associated with impaired immune function, poor postoperative recovery, higher complication rates, and a microenvironment more conducive to tumor recurrence, thus increasing recurrence risk [35]. Solid tumors are characterized by high cellular density and strong angiogenic potential, which facilitate dissemination via the blood or lymphatic system, increasing the risk of recurrence [35]. Increasing evidence has shown that ground-glass components is associated with a better prognosis. For instance, Hattori et al. [36, 37], in an analysis of 671 patients with stage IA NSCLC from the JCOG0201 trial, demonstrated that across all IA substages, patients with ground-glass opacity (GGO) components had higher 5-year survival rate compared with those with purely solid nodules, regardless of the proportion of solid components within mixed nodules. Similarly,

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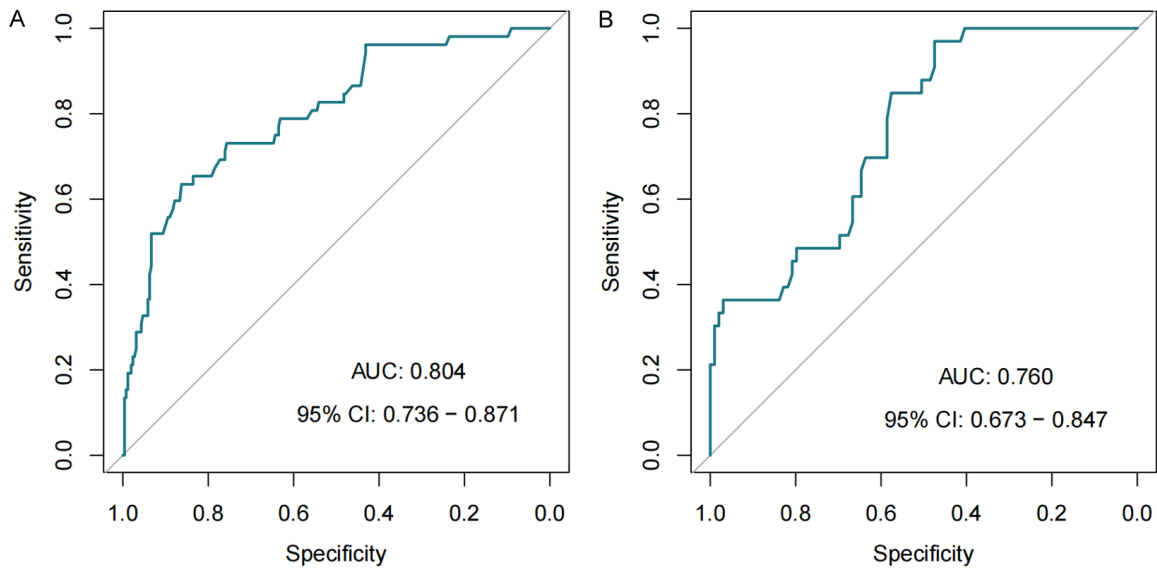


Figure 5. ROC curves for the nomogram in predicting recurrence in training set (A) and validation set (B).

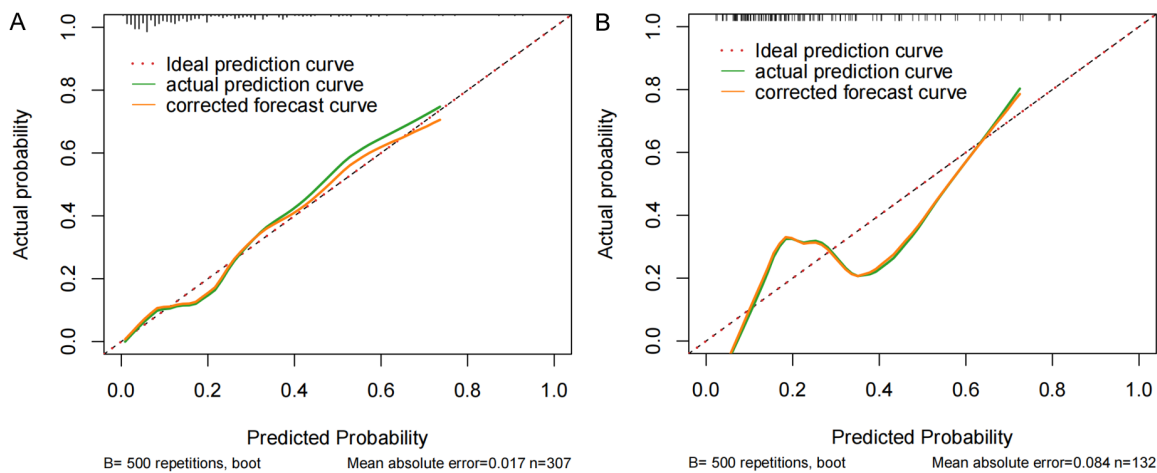


Figure 6. Calibration curves for the nomogram in training set (A) and validation set (B).

other researchers have reported a 5-year cumulative recurrence rate of only 7.5% in patients with lung adenocarcinoma harboring ground-glass components, markedly lower than the 24.5% recurrence observed in patients without GGO [38].

CYFRA21-1, a fragment of cytokeratin 19 mainly released by tumor cells into the bloodstream, is an important diagnostic biomarker for lung cancer and is closely related to postoperative recurrence and prognosis [39-41]. This study found that the risk of postoperative recurrence in early-stage lung cancer patients increases with the elevation of CYFRA21-1 levels, similar

to the results of Zhang et al. [42]. Normally, CYFRA21-1 is distributed in lung epithelial cells but not released into circulation; however, during carcinogenesis it is released into the blood. Elevated levels may indicate aggressive tumor biology, higher tumor burden, and greater cellular heterogeneity, thereby increasing postoperative recurrence risk [43-45].

CA19-9 and CA125 are two widely used tumor markers used in the diagnosis, treatment monitoring, and prognosis assessment of various malignant tumors. Initially, CA19-9 was mainly used for the detection of pancreatic cancer and cholangiocarcinoma, while CA125 was com-

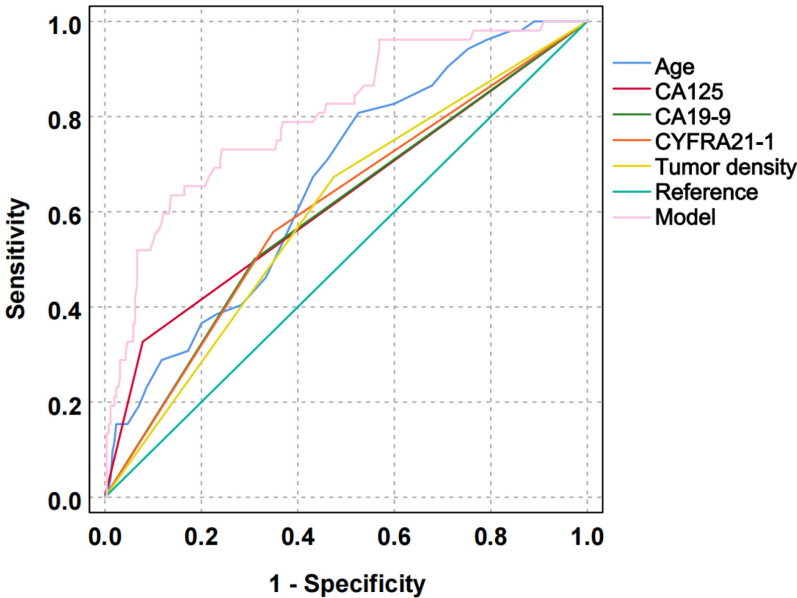


Figure 7. Comparison of predictive efficacy.

Table 6. Comparison of predictive efficacy

Indicators	AUC	Cut off value	95% CI	Z	P
Model	0.804	0.264	0.736-0.871	-	-
Age	0.663	54	0.607-0.716	3.862	0.000
Tumor density is solid	0.599	1	0.542-0.655	4.297	0.000
CYFRA21-1	0.604	1	0.547-0.659	4.795	0.000
CA19-9	0.594	1	0.538-0.650	4.831	0.000
CA125	0.624	1	0.567-0.679	5.348	0.000

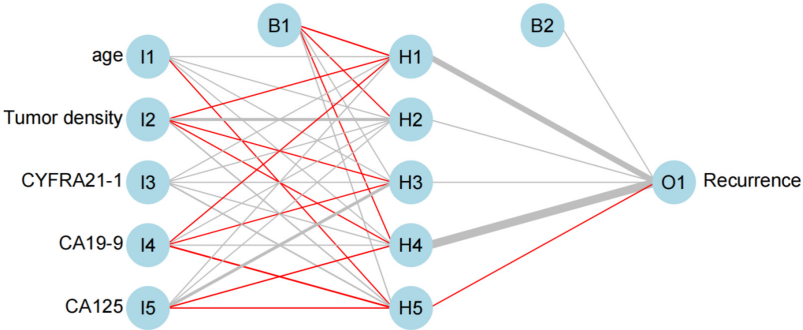


Figure 8. Neural network diagram.

monly used for the monitoring of ovarian cancer [46-48]. In recent years, the clinical significance of these two markers in lung cancer patients has also been confirmed [49]. CA125 may affect intercellular signal transduction through its interaction with cell surface receptors, thereby promoting the invasion and

metastasis of tumor cells [49]. Our study suggest that elevated CA19-9 and CA125 can also predict postoperative recurrence risk in early-stage lung cancer patients. Sun et al. [49] demonstrated significant differences in CA19-9 and CA125 levels between lung cancer patients before and 6 months after surgery, with both markers associated with prognosis.

Currently, in clinical practice, postoperative risk assessment for lung cancer patients is largely based on TNM stage and histopathological type. However, compared with the 7th edition, the 8th edition of TNM staging system reclassified stage IB disease into stage IB (3 cm <T2a≤4 cm) and stage IIA (4 cm <T2b≤5 cm). For these substages, especially stage IB, the role of postoperative adjuvant therapy remains controversial [50]. Although recurrence rates are generally higher in patients with more advanced stages, our study found no significant difference in recurrence among different stages. This may be related to some patients receiving adjuvant therapy. According to the NCCN guidelines, surgical resection is recommended for stage I NSCLC, while stage II patients are recom-

mended for surgery followed by adjuvant therapy. In addition, adjuvant therapy may be considered for high-risk stage IB patients [51]. The 2020 JCOG0802 trial included 1106 patients and demonstrated comparable 5-year recurrence-free survival and overall survival between lobectomy and sublobar resection [52].

Imaging features and clinical marker of early lung cancer

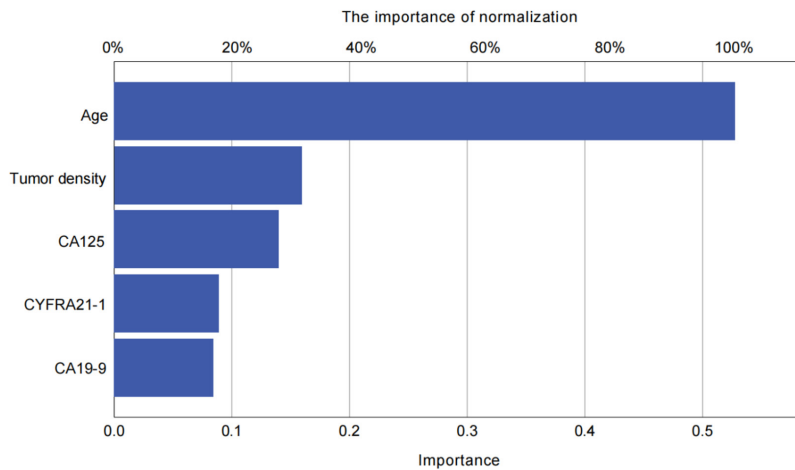


Figure 9. Importance ranking of independent variables.

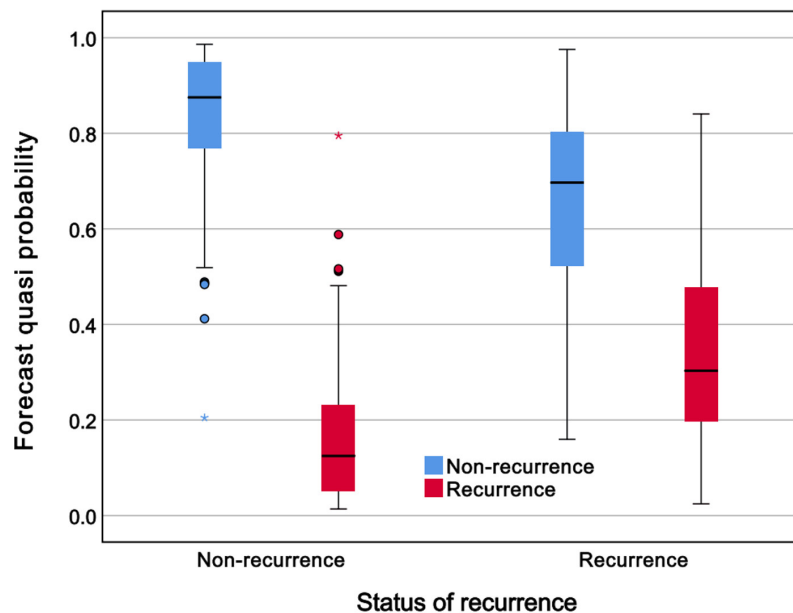


Figure 10. Predicted quasi-probability plots.

Similarly, the 2023 CALGB140503 trial found no difference in the 5-year disease-free survival between lobectomy and sublobar resection when the tumor diameter was ≤ 2 cm [53]. In line with these findings, our study observed no significant difference in postoperative recurrence among patients of different surgical types. This may reflect real-world clinical practice, in which treatment plans are tailored according to individual stage and condition, with adjuvant therapy administered when necessary. However, the absence of differences may also be attributable to the limited sample

size in our cohort. Additionally, traditional imaging features such as spiculation and pleural indentation were not significantly associated with recurrence in the univariate analysis. These features may have greater prognostic relevance in advanced-stage lung cancer, and further studies are warranted to clarify their role in early-stage disease.

Disease prediction models are used to predict health conditions, disease risks, or disease progression. Among them, logistic regression and neural networks are two of the most commonly used models [54-61]. In this study, we developed both models to predict postoperative recurrence in early-stage lung cancer patients. The logistic regression model achieved an AUC of 0.804 in the training set and 0.760 in the validation set, showing good discrimination and prediction accuracy. The neural network model achieved an AUC of 0.882 in the training set and 0.734 in the validation, also demonstrating good predictive performance. These results indi-

cate that both models have good accuracy and reliability in predicting recurrence risk of early-stage lung cancer after surgery.

Limitations and prospects

This study has several limitations. First, the sample size was relatively limited; although the models performed well in internal and external validation, their generalizability requires further assessment in larger multicenter cohorts. Second, the follow-up periods of the study subjects were not fully consistent, which may affect

Imaging features and clinical marker of early lung cancer

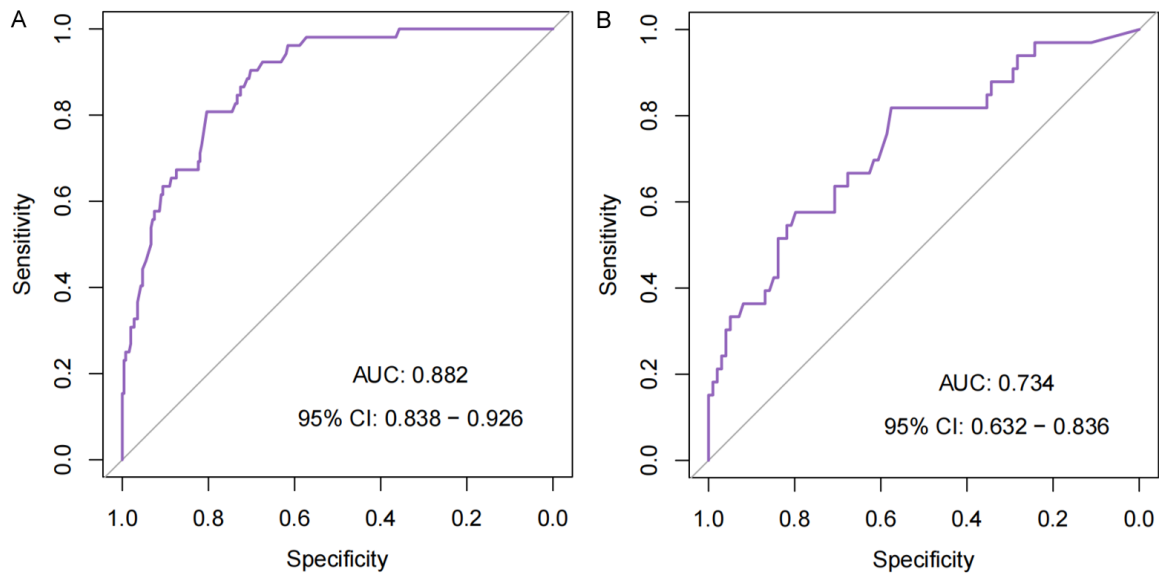


Figure 11. ROC curves of the neural network model in predicting recurrence risk in training set (A) and validation set (B).

Table 7. Validation of the model

Model	Forecast situation	Actual recurrence situation		Total
		Recurrence	Non-recurrence	
Nomogram model	Recurrence	29	45	74
	Non-recurrence	10	127	137
Total		39	172	211
Neural network model	Recurrence	31	54	85
	Non-recurrence	8	118	126
Total		39	172	211

the reliability of recurrence assessment. Future prospective studies with uniform follow-up periods are needed to address this issue. Third, the models primarily relied on static preoperative and postoperative data and did not incorporate dynamic monitoring indicators during follow-up. Future research could incorporate postoperative dynamic monitoring data to further enhance the predictive performance of the model.

Conclusions

The nomogram model and neural network model constructed in this study both showed high predictive efficiency and effectively identified patients at elevated recurrence risk. This provides strong support for clinicians in developing individualized treatment plans. For patients with a higher risk of recurrence, more

intensive follow-ups (e.g., shortening the regular 6-month interval to 3 months) and timely adjuvant treatments - determined by a multidisciplinary team based on a comprehensive assessment of the patient's specific condition - may reduce the risk of recurrence. Conversely, for low-risk patients, follow-up

frequency can be appropriately reduced to alleviate the psychological and economic burdens on the patients.

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Disclosure of conflict of interest

None.

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