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Clinical Characteristics and Prognosis of Non-Small Cell Lung Cancer with Coexisting Pulmonary Tuberculosis: A Retrospective Matched-Cohort Study

Jing Zheng[1,2,*], Haoran Xie[3,*], Guocan Yu[1,2], Likui Fang[1,2], Min Gao[1,2], Fangming Zhong[1,2], Bo Ye[3], Wenfeng Yu[1,2]

[1]Department of Tuberculosis, Hangzhou Red Cross Hospital, Hangzhou, Zhejiang, 310003, People's Republic of China; [2]Department of Thoracic Surgery, Hangzhou Red Cross Hospital, Hangzhou, Zhejiang, 310003, People's Republic of China; [3]The Affiliated Hospital of Hangzhou Normal University, Hangzhou, Zhejiang, 310003, People's Republic of China

*These authors contributed equally to this work

Correspondence: Wenfeng Yu, Email ywf1078@163.com

Background: Pulmonary tuberculosis (PTB) may coexist with non-small cell lung cancer (NSCLC), yet the clinical implications of this coexistence, including its prognostic impact, remain understudied.

Methods: We performed a retrospective 1:1 matched cohort study of 132 patients (66 PTB-NSCLC cases and 66 NSCLC-only controls) diagnosed between 2017 and 2023. Cases and controls were matched on age (±5 years) and TNM stage. Kaplan–Meier analysis evaluated survival differences, with hazard ratios derived from Cox proportional hazards regression.

Results: Between 2017 and 2023, patients with simultaneously diagnosed PTB and NSCLC (PTB-NSCLC) cases constituted approximately 4.7% of all diagnosed NSCLC patients. PTB-NSCLC patients exhibited higher erythrocyte sedimentation rates ($p = 0.002$) and lower serum albumin levels ($p = 0.032$) than controls. Elevated erythrocyte sedimentation rate was associated with poor survival in univariate analysis ($p = 0.037$), while a high modified Glasgow Prognostic Score (mGPS) remained an independent predictor of adverse outcomes in multivariable analysis (HR: 2.55, 95% CI: 1.12–5.84; $p = 0.026$). Kaplan-Meier analysis revealed that patients with PTB-NSCLC coexistence had significantly worse overall survival compared to matched controls (median OS: 32 vs 72 months; HR: 2.879, 95% CI: 1.728–4.797; $p < 0.001$). Furthermore, in multivariable analysis, surgical intervention was associated with significantly improved survival (HR: 0.34, 95% CI: 0.14–0.81; $p = 0.015$).

Conclusion: PTB-NSCLC confers worse survival outcomes. The mGPS provides independent prognostic value, while surgical intervention was associated with a significant survival benefit, highlighting the importance of integrated management.

Keywords: non-small cell lung cancer, pulmonary tuberculosis, comorbidity, prognosis

Introduction

Tuberculosis(TB) remains a significant fatal infectious disease globally, with China being a high-incidence country for the disease.[1] Among organs affected by tuberculosis, the lungs are the primary site of involvement, accounting for approximately 80% of tuberculosis cases.[2] Concurrently, lung cancer is the most prevalent malignant tumor worldwide for both incidence and mortality, with non-small cell lung cancer (NSCLC) accounting for over 80% of lung cancer cases.[3] Driven by lifestyle changes, air pollution, and population aging, NSCLC incidence continues to rise, imposing a substantial burden on public health systems.[4] As two of the most devastating pulmonary diseases, NSCLC and pulmonary tuberculosis(PTB) may coexist clinically.[5] These conditions share common risk factors, including smoking, structural lung damage, and environmental exposures.[6,7] Chronic inflammation and immune dysregulation may drive

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synergistic pathogenesis between the two, presenting complex clinical challenges.[8] Active tuberculosis infection induces persistent systemic inflammation and immune dysfunction, thereby fostering a microenvironment that supports lung cancer development.[9] Post-tuberculosis pulmonary scar tissue may likewise serve as a potential nidus for lung carcinogenesis and is frequently associated with nutritional depletion and metabolic dysregulation.[10] Clinically, these alterations often manifest as weight loss and hypoalbuminemia. Moreover, tuberculosis and lung cancer exhibit bidirectional interplay: tuberculosis-related inflammation can promote tumor progression, whereas immunosuppression resulting from lung cancer or its treatment may elevate the risk of tuberculosis reactivation.[11,12] Together, these interactions amplify the systemic inflammatory burden and worsen nutritional status in affected patients.

Existing research confirms that a history of tuberculosis increases lung cancer risk, while lung cancer patients, particularly those undergoing immunosuppressive therapy, are more susceptible to recurrent or new tuberculosis infections.[13,14] Based on large-scale cohort studies, the estimated incidence of PTB-NSCLC coexistence is approximately 3%, a figure that may be elevated in high-TB-burden settings.[15,16] This evidence corroborates the clinical coexistence of both diseases and underscores the need to investigate their combined prognostic implications. Retrospective studies indicate a markedly elevated mortality risk among patients with coexisting pulmonary tuberculosis and lung cancer.[17] The one-year mortality rate for tuberculosis patients with concurrent lung cancer was 11.4%, significantly higher than the 1.0% observed in tuberculosis patients without lung cancer.[18] A separate analysis of the squamous cell carcinoma subgroup further confirmed that patients with lung squamous cell carcinoma and concurrent tuberculosis exhibited a significantly shorter median overall survival (1.7 years vs 3.4 years, $p<0.01$).[19] However, previous studies on the impact of PTB-NSCLC comorbidity on patient prognosis remain significantly limited in three key aspects. Firstly, research primarily focuses on epidemiological associations or clinical diagnostic challenges, with insufficient attention to the direct effect of comorbidity on patient survival outcomes, rendering conclusions difficult to directly inform prognostic management. Secondly, existing studies generally fail to adequately control for key confounding factors. Variables such as inflammatory biomarkers and nutritional status have demonstrably been shown to independently influence cancer patient prognosis; neglecting their confounding effects may introduce bias into results. Thirdly, research gaps exist regarding specific prognosis-related indicators. For instance, systemic inflammatory markers such as erythrocyte sedimentation rate (ESR) and modified Glasgow Prognostic Score (mGPS) hold significant importance in studies examining tuberculosis and cancer separately. However, specific research evaluating these markers in the context of coexisting PTB and NSCLC remains scarce. Therefore, to clarify the prognostic impact of PTB-NSCLC comorbidity and to evaluate the predictive value of systemic inflammatory markers in this population, we conducted a retrospective matched-cohort study. This study aimed to (1) compare the clinical characteristics and overall survival between patients with PTB-NSCLC and matched patients with NSCLC alone, and (2) assess the prognostic utility of the ESR and mGPS. We hypothesized that patients with PTB-NSCLC have a worse prognosis than those with NSCLC alone, and that ESR and mGPS serve as independent prognostic predictors in this comorbid population.

Materials and Methods

Study Design and Subjects

This retrospective matched-cohort study was conducted at Hangzhou Red Cross Hospital between December 2017 and December 2023. Patients were eligible if they had a confirmed diagnosis of both NSCLC and PTB. Exclusion criteria included: (1) other primary malignancies; (2) incomplete medical records; and (3) loss to follow-up. The sample size was determined by the number of eligible PTB-NSCLC cases identified during the study period, consistent with similar retrospective studies in this field. After applying these criteria, 66 patients with co-existent NSCLC and PTB constituted the PTB-NSCLC case group (see Figure 1 for the selection flowchart). To be included in the case group, patients must have a confirmed histological diagnosis of NSCLC after or concurrent with a bacteriologically or clinically confirmed diagnosis of PTB. For the control group, 66 patients with NSCLC-only were selected from the same institution and time period. The controls were matched to the cases in a 1:1 ratio based on age (±5 years) and clinical TNM stage at diagnosis (according to the 8th edition of the AJCC Cancer Staging Manual). Age and TNM stage were selected as primary matching variables because they are among the strongest determinants of survival in NSCLC and are routinely available

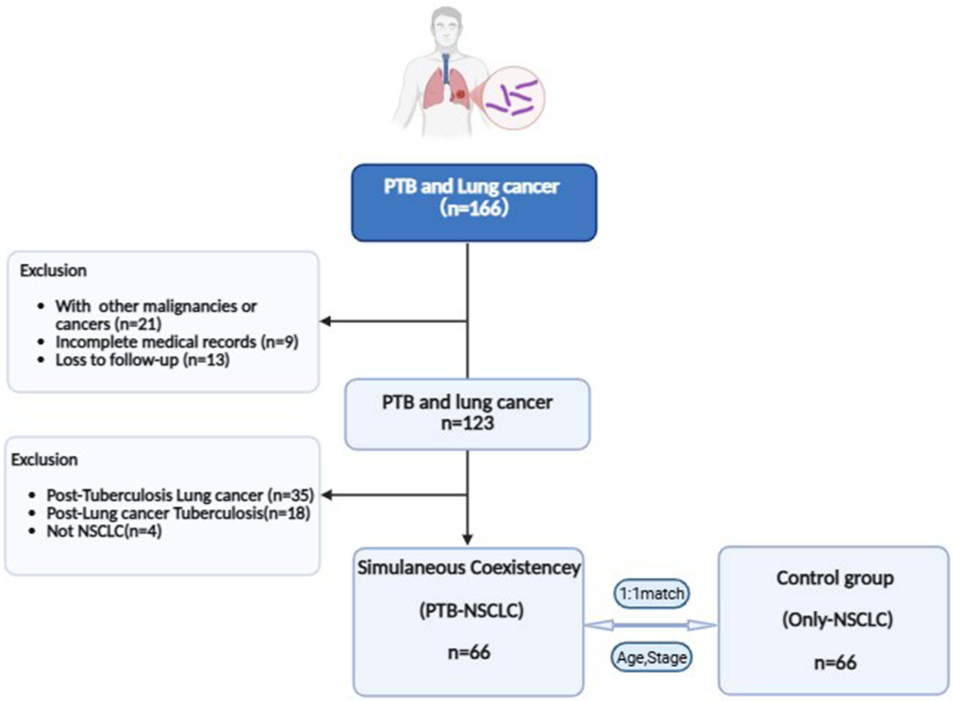

Figure 1 Flow Chart.

in clinical records. Although sex, comorbidities, and histological subtype also influence prognosis, we prioritized matching on age and stage to ensure balance on these fundamental prognostic factors while maintaining the feasibility of matching in our cohort. We acknowledge that residual confounding from unmatched variables may persist, and this is discussed as a study limitation. This study was reported in accordance with the REporting of Studies Conducted using Observational Routinely-collected Data (RECORD) statement.[20]

Diagnostic Criteria

Lung Cancer

Confirmed by histopathology from bronchoscopy biopsy, CT-guided needle biopsy, surgical resection, or cytology (with identified malignant cells). Histological subtypes included adenocarcinoma, squamous cell carcinoma, small cell carcinoma, and rare types.

Tuberculosis

Diagnosed per the Chinese WS 288–2017 criteria:

1. Microbiological Evidence (Preferred for Confirmation): Positive detection of Mycobacterium tuberculosis (MTB) in sputum, bronchoalveolar lavage fluid (BALF), tissue, or pleural fluid via culture, PCR, or nucleic acid testing;
2. Pathological Evidence: Granulomas with caseous necrosis identified via biopsy;
3. Imaging and Clinical Evidence (for Clinical Diagnosis): In the absence of microbiological or pathological confirmation, PTB was diagnosed based on typical radiological features (eg, upper-lobe cavities, miliary nodules) accompanied by chronic symptoms suggestive of TB (eg, cough, fever, night sweats, weight loss) and documented clinical/radiological improvement after a full course of anti-tuberculosis therapy. This approach is consistent with the Chinese WS 288–2017 diagnostic guidelines.

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Patients were categorized into three groups based on the temporal relationship between TB and lung cancer:

(1) Simultaneous Coexistence (PTB-LC), defined as concurrent diagnosis of both conditions within a six-month window;
(2) Post-Tuberculosis Lung Cancer (PTB→LC), referring to lung cancer developing against a backdrop of prior TB sequelae;
(3) Post-Lung Cancer Tuberculosis (LC→PTB), denoting active TB occurring during or following lung cancer treatment.

This temporal classification was used to describe the spectrum of PTB–NSCLC coexistence in our cohort. For the primary survival analysis, we focused on patients with "simultaneous coexistence" as this group most directly reflects the clinical scenario of active comorbidity and its potential impact on concurrent management and prognosis. The "post-tuberculosis lung cancer" and "post-lung cancer tuberculosis" groups were described for completeness but were not included in the matched comparative survival analysis.

Data Collection and Variables

Demographic, clinical, and laboratory data were extracted from electronic medical records using a standardized case report form. Key variables included age, sex, body mass index (BMI), smoking history, comorbidities (eg, chronic obstructive pulmonary disease, diabetes), cancer stage (AJCC 8th edition), histologic subtype, and treatment modalities. For NSCLC, this included specific regimens (platinum-based chemotherapy, immunotherapy agents such as PD-1/PD-L1 inhibitors) and surgical procedures. For tuberculosis, the treatment of tuberculosis follows national guidelines. In brief, the anti-tuberculosis chemotherapy initially uses four drugs: rifampicin, isoniazid, pyrazinamide, and ethambutol, and lasts for at least 6 months. Inflammatory biomarkers—erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and serum albumin—were recorded at diagnosis. The modified Glasgow Prognostic Score (mGPS) was calculated (0: C-reactive protein $\leq$ 10 mg/L and albumin $\geq$ 35 g/L; 1: C-reactive protein > 10 mg/L or albumin < 35 g/L; 2: C-reactive protein > 10 mg/L and albumin < 35 g/L). Among them, 0 was assigned to the low mGPS group, and 1 and 2 were assigned to the high mGPS group.

Statistical Analysis

Categorical variables were summarized as frequencies (percentages) and compared using chi-square or Fisher's exact tests. Continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range [IQR]) and analyzed with Student's *t*-test or Mann–Whitney *U*-test, as appropriate. Exploratory cut-off values for continuous variables were determined by the X-tile software using the minimal P-value approach; we note that such data-driven cutoffs carry a risk of overfitting. Therefore, primary conclusions are based on established variables (eg, mGPS categories and cancer stage), while these exploratory cutoffs (eg, for ESR) are presented to describe risk stratification within our cohort and require external validation. Survival analysis was performed using the Kaplan–Meier method, with differences assessed by Log rank tests. Cox proportional hazards regression models were employed to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for overall survival, adjusting for covariates with $p < 0.1$ in univariate analysis. All analyses were two-sided, with $p < 0.05$ considered statistically significant, and performed in R software (version 4.2.0).

Results

Patient Selection and Baseline Characteristics

Between 2017 and 2023, 1414 patients were diagnosed with NSCLC at our institution. From this population, 66 patients (4.7%) were identified as having coexisting PTB and formed the PTB-NSCLC case cohort. Each case was then matched 1:1 with a control patient diagnosed with NSCLC only, resulting in a final analytic cohort of 132 patients. The median age was 63.00 years (range, 54.25–68.75) in the PTB-NSCLC group and 64.00 years (range, 58.25–71.00) in the control group. Both groups were predominantly male, accounting for 74.24% and 77.27% of the PTB-NSCLC and control groups, respectively. No significant differences were observed between the groups regarding gender, smoking index, alcohol consumption history, hypertension, diabetes mellitus, or chronic obstructive pulmonary disease (COPD) (all $p > 0.05$) (Table 1). However, body weight was significantly lower in the PTB-NSCLC group compared to the control group ($p = 0.021$). The body mass index was also lower in the PTB-NSCLC group, though this difference did not reach statistical significance (20.52 ± 2.73 vs 21.40 ± 3.27, $p = 0.096$).

Clinical, Pathological, and Imaging Characteristics

In the entire cohort, the distribution of NSCLC stages was as follows: Stage I, 31.82%; Stage II, 28.79%; Stage III, 22.73%; and Stage IV, 16.67%. In the control group, 38 cases (57.58%) were adenocarcinoma and 28 cases (42.42%) were squamous cell carcinoma; in the PTB-NSCLC group, 31 cases (46.97%) were adenocarcinoma and 35 cases (53.03%) were squamous cell carcinoma (Table 2). Computed tomography (CT) analysis revealed that lung cavities were significantly more prevalent in the PTB-NSCLC group (31.82%), whereas mass lesions and nodules were more common in the control group (39.39% and 46.97%, respectively). The proportions of patients receiving chemotherapy or surgery were comparable between the groups. However, symptomatic presentation differed significantly ($p < 0.001$). A higher proportion of patients in the control group were asymptomatic at diagnosis (40.91%), compared to only 12.12% in the PTB-NSCLC group. Cough (39.39%) and haemoptysis (21.21%) were the most common symptoms in the PTB-NSCLC group.

Inflammatory, Biochemical, and Tumour Marker Characteristics

A comparative analysis of laboratory parameters was conducted between the two groups (Table 3). Patients in the PTB-NSCLC group exhibited significantly lower serum albumin (ALB) levels (36.18 ± 6.07 vs 38.65 ± 5.24, $p = 0.032$) and a significantly higher erythrocyte sedimentation rate (ESR) (median, 40.50 mm/h vs 22.00 mm/h, $p = 0.002$). Regarding liver function, the PTB-NSCLC group exhibited significantly lower levels of alanine aminotransferase (ALT) (median, 14.00 U/L vs 21.00 U/L, $p = 0.011$) and total bilirubin (TBiL) (median, 9.15 μmol/L vs 12.00 μmol/L, $p = 0.011$). No significant intergroup differences were observed in white blood cell count, neutrophil count, lymphocyte count, C-reactive protein levels, or the tumour markers CEA, CA-125, and CA-199 (all $p > 0.05$).

Table 1 Baseline Demographic and Clinical Characteristics of Patients

Variables	Total (n = 132)	Control Group (n = 66)	PTB-NSCLC (n = 66)	*P*
BMI, Mean ± SD	20.96 ± 3.03	21.40 ± 3.27	20.52 ± 2.73	0.096
Age, M (Q_1, Q_3)	64.00 (56.00, 71.00)	64.00 (58.25, 71.00)	63.00 (54.25, 68.75)	0.086
Height, M (Q_1, Q_3)	169.00 (160.00, 173.00)	170.00 (162.25, 173.75)	168.00 (160.00, 172.00)	0.224
Weight, M (Q_1, Q_3)	58.00 (51.38, 65.00)	60.00 (55.00, 66.75)	55.00 (50.00, 62.75)	0.021
Gender, n (%)				0.685
Female	32 (24.24)	15 (22.73)	17 (25.76)	
Male	100 (75.76)	51 (77.27)	49 (74.24)	
Smoking index, n (%)				0.080
<400	72 (54.55)	31 (46.97)	41 (62.12)	
>400	60 (45.45)	35 (53.03)	25 (37.88)	
Drinking, n (%)				0.709
No	90 (68.18)	44 (66.67)	46 (69.70)	
Yes	42 (31.82)	22 (33.33)	20 (30.30)	
Hypertension, n (%)				0.546
No	99 (75.00)	51 (77.27)	48 (72.73)	
Yes	33 (25.00)	15 (22.73)	18 (27.27)	
Diabetes, n (%)				0.083
No	113 (85.61)	60 (90.91)	53 (80.30)	
Yes	19 (14.39)	6 (9.09)	13 (19.70)	
COPD, n (%)				0.612
No	114 (86.36)	58 (87.88)	56 (84.85)	
Yes	18 (13.64)	8 (12.12)	10 (15.15)	

Abbreviations: SD, standard deviation; M, Median; Q_1, 1st Quartile; Q_3, 3st Quartile.

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Table 2 Clinical and Pathological Characteristics of the Study Population Stratified by Tuberculosis Status

Variables	Total (n = 132)	Control Group (n = 66)	PTB-NSCLC (n = 66)	*P*
Pathology, n (%)				0.223
Adenocarcinoma	69 (52.27)	38 (57.58)	31 (46.97)	
Squamous carcinoma	63 (47.73)	28 (42.42)	35 (53.03)	
Staging, n (%)				1.000
I	42 (31.82)	21 (31.82)	21 (31.82)	
II	38 (28.79)	19 (28.79)	19 (28.79)	
III	30 (22.73)	15 (22.73)	15 (22.73)	
IV	22 (16.67)	11 (16.67)	11 (16.67)	
CT, n (%)				<0.001
Ground-glass opacity	16 (12.12)	6 (9.09)	10 (15.15)	
Massy	41 (31.06)	26 (39.39)	15 (22.73)	
Nodule	51 (38.64)	31 (46.97)	20 (30.30)	
Pulmonary cavity	24 (18.18)	3 (4.55)	21 (31.82)	
Chemotherapy, n (%)				0.596
No	77 (58.33)	40 (60.61)	37 (56.06)	
Yes	55 (41.67)	26 (39.39)	29 (43.94)	
Operation, n (%)				0.375
No	53 (40.15)	24 (36.36)	29 (43.94)	
Yes	79 (59.85)	42 (63.64)	37 (56.06)	
Symptoms, n (%)				<0.001
Asymptomatic	35 (26.52)	27 (40.91)	8 (12.12)	
Chest pain	15 (11.36)	8 (12.12)	7 (10.61)	
Cough	49 (37.12)	23 (34.85)	26 (39.39)	
Feeble	4 (3.03)	0 (0.00)	4 (6.06)	
Fever	8 (6.06)	1 (1.52)	7 (10.61)	
Hemoptysis	21 (15.91)	7 (10.61)	14 (21.21)	

Table 3 Comparative Analysis of Inflammatory Biomarkers, Biochemical Parameters, and Tumor Markers in Tuberculosis-Associated Non-Small Cell Lung Cancer (TB-NSCLC) versus the Control Group

Variables	Total (n = 132)	Control Group (n = 66)	PTB-NSCLC (n = 66)	*P*
TP, Mean ± SD	67.56 ± 7.22	68.01 ± 7.45	67.27 ± 7.12	0.607
ALB, Mean ± SD	37.14 ± 5.86	38.65 ± 5.24	36.18 ± 6.07	0.032
WBC, M (Q_1, Q_3)	6.35 (5.00, 7.70)	6.55 (4.75, 7.92)	6.20 (5.10, 7.57)	0.875
NEC, M (Q_1, Q_3)	4.35 (3.10, 5.80)	4.48 (3.02, 5.80)	4.25 (3.30, 5.99)	0.574
LYN, M (Q_1, Q_3)	1.20 (0.90, 1.40)	1.25 (1.00, 1.48)	1.10 (0.70, 1.40)	0.104
CRP, M (Q_1, Q_3)	8.73 (1.73, 29.97)	4.50 (1.47, 22.86)	12.11 (2.20, 46.25)	0.112
ESR, M (Q_1, Q_3)	31.00 (12.00, 56.75)	22.00 (6.00, 39.50)	40.50 (19.25, 65.00)	0.002
ALT, M (Q_1, Q_3)	17.00 (12.00, 25.00)	21.00 (14.25, 27.75)	14.00 (11.00, 22.00)	0.011
AST, M (Q_1, Q_3)	22.00 (17.00, 25.25)	22.00 (18.00, 27.50)	21.50 (17.00, 25.00)	0.485
TBiL, M (Q_1, Q_3)	10.25 (7.70, 14.12)	12.00 (8.85, 16.23)	9.15 (6.82, 12.78)	0.011
Cr, M (Q_1, Q_3)	79.70 (68.88, 87.50)	82.30 (73.10, 88.40)	76.20 (66.28, 87.20)	0.125
CEA, M (Q_1, Q_3)	2.36 (1.30, 4.06)	2.65 (1.56, 4.51)	2.15 (1.15, 3.52)	0.289
CA-125, M (Q_1, Q_3)	16.75 (9.83, 51.67)	14.05 (8.28, 51.00)	20.45 (11.88, 51.67)	0.078
CA-199, M (Q_1, Q_3)	12.55 (8.44, 21.42)	12.88 (8.75, 21.54)	12.28 (8.17, 21.11)	0.890

Abbreviations: SD, standard deviation; M, Median; Q_1, 1st Quartile; Q_3, 3st Quartile.

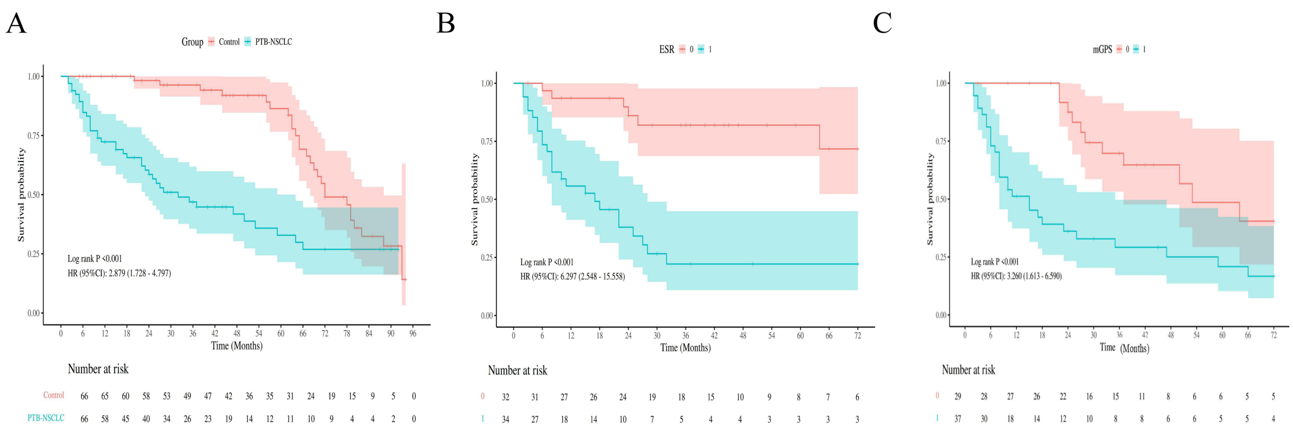

Figure 2 Kaplan-Meier Survival Analysis Stratified by Key Prognostic Factors.
Note: Kaplan-Meier curves depict overall survival probabilities over time for patients with NSCLC and PTB, stratified by different prognostic variables. (**A**) Comparison between study groups (PTB-NSCLC vs Control group). (**B**) Stratification by erythrocyte sedimentation rate (ESR) levels (1-high vs 0-low). (**C**) Stratification by modified Glasgow Prognostic Score (mGPS) (1-high vs 0-low). Hazard ratios (HR) with 95% confidence intervals are presented for each comparison, derived from Cox proportional hazards regression. The number of patients at risk during follow-up is shown below each graph. Statistical significance was determined using the Log rank test, with $p < 0.05$ considered statistically significant.

Survival Analysis and Prognostic Factors

Kaplan-Meier survival curves illustrated the impact of concurrent pulmonary tuberculosis on survival in patients with NSCLC (Figure 2A). The median overall survival (OS) was 32 months in the PTB-NSCLC group versus 72 months in the control group, indicating a significantly poorer prognosis for PTB-NSCLC patients (HR: 2.879; 95% CI: 1.728–4.797; *p* < 0.001). For subgroup survival analysis within the PTB-NSCLC cohort, ESR was converted into a categorical variable using X-tile software, dividing patients into high- (≥39 mm/h) and low- (<39 mm/h) ESR groups. The high-ESR group demonstrated a significantly poorer prognosis (HR: 6.297; 95% CI: 2.548–15.558, p < 0.001)(Figure 2B). Similarly, patients with high mGPS scores in the PTB-NSCLC cohort demonstrated poorer outcomes (HR: 3.260; 95% CI: 1.613–6.590, p < 0.001) (Figure 2C). Univariate Cox regression analysis identified advanced cancer staging (stage III–IV vs stage I–II; HR: 8.39, 95% CI: 3.87–18.18, p < 0.001) and ESR (HR: 0.42, 95% CI: 0.18–0.95, p = 0.037) as significant factors associated with survival (Table 4). In the multivariable Cox regression model, after adjusting for covariates, advanced cancer staging (HR: 10.53, 95%

Table 4 Univariate and Multivariable Cox Regression Analyses of Factors Associated with Overall Survival in Patients with Non-Small Cell Lung Cancer and Pulmonary Tuberculosis

Variables	**Univariable analysis**		**Multivariable analysis**	
	P	**HR (95% CI)**	***P***	**HR (95% CI)**
Age	0.820	1.00 (0.98 ~ 1.02)	0.907	1.00 (0.97 ~ 1.03)
Staging				
I–II		1.00 (Reference)		1.00 (Reference)
III–IV	<0.001	8.39 (3.87 ~ 18.18)	<0.001	10.53 (4.20 ~ 26.39)
ESR				
Low ESR		1.00 (Reference)		1.00 (Reference)
High ESR	0.037	0.42 (0.18 ~ 0.95)	0.286	0.60 (0.23 ~ 1.54)
mGPS				
Low score		1.00 (Reference)		1.00 (Reference)
High score	0.075	1.78 (0.94 ~ 3.37)	0.026	2.55 (1.12 ~ 5.84)
Chemotherapy				
No		1.00 (Reference)		1.00 (Reference)
Yes	0.853	1.06 (0.56 ~ 2.00)	0.055	0.45 (0.20 ~ 1.02)
Operation				
No		1.00 (Reference)		1.00 (Reference)
Yes	0.317	0.72 (0.39 ~ 1.36)	0.015	0.34 (0.14 ~ 0.81)

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CI: 4.20–26.39, p < 0.001) and an elevated modified Glasgow Prognosis Score (HR: 2.55, 95% CI: 1.12–5.84, p = 0.026) remained independent predictors of poorer survival. Conversely, undergoing surgery was significantly associated with an improved prognosis (HR: 0.34, 95% CI: 0.14–0.81, p = 0.015).

Discussion

This study investigated the impact of comorbid active pulmonary tuberculosis (PTB) and non-small cell lung cancer (NSCLC) on clinicopathological characteristics and long-term prognosis through a retrospective matched-cohort analysis. Our findings confirm that PTB-NSCLC comorbidity is an independent risk factor for poor prognosis, highlighting the significant prognostic value of the erythrocyte sedimentation rate (ESR) and the modified Glasgow Prognostic Score (mGPS) in this patient population. Compared with patients with NSCLC alone, those with PTB-NSCLC exhibited significantly worse survival outcomes, with a median overall survival reduced by more than half and a nearly 2.9-fold increase in mortality risk. These patients also presented with lower body weight, a greater symptom burden (cough and hemoptysis), and a higher incidence of cavitary lesions on radiology. Notably, they demonstrated a clinical profile characterized by systemic inflammation and malnutrition, including elevated ESR, hypoalbuminemia, and low body mass. Importantly, mGPS, which integrates inflammatory and nutritional markers, was validated as a robust independent prognostic predictor in this cohort.

Our results align with and extend existing literature. Regarding the association between comorbidity and adverse outcomes, our findings are consistent with those of Zheng et al[18] and Zhou et al,[19] all indicating increased mortality in lung cancer patients with concurrent tuberculosis. By rigorously matching for age and clinical stage, this study minimized key confounding variables, thereby providing stronger evidence that active PTB is an independent prognostic factor in NSCLC. A key contribution of this study is the extension of prognostic utility for inflammation-related markers to the complex setting of PTB-NSCLC comorbidity. ESR is well-established in tuberculosis diagnosis,[21,22] while mGPS —based on C-reactive protein and albumin levels—provides a composite measure of systemic inflammation and nutritional status, serving as a reliable tool for evaluating cancer cachexia and prognosis.[23,24] This study demonstrates that both ESR and mGPS retain strong prognostic stratification capacity even under the dual disease burden. While other systemic inflammatory indices, such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), are valuable in general oncology prognostication, the mGPS may offer a more comprehensive reflection of the combined inflammatory and catabolic state characteristic of PTB-NSCLC comorbidity, potentially explaining its retained independent significance in our multivariable model. Another noteworthy finding of our study is the differential significance of erythrocyte sedimentation rate (ESR) in univariate and multivariable analyses. While an elevated ESR was associated with poorer survival in the univariate model, it did not retain independent prognostic significance in the multivariable Cox regression that included cancer stage and mGPS. This observation can be plausibly explained by the phenomenon of statistical confounding or shared variance. Specifically, ESR, as a non-specific marker of systemic inflammation, is known to be elevated in both active tuberculosis and advanced cancer. It is highly likely that the prognostic information carried by ESR is not unique but is instead captured, to a substantial degree, by the variables it correlates with. The modified Glasgow Prognostic Score (mGPS), which integrates both an acute-phase reactant (C-reactive protein) and a nutritional marker (albumin), provides a more comprehensive reflection of the systemic inflammatory and nutritional status.[25] Consequently, when mGPS is included in the model, it may absorb or account for the inflammatory component of the risk that ESR alone would indicate. Similarly, advanced tumor stage is a powerful driver of both systemic inflammation and poor outcomes, further diluting the independent contribution of ESR when all factors are considered together. Therefore, the loss of significance for ESR in the multivariable model does not negate its clinical value as a readily available risk indicator, but rather refines our understanding by positioning mGPS as a more robust and integrative independent prognostic factor in this patient population.

In patients with PTB-NSCLC, the chronic inflammatory microenvironment driven by active tuberculosis infection appears to serve as a critical biological link between the two conditions, contributing to unfavorable outcomes. Persistent immune activation due to Mycobacterium tuberculosis infection can lead to excessive production of reactive oxygen and nitrogen species, causing direct DNA damage in lung epithelial cells and impairing repair mechanisms, thereby promoting genomic instability and carcinogenesis.[9,26] Concurrently, chronic inflammation facilitates M2 macrophage polarization and recruits immunosuppressive cell populations such as PD-1^+ exhausted T cells and $ARG1^+$ myeloid-derived suppressor cells via signaling pathways like TLR2/MyD88, fostering a local microenvironment conducive to both latent tuberculosis persistence and tumor immune evasion.[27,28] Additionally, post-tuberculosis fibrotic scarring may activate the Hippo signaling pathway and epithelial-mesenchymal transition, creating a pathological foundation for lung cancer development.[29] Thus, the elevated ESR and prognostic relevance of mGPS observed in this study reflect sustained systemic and local inflammatory activation, supporting the central role of chronic inflammation in driving poor outcomes in PTB-NSCLC patients.

Among patients with comorbidity, the surgical resection rate was 56% (37/66). Multivariate Cox regression confirmed surgical intervention as an independent protective factor for overall survival (HR: 0.34; 95% CI: 0.14–0.81; p = 0.015), indicating a significant survival benefit for selected patients even after adjusting for tumor stage. This observation is consistent with prior studies.[30] Based on these findings and clinical experience, we recommend individualized surgical decision-making: for patients with positive sputum smear or extensive active tuberculosis alongside resectable NSCLC, initiation of standard anti-tuberculosis therapy is advised, followed by surgical resection upon disease control; if rapid control is not achieved, neoadjuvant therapy should be considered. Lung cancer surgery or neoadjuvant treatment is typically performed within one month of starting anti-tuberculosis therapy. For stage I–IIA NSCLC patients with negative sputum smear or localized tuberculous lesions, surgical evaluation may proceed after a short course of anti-tuberculosis treatment. In patients with NSCLC and only healed tuberculosis lesions, no additional anti-tuberculosis therapy is required, and treatment planning should be based solely on lung cancer staging.[31] However, this observed benefit must be interpreted with caution, as it may be influenced by confounding by indication and selection bias. Patients selected for surgery likely had better performance status, more localized disease, and controlled tuberculosis, factors not fully captured by our matching and adjustment.

An unexpected finding was that alanine aminotransferase (ALT) and total bilirubin (TBiL) levels were significantly lower in the PTB-NSCLC group, contrary to the typical association of severe illness with hepatic impairment. This may be attributed to more proactive hepatoprotective strategies during anti-tuberculosis treatment,[32] whereas liver-protective agents are not routinely administered to cancer patients without baseline hepatic abnormalities.

These findings have important implications for clinical practice. First, active screening and integrated management of both diseases should be prioritized in high-burden regions. Upon diagnosis, multidisciplinary collaboration is essential, and surgical intervention should be actively pursued for eligible patients. Second, ESR and mGPS may serve as practical tools for routine prognostic assessment. High-risk patients (ESR $\geq$ 39 mm/h or mGPS 1–2) should receive intensified monitoring, nutritional support, and individualized treatment planning. Collectively, our findings advocate for the development of integrated TB-oncology clinical pathways in high-burden settings. Implementing routine prognostic stratification using simple markers like mGPS could help identify high-risk patients needing intensified multidisciplinary management, thereby optimizing resource allocation and improving outcomes in this complex population.

This study has several limitations. Firstly, its retrospective and single-center nature may introduce selection bias and limit the generalizability of our findings. Secondly, although we adhered to national diagnostic guidelines, the inclusion of PTB cases diagnosed on clinical and radiological grounds alone, without microbiological or pathological confirmation, may introduce diagnostic misclassification bias. Given the symptomatic and imaging overlap between PTB and lung cancer, some cases could have been misclassified, potentially affecting the accuracy of prevalence estimates and prognostic comparisons. Third, while we identified the mGPS as a significant prognostic factor, our analysis did not include other established systemic inflammatory indices, such as the neutrophil-to-lymphocyte ratio (NLR) or platelet-to-lymphocyte ratio (PLR). Fourth, although we matched cases and controls on age and TNM stage, residual confounding may exist due to variables not included in matching, such as sex, specific comorbidities, histological subtypes, and socioeconomic factors. These could influence both the risk of PTB-NSCLC coexistence and survival outcomes. Fifth, due to the limited sample size of the PTB-NSCLC cohort, our study was not powered to conduct robust subgroup analyses based on histological subtype or specific comorbidities. Sixth, our study lacks detailed data on anti-tuberculosis treatment regimens (eg, specific drugs, duration, adherence) and molecular profiling of tumors (eg, EGFR, ALK status), which could influence both tuberculosis activity and cancer prognosis. Therefore, future large-scale, prospective, and multicenter studies are warranted to validate the prognostic impact of PTB-NSCLC coexistence and to further explore

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potential differential outcomes across clinically relevant subgroups. Incorporating an expanded panel of systemic inflammatory and nutritional biomarkers in such studies would also help to comparatively assess their prognostic utility and refine risk stratification in this complex patient population. Furthermore, the variability in the temporal sequence and interval between PTB and NSCLC diagnoses (simultaneous coexistence, post-TB, post-LC) represents a unique aspect of this comorbidity. While we focused our primary analysis on simultaneous coexistence to homogenize the clinical scenario, this inherent variability could influence treatment strategies, host immune responses, and ultimately survival outcomes in ways our study was not designed to dissect.

In conclusion, this study establishes active pulmonary tuberculosis as an independent adverse prognostic factor in NSCLC. PTB-NSCLC comorbidity is associated with distinct clinical features and a pronounced inflammation-malnutrition phenotype. ESR and mGPS are simple yet effective biomarkers for prognostic stratification in this population. Future clinical efforts should emphasize coordinated management and personalized treatment strategies guided by systemic inflammatory markers to improve patient survival.

Conclusion

PTB-NSCLC comorbidity was associated with worse survival, a distinct systemic inflammatory and nutritional phenotype, and a potential survival benefit from surgical intervention in selected patients. The modified Glasgow Prognostic Score (mGPS) was identified as an independent prognostic biomarker in this setting. These preliminary results support the consideration of integrated management approaches that include prognostic assessment using inflammatory markers and the evaluation of surgical candidacy. Our findings highlight the need for prospective, multicenter studies to validate these observations and to further define optimal management strategies for this complex patient population.

Data Sharing Statement

The data of the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the Clinical Research Ethics Committee of the Hangzhou Red Cross Hospital (No.031-001, 2025) and conducted in accordance with the Declaration of Helsinki (as revised in 2013) and Good Clinical Practice Guidelines. Due to the retrospective nature of the study and without any specific intervention, informed consent has been agreed to be waived. The data were maintained with confidentiality.

Patient Consent for Publication

Informed consent was waived for the retrospective data by the Clinical Research Ethics Committee of the Hangzhou Red Cross Hospital.

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Author Contributions

Conceptualization: Wenfeng Yu, Haoran Xie, Jing Zheng.

Data curation:Fangming Zhong, Bo Ye, Min Gao.

Formal analysis: Likui Fang, Guocan Yu.

Writing – original draft: Guocan Yu.

Writing – review & editing: Min Gao.

All authors took part in either drafting or revising the manuscript. All authors gave final approval of the version to be published, have agreed on the journal to which the article has been submitted, and agreed to be 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.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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