

Original Article

**Airflow Obstruction in Post-tuberculosis Lung Disease: A 5-year Prospective Cohort Study**

Zikang Sheng^{1,&}, Wenli Cao^{2,&}, Hongling Chu³, Yanqing Le¹, Junfeng Wu², Yue Zhang¹, Yafei Rao¹,
Brian Allwood⁴, Yongchang Sun^{1,#}, and Xiaoyan Gai^{1,#}

1. Department of Respiratory and Critical Care Medicine, Peking University Third Hospital; Chronic Airway Diseases Research Center, Peking University Health Science Center; Beijing 100191, China; 2. Tuberculosis Department, Beijing Geriatric Hospital, Beijing 100095, China; 3. Clinical Epidemiology Research Center, Peking University Third Hospital, Beijing 100191, China; 4. Division of Pulmonology, Department of Medicine, Stellenbosch University & Tygerberg Academic Hospital, Cape Town, South Africa

Abstract

Objective Post tuberculosis lung disease (PTLD) manifests in various forms, including tuberculosis-associated chronic obstructive pulmonary disease (TB-COPD), yet the clinical features of PTLD remain undercharacterized. This study aimed to assess longitudinal changes in lung function over a 5-year period and to identify predictors of airflow obstruction in a cohort of patients treated for active pulmonary TB.

Methods Patients with active pulmonary TB were enrolled in this study and were followed during treatment, at treatment completion and five years post-treatment. Assessments included lung function and chest CT, analyzing longitudinal trends and airflow obstruction risk factors.

Results Among 53 patients (mean age 36.9 ± 13.9 years; 64.2% male), 7 patients (13.2%) exhibited airflow obstruction. At the 5-year follow-up, the mean FEV_1/FVC declined significantly ($76.27\% \pm 12.04\%$ vs. $80.23\% \pm 11.02\%$, $P < 0.001$) and 9 patients (17.0%) exhibited airflow obstruction. Seven of these patients predominantly showed air trapping consistent with small airway disease on chest CT, aligning with TB-COPD phenotype. Notably, four young-to-middle-aged patients (< 60 years old) had persistent obstruction over the five years.

Conclusion The initial test revealed that 13.2% of patients presented with airflow obstruction. By the 5-year follow-up, this proportion had increased to 17.0%, with most cases demonstrating imaging findings aligning with TB-COPD, even among younger, non-smoking individuals. These findings emphasize the importance of long-term follow-up and routine lung function assessments in TB survivors.

Key words: Post tuberculosis; TB-associated COPD; Lung function; Airflow obstruction; Chest CT

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[&]These authors contributed equally to this work.

[#]Correspondence should be addressed to Xiaoyan Gai, Associate Professor, Tel: 86-13522708870, E-mail: GXy81WFL79@163.com; Yongchang Sun, Professor, Tel: 86-10-82265020, E-mail: suny@bjmu.edu.cn

Biographical notes of the first authors: Zikang Sheng, MD, majoring in disease of respiratory system, E-mail: s13721332691@163.com; Wenli Cao, Professor, majoring in disease of pulmonary tuberculosis, E-mail: yangqiang@tsinghua.org.cn

INTRODUCTION

Tuberculosis (TB) remains one of the leading infectious causes of mortality worldwide, with an estimated one-quarter of the global population harboring *Mycobacterium TB* (Mtb) infection^[1,2]. According to the 2024 World Health Organization (WHO) report, there were 10.8 million new TB cases and 1.25 million deaths in 2023^[3]. A proportion of patients experience chronic respiratory sequelae following treatment, termed post TB lung disease (PTLD), characterized by persistent respiratory symptoms, radiological abnormalities, and pulmonary dysfunction^[4,5].

The First International PTLD Symposium in 2019 defined PTLD as chronic respiratory abnormalities attributable to prior pulmonary TB, regardless of the presence of current symptoms^[6]. The pathogenesis of PTLD involves the direct damage caused by Mtb, immune-mediated injury, and environmental exposures, leading to airway remodeling, reduced lung elasticity, and vascular injury^[7-9]. Pathological examinations have indicated that PTLD is characterized by granulomatous inflammation and fibrosis predominantly concentrated around the small bronchovascular bundles, accompanied by significant perilesional fibrosis, which directly damages small airway structures and consequently impairs lung function^[8,10]. Lung function impairment in PTLD may manifest as obstructive, restrictive, or mixed patterns^[9,11]. A longitudinal study from Malawi involving 405 TB patients found that 34.2% had impaired lung function at treatment completion, with the impairment persisting in 27.9% of patients after three years^[11,12]. In recent years, pulmonary TB has been increasingly recognized as an independent and significant risk factor for the development of chronic obstructive pulmonary disease (COPD), termed TB-associated COPD (TB-COPD)^[8,13]. Moreover, individuals with a history of TB are approximately 4-fold higher risk to develop COPD compared to those without TB (25.7% vs. 8.3%)^[14]. TB-COPD is a distinct phenotype of airflow obstruction that develops as a sequela of pulmonary TB, characterized by persistent airflow limitation and radiological signs of small airway involvement^[15]. In China, a cross-sectional study involving 8,680 individuals revealed that 21.3% of participants with radiologic evidence of prior TB exhibited airflow obstruction^[16]. However, prospective data on the development and long-term progression of TB-COPD following anti-TB treatment remain limited.

China has a high burden of tuberculosis, but no

prospective cohort studies have yet been conducted to evaluate lung function models in pulmonary TB patients. This study aimed to assess longitudinal changes in lung function over a 5-year period and to identify predictors of airflow obstruction in a cohort of patients treated for active pulmonary TB^[17].

MATERIALS AND METHODS

Study Design and Participants

In this prospective cohort study, we enrolled 178 patients diagnosed with active pulmonary TB from the TB Outpatient Clinic of Beijing Geriatric Hospital between 1 January 2017 to 31 December 2019. Follow-up evaluations were conducted after anti-TB treatment to assess the development of TB-COPD. The diagnosis of pulmonary TB was confirmed by microbiological detection of Mtb in bodily fluids (e.g., sputum, bronchoalveolar lavage fluid, or pleural effusion) or histopathological confirmation from lung or pleural biopsy in patients with clinical symptoms and chest CT findings^[1]. Inclusion Criteria: (1) Age 18 to 70 years; (2) Permanent residency in Beijing or surrounding areas to ensure long-term follow-up compliance; (3) Willingness to undergo serial lung function testing. Exclusion Criteria: (1) HIV positivity, malignancies (e.g., lung cancer), or severe cardiovascular / cerebrovascular diseases; (2) Inability to complete long-term follow-up. TB-COPD should be considered when airflow limitation ($FEV_1/FVC < 70\%$) develops in patients with prior TB, along with imaging findings suggestive of small airway disease (typically manifested as air trapping, mosaic attenuation, fibrotic scars, etc)^[15,18,19].

At enrollment, baseline data were collected, including age, gender, height, weight, comorbidities, smoking history, as well as initial imaging and laboratory results (chest CT, blood routine test, and serum albumin). Based on lung function test results, patients were categorized into three groups: normal airflow group, low FVC group and airflow obstruction group.

Clinical follow-up was conducted at Beijing Geriatric Hospital at two time points: (1) At completion of anti-TB treatment: primary follow-up assessments included chest CT and blood routine test. (2) Five years after treatment completion (5-year follow-up): comprehensive follow-up evaluations were performed, including: updated baseline data (age, BMI, newly developed comorbidities), respiratory symptom assessments [St. George's Respiratory Questionnaire (SGRQ)],

COPD Assessment Test (CAT), modified Medical Research Council (mMRC) dyspnea scale], lung function test, Chest CT scan, and blood routine test (Figure 1). A total of 53 patients completed the 5-year follow-up.

This prospective cohort study has been registered with ClinicalTrials.gov (NCT 05426720). Written informed consent was obtained from all participating patients.

Lung Function Test

Lung function test was performed by experienced technicians according to internationally standardized protocol^[20]. Parameters assessed included: forced expiratory volume in 1 second (FEV₁), forced vital capacity (FVC), FEV₁/FVC, forced expiratory flow at 25%–75% (FEF_{25%–75%}), forced expiratory flow at 50% (FEF_{50%}), and forced expiratory flow at 75% (FEF_{75%}); lung volume parameters: total lung capacity (TLC), residual volume (RV) and RV/TLC; diffusion function parameter: diffusing capacity of the lungs for carbon monoxide (DLCO). % predicted (% pred) is expressed as a percentage of predicted values^[9]. All testing was performed in accordance with ATS/ERS guidelines^[21].

Airway patterns were categorized as follows: normal airflow group (post-bronchodilator FEV₁/FVC ≥ 70% and FVC% pred ≥ 80%); airflow obstruction group (post-bronchodilator FEV₁/FVC < 70%); low FVC group (FEV₁/FVC ≥ 70% but FVC % pred < 80%); TLC % pred < 80% was defined as low TLC; small airway dysfunction have been defined as ≥ 2 of FEF_{25%–75%} pred, FEF_{50%} pred or FEF_{75%} pred < 65%.

Additionally, DLCO% pred < 80% was defined as low DLCO^[22].

Chest CT Imaging

Longitudinal chest CT examinations were performed for all pulmonary TB patients at three critical time points: (1) Baseline phase; (2) At treatment completion; (3) At the 5-year follow-up. Based on validated TB imaging scoring systems^[11,23,24], CT evaluation was conducted to assess the characteristics and severity of imaging findings:

(1) Extent scoring: Each lung is divided into three zones (upper, middle, lower), with the lingula counted separately. Each zone is scored on a 0–4 scale based on the degree of parenchymal involvement. The total score ranged from 0 (no disease) to 24 (extensive bilateral involvement), see Supplementary Data 1^[23].

(2) Feature-based scoring: Quantitative assessments were performed for specific pathological features, including fibrosis, calcification, emphysema, bronchiectasis, cavitation, micronodules, consolidation, infiltrates, mosaic attenuation, collapse, and volume loss. Additional findings such as pleural thickening or effusion and mediastinal lymphadenopathy were documented. Moreover, the extent of disease involvement (i.e., unilateral vs. bilateral) was recorded (Supplementary Data 1)^[11,24]. All three serial chest CT examinations were reported independently by a radiologist, pulmonologist, and TB specialist. Where there were disagreements in the presence or type of radiological

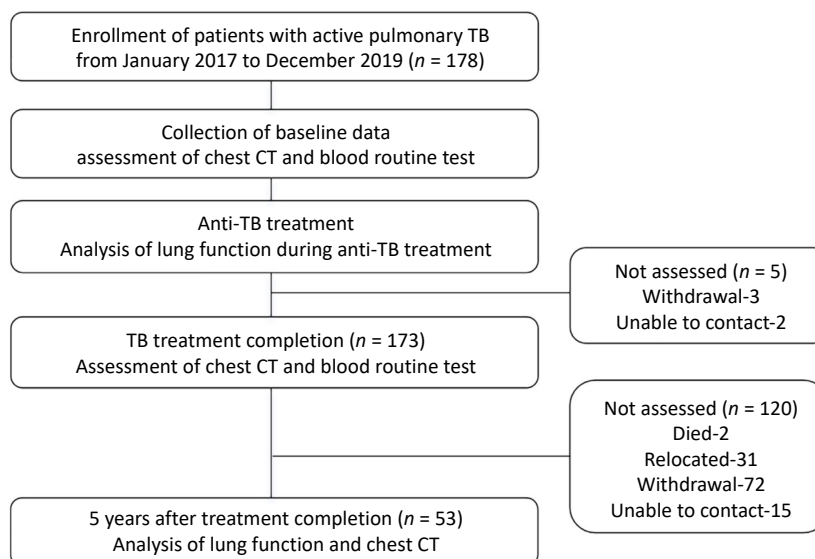


Figure 1. Flowchart of study design.

abnormality, discrepancies were resolved by consensus read. CT scoring and lung function assessments were performed in a blinded manner.

Statistical Analysis

Data were analyzed using SPSS version 25 (IBM Corp., Armonk, NY). Normally distributed continuous variables were presented as mean \pm standard deviation, while non-normally distributed variables were expressed as median (inter-quartile range). Continuous variables were compared using student's *t*-tests or non-parametric tests. Categorical variables were expressed as frequencies and percentages and compared using χ^2 test.

Patients were stratified by lung function status, focusing on comparisons between the normal airflow and airflow obstruction groups. Univariable and multivariable logistic regression analyses were conducted to identify predictors of airflow obstruction. Based on previous studies, we selected potential influencing factors on lung function as independent variables, including age, sex, BMI, smoking history, previous TB, multidrug resistance (MDR)^[8,25]. The odds ratio (OR), 95% confidence interval (CI) and *p* value were reported. A *P* value < 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

A total of 178 patients were initially enrolled in this study, with a mean age of 37.5 \pm 15.0 years, 108 (60.7%) were male. At baseline, the radiological score was 4.8 (IQR: 3.0–8.0), the mean FEV₁ was 3.05 \pm 0.98 L, FVC was 3.74 \pm 1.04 L, and FEV₁/FVC ratio was 81.08% \pm 11.50%. However, only 53 patients completed the 5-year follow-up. Therefore, the primary analysis focused on these 53 patients, evaluating changes in lung function over the 5-year period. A comparison of baseline characteristics between these 53 patients and the 125 who were lost to 5-year follow-up revealed no significant differences in sex, age, radiological score, or lung function parameters (Supplementary Table S1), suggesting that the follow-up group was representative of the overall cohort.

The baseline characteristics of the 53 patients were as follows: The mean age at initial treatment was 36.9 \pm 13.9 years, and 34 patients (64.2%) were male. Seven patients (13.2%) had a TB history and had received prior anti-TB treatment. Comorbidities included diabetes mellitus in two patients (3.8%),

and hypertension in five (9.4%). Among male patients, 18 (34.0%) had a long-term smoking history. The overall smoking pack-years were 0 (IQR: 0–3.3) across all patients, and 7.4 (IQR: 2.3–35.0) among smokers. None of the female patients had a history of smoking. All patients underwent sputum smear and culture tests at baseline. 7 (13.2%) had positive sputum smears, and 11 (20.8%) had positive sputum cultures. The baseline radiological score was 4.0 (IQR: 2.8–6.3) (Table 1).

Clinical Characteristics, Lung Function Features at Baseline and 5-Year Follow-up

Lung Function at Baseline The first lung function test was performed in all 53 patients during anti-TB treatment after sputum smear conversion to negative, serving as baseline lung function (initial test). The time from treatment initiation to first spirometry was 5.5 (3.8–7.6) months. The mean FEV₁ was 3.06 \pm 1.01 L, FVC was 3.76 \pm 1.03 L, and

Table 1. Baseline characteristics of patients with pulmonary TB at initial test

Characteristics Items (n = 53)	Baseline characteristic
Male	34 (64.2)
Age (years)	36.9 \pm 13.9
BMI (kg/m ²)	21.41 \pm 2.79
Smoking status	
Never smoker	35 (66.0)
Smoker	18 (34.0)
Pack-years of smoking for all patients	0 (0–3.3)
Pack-years of smoking for smokers	7.4 (2.3–35.0)
Occupational dust exposure	1 (0.6)
Comorbidities	
Diabetes	2 (3.8)
Hypertension	5 (9.4)
Previous TB	7 (13.2)
MDR	3 (5.7)
IGRA positive	35 (66.0)
Sputum smear (+)	7 (13.2)
Sputum culture (+)	11 (20.8)
Radiological score	4.0 (2.8–6.3)

Note. The data in the table are presented as *n* (%) or mean (standard deviation) or median (IQR). BMI, body mass index; TB, tuberculosis; MDR, multidrug resistance; IGRA, interferon gamma release assay.

FEV₁/FVC ratio was 80.23% ± 11.02% (Table 2). Based on spirometric pattern, 43 (81.1%) patients had normal airflow, 7 (13.2%) had airflow obstruction, and 3 (5.7%) had low FVC. Among the 7 patients with airflow obstruction, 5 (71.4%) were male, and 2 were smokers (both male). Patients with airflow obstruction had significantly higher radiological score at baseline compared to those with normal airflow [8.0 (5.0–16.5) vs. 3.5 (2.0–5.0), $P = 0.002$]. No significant differences were observed in other baseline characteristics (all $P > 0.05$) (Supplementary Table S2).

Lung Function At 5-Year Follow-up At the 5-year follow-up, 53 patients underwent a second lung function test. The mean FEV₁ was 2.97 ± 1.09 L, FVC was 3.83 ± 1.16 L, and FEV₁/FVC ratio was 76.27% ± 12.04% (Table 2). Forty-one patients had normal airflow, 9 (17.0%) exhibited airflow obstruction, 3 (5.7%) had low FVC, 26 (49.1%) had small airway dysfunction, 9 (17.0%) had low TLC and 14 (26.4%) had low DLCO. Patients in the airflow obstruction group were significantly older than those with normal airflow (54.7 ± 13.5 years old vs. 40.1 ± 12.7 years old, $P = 0.003$). Quality of life scores were significantly worse in the airflow obstruction group,

with higher median scores on the SGRQ [29.0 (13.0–36.5) vs. 3.0 (0–6.0)], CAT [22.0 (12.0–24.5) vs. 10.0 (8.0–12.5)], and mMRC [2.0 (1.5–3.0) vs. 0 (0–1.0)] (all $P < 0.05$). Although pack-years of smoking, IGRA positivity, sputum smear positivity, and sputum culture positivity, were slightly higher in the airflow obstruction group, the differences were not statistically significant. Additionally, the radiological score at the 5-year follow-up was significantly higher in the airflow obstruction group compared to the normal airflow function group [5.8 (2.5–12.3) vs. 1.5 (1.0–2.8), $P = 0.008$] (Table 3).

Longitudinal Changes in Lung Function Over 5 Years

Over the 5-year period, the number of patients with normal airflow decreased from 43 to 41 cases, while those with airflow obstruction increased from 7 to 9 cases; the number with low FVC remained unchanged ($n = 3$). Four initially normal patients have developed dysfunction, 1 progressed to low FVC, 3 developed airflow obstruction, 1 patient each from low FVC and airflow obstruction groups normalized (Figure 2).

Lung airflow function analysis: Compared to baseline, there was a significant reduction in FEV₁ (2.97 ± 1.09 L vs. 3.0 ± 1.01 L, $P = 0.035$), FVC % pred

Table 2. Longitudinal lung function changes in patients over 5 years

Parameters	Initial test (n = 53)	5-year follow-up (n = 53)	Mean difference (95% CI)	P value
Spirometry				
FEV ₁ (L)	3.06 ± 1.01	2.97 ± 1.09	-0.09 (-0.17, -0.01)	0.035*
FEV ₁ % pred (%)	88.36 ± 20.28	86.70 ± 21.65	-1.66 (-9.75, 6.42)	0.684
FVC (L)	3.76 ± 1.03	3.83 ± 1.16	0.07 (-0.02, 0.16)	0.107
FVC% pred (%)	102.19 ± 18.93	94.23 ± 18.11	-7.97 (-15.10, 0.83)	0.029*
FEV ₁ /FVC (%)	80.23 ± 11.02	76.27 ± 12.04	-3.97 (-5.38, -2.55)	< 0.001*
FEF _{25%-75%} pred (%)	63.70 ± 25.12	64.16 ± 28.80	0.46 (-3.51, 4.44)	0.816
FEF _{50%} pred (%)	58.91 ± 22.70	68.25 ± 31.18	9.33 (-1.21, 19.88)	0.082
FEF _{75%} pred (%)	49.46 ± 23.39	75.54 ± 30.97	26.08 (15.43–36.72)	< 0.001*
Plethysmography				
TLC (L)	6.42 ± 1.63	7.61 ± 12.66	1.19 (-2.29, 4.67)	0.504
TLC% pred (%)	119.81 ± 20.04	96.64 ± 22.22	-23.17 (-31.43, -14.91)	< 0.001*
RV (L)	2.79 ± 1.16	2.23 ± 0.93	-0.56 (-0.97, -0.15)	0.001*
RV/TLC (%)	42.65 ± 10.39	41.68 ± 21.37	-0.97 (-7.48, 5.53)	0.728
Diffusion capacity				
DLCO% pred (%)	75.84 ± 26.94	84.17 ± 18.92	9.24 (1.97, 16.50)	0.014*

Note. FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; FEF_{25%-75%}, forced expiratory flow at 25%–75%; FEF_{50%}, forced expiratory flow at 50%; FEF_{75%}, forced expiratory flow at 75%; TLC, total lung capacity; RV, residual volume; DLCO, diffusing capacity of the lungs for carbon monoxide; % pred, % predicted; * $P < 0.05$.

(94.23% ± 18.11% vs. 102.19% ± 18.93%, $P = 0.029$) and FEV₁/FVC Ratio (76.27% ± 12.04% vs. 80.23% ± 11.02%, $P < 0.001$), with a non-significant increase in FVC (3.83 ± 1.16 L vs. 3.76 ± 1.03 L, $P = 0.107$) (Figure 3A–C).

Lung volume analysis: RV significantly decreased (2.23 ± 0.93 L vs. 2.79 ± 1.16 L, $P = 0.001$), and TLC% pred decreased significantly (96.64% ± 22.22% vs.

119.81% ± 20.04%, $P < 0.001$).

Small airway function: A marked improvement in small airway function was observed, particularly in FEF_{75%} pred (75.54% ± 30.97% vs. 49.46% ± 23.39%, $P < 0.001$) (Table 2).

DLCO Trends Over 5 Years At baseline, 34 (64.2%) patients exhibited reduced DLCO. The low DLCO group had significantly lower FEV₁/FVC (77.81% ±

Table 3. Comparison between normal airflow and airflow obstruction groups at 5-year follow-up

Items	Total (n = 53)	Normal airflow (n = 41)	Airflow obstruction (n = 9)	P value
Male (%)	34 (64.2)	28 (68.3)	6 (66.7)	1.000
Age (years)	43.2 ± 13.8	40.1 ± 12.7	54.7 ± 13.5	0.003*
BMI (kg/m ²)	22.00 ± 2.95	21.97 ± 2.92	22.64 ± 3.11	0.541
Smoking history (%)	18 (34.0)	14 (34.1)	4 (44.4)	0.842
Pack-years of smoking	0 (0–5.5)	0 (0–4.5)	0 (0–35.0)	0.343
Diabetes history (%)	2 (3.8)	1 (2.4)	1 (11.1)	0.414
Hypertension history (%)	5 (9.4)	3 (7.3)	1 (11.1)	0.492
Newly Diagnosed Diabetes (%)	3 (5.7)	3 (7.3)	0 (0)	0.267
Newly Diagnosed Hypertension (%)	2 (3.8)	2 (4.9)	0 (0)	0.368
Previous TB (%)	7 (13.2)	4 (9.8)	1 (11.1)	0.904
MDR (%)	3 (5.7)	3 (7.3)	0 (0)	0.267
IGRA positive (%)	35 (66.0)	29 (70.7)	5 (55.6)	0.625
Sputum smear (+) (%)	7 (13.2)	5 (12.2)	2 (22.2)	0.799
Sputum culture (+) (%)	11 (20.8)	8 (19.5)	3 (33.3)	0.644
Quality of life				
SGRQ score (median, IQR)	4.0 (0–9.5)	3.0 (0–6.0)	29.0 (13.0–36.5)	< 0.001*
CAT score (median, IQR)	8.0 (10.0–16.0)	10.0 (8.0–12.5)	22.0 (12.0–24.5)	< 0.001*
mMRC (median, IQR)	0 (0–1.0)	0 (0–1.0)	2.0 (1.5–3.0)	< 0.001*
Radiological score	1.5 (1.0–3.0)	1.5 (1.0–2.8)	5.8 (2.5–12.3)	0.008*
Lung function parameters				
FEV ₁ /FVC (%)	76.27 ± 12.04	80.31 ± 7.19	56.26 ± 9.23	—
FEV ₁ (L)	2.97 ± 1.09	3.37 ± 0.85	1.65 ± 0.75	< 0.001*
FEV _{1%} pred (%)	86.70 ± 21.65	95.35 ± 11.64	55.98 ± 25.50	< 0.001*
FVC (L)	3.83 ± 1.16	4.20 ± 0.96	2.84 ± 0.98	< 0.001*
FVC% pred (%)	94.23 ± 18.11	99.89 ± 10.40	78.31 ± 28.02	< 0.001*
RV (L)	2.23 ± 0.95	2.15 ± 0.96	2.59 ± 0.90	0.211
TLC (L)	5.83 ± 1.39	6.10 ± 1.31	5.29 ± 1.46	0.111
TLC % pred (%)	97.37 ± 22.54	98.86 ± 20.78	91.12 ± 29.50	0.361
RV/TLC (%)	40.99 ± 21.83	39.09 ± 23.33	49.03 ± 11.56	0.223
DLCO% pred (%)	84.17 ± 18.92	85.31 ± 17.69	74.90 ± 23.92	0.162

Note. BMI, body mass index; TB, tuberculosis; MDR, multidrug resistance; IGRA, interferon gamma release assay; SGRQ, St. George's Respiratory Questionnaire; CAT, COPD Assessment Test; mMRC, modified Medical Research Council; The definition of lung function parameters are consistent with the above mentioned; * $P < 0.05$.

11.42% vs. 84.57% ± 8.99%, $P = 0.031$).

At the 5-year follow-up, 14 (26.4%) patients maintained reduced DLCO impairment. Patients with persistent DLCO impairment had significantly lower absolute FVC values (3.33 ± 1.07 L vs. 4.04 ± 1.08 L, $P = 0.042$), but not lower FEV₁/FVC Ratio (Supplementary Table S3). Overall, DLCO% pred improved over the 5 years ($84.17\% \pm 18.92\%$ vs. $75.84\% \pm 26.94\%$, $P = 0.014$) (Table 2).

Analysis of Chest CT Scans at Initial Treatment, Treatment Completion, and 5-year Follow-up

Across the three time points, the airflow

obstruction group consistently showed significantly higher radiological score compared to the normal airflow group. At the 5-year follow-up, the airflow obstruction group had greater extent of emphysema, bronchiectasis, and mosaic attenuation (all $P < 0.05$). In the airflow obstruction group, 100% of patients had bilateral disease at baseline and 83.3% had bilateral disease at 5-year follow-up, compared with 46.6% ($P = 0.023$) and 43.8% ($P = 0.136$) in the normal airflow group, respectively (Supplementary Tables S4–S6). Additionally, we compared radiological scores between small airway dysfunction and normal small airway function groups

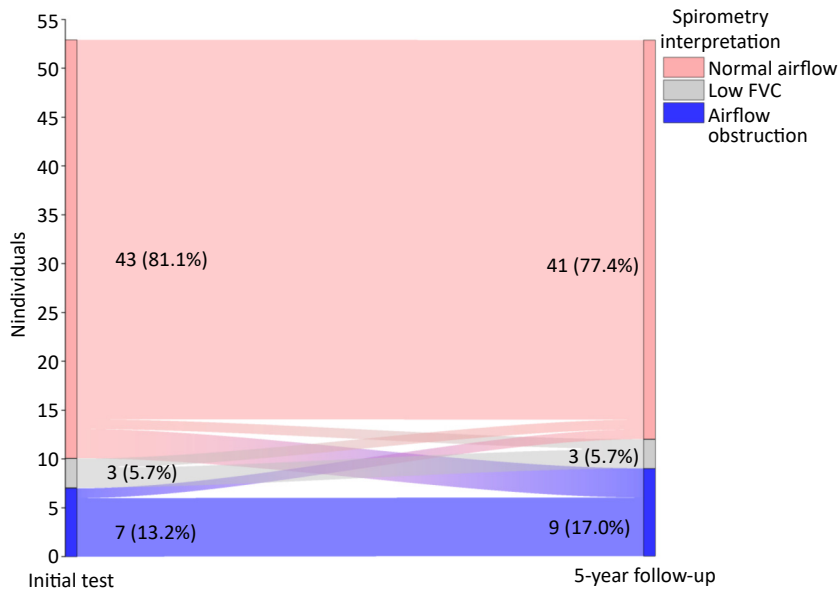


Figure 2. Sankey plot showing change of spirometry pattern.

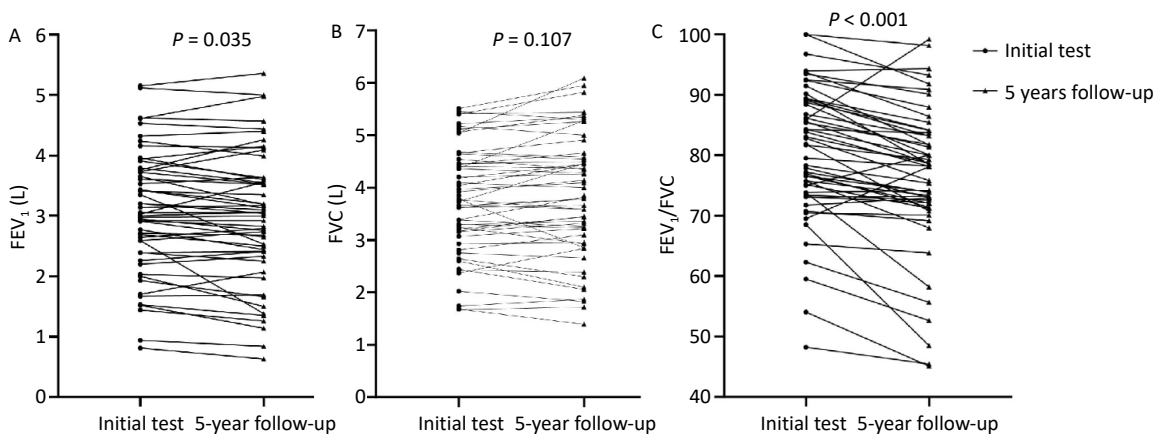


Figure 3. Comparison of key lung function indicators between the two assessments of the patient. (A) Comparison of FEV₁ Initial test and 5-year follow-up. (B) Comparison of FVC initial test and 5-year follow-up. (C) Comparison of FEV₁/FVC initial test and 5-year follow-up.

at the 5-year follow-up. The results revealed that small airway dysfunction group had greater extent of emphysema, micronodules, mosaic attenuation and radiological score (Supplementary Table S7).

Univariable and Multivariable Analyses of Factors Influencing Airflow Obstruction at 5-year Follow-up

Univariable logistic regression identified age (*OR*: 1.079, 95% *CI*: 1.019–1.142, *P* = 0.009), and radiological score (*OR*: 1.445, 95% *CI*: 1.063–1.966, *P* = 0.019) at 5-year follow-up were associated with airflow obstruction. However, these associations were no longer significant on multivariable analysis (Table 4). Additionally, when patients were stratified by the median age and the median radiological score at 5-year follow-up, the older age and high radiological score groups exhibited significantly worse lung function compared to the younger age and low radiological score groups (Supplementary Tables S8–S9).

Chest Imaging Findings, Symptom Assessment, and Lung Function Characteristics in Patients with Airflow Obstruction

At the 5-year follow-up, the 9 patients with airflow obstruction had a mean age of 54.7 ± 13.5 years, including 6 males. Among them, four (all male) had a smoking history, with a median smoking exposure of 35.0 pack-years (IQR: 26.3–62.5). The mean FEV₁/FVC ratio was $56.26\% \pm 9.23\%$, with mean FEV₁ and FVC of 1.65 ± 0.75 L, and 2.84 ± 0.98 L, respectively. Chest CT imaging of these 9 patients revealed a variety of abnormalities: one female patient with a destroyed left lung and underwent lobectomy, and one male patient with a long-term history of coal dust exposure, presenting

typical pneumoconiotic micronodular lesions (Cases 8–9). The remaining 7 cases predominantly exhibited imaging features such as air trapping, emphysema, and small airway disease. Three non-smoking middle-aged patients (Cases 1–3) primarily exhibited significant air trapping on chest CT without other notable abnormalities, suggesting that their airflow obstruction was mainly caused by small airway disease secondary to TB. Meanwhile, the other four older patients with long-term smoking histories (Cases 4–7) showed coexisting emphysema and small airway disease on imaging, indicating that their airflow obstruction likely resulted from the combined effects of smoking and prior TB infection. Representative chest CT images of a middle-aged non-smoking female (Case 1) and an older smoking male (Case 4) are presented in Figure 4. Notably, four of these patients (aged < 60 years) maintained persistent airflow obstruction over the 5-year follow-up period (Table 5).

Case 1: A female patient with no smoking history was diagnosed with pulmonary TB at 30 years of age. Initial chest CT demonstrated multiple patchy opacities with diffuse mosaic attenuation in both lungs. Lung function test revealed airflow obstruction, with FEV_{1%} pred of 50.20%, FEV₁/FVC ratio of 59.50%, and DLCO% pred of 69.90%. At the 5-year follow-up, chest CT demonstrated scattered residual fibrocalcific nodules in both lungs, with no significant improvement in the diffuse mosaic attenuation. Lung function showed a decline in FEV_{1%} pred to 46.4%, and FEV₁/FVC ratio to 52.63% (A–D).

Case 4: A male patient with a 67 pack-year smoking history was diagnosed with pulmonary TB at the age of 56. Initial chest CT revealed a cavitary

Table 4. Univariable and multivariable analyses of factors influencing airflow obstruction at 5-year follow-up

Characteristics	Univariable analysis		Multivariable analysis	
	<i>OR</i> (95% <i>CI</i>)	<i>P</i> value	<i>aOR</i> (95% <i>CI</i>)	<i>P</i> value
Age (years)	1.079 (1.019–1.142)	0.009*	1.099 (0.986–1.225)	0.088
Sex	0.929 (0.200–4.306)	0.925	0.789 (0.029–21.701)	0.889
BMI (kg/m ²)	1.086 (0.838–1.407)	0.533	0.725 (0.425–1.237)	0.238
Smoking history	1.543 (0.357–6.675)	0.562	0.371 (0.002–66.581)	0.708
Previous TB	1.156 (0.114–11.774)	0.902	0.487 (0.004–65.859)	0.774
MDR	—	0.999	—	0.999
Radiological score	1.445 (1.063–1.966)	0.019*	1.539 (0.869–2.724)	0.139

Note. *OR*, odds ratio; 95% *CI*, 95% confidence interval; *aOR*, adjusted odds ratio; BMI, body mass index; TB, tuberculosis; MDR, multidrug resistance; **P* < 0.05.

lesion in the right upper lobe accompanied by bilateral emphysema. Lung function tests demonstrated airflow obstruction, with FEV_{1%} pred of 29.70%, FEV₁/FVC ratio of 54.02%, and DLCO% pred of 22.90%. At the 5-year follow-up, the cavity had resolved, but bilateral emphysema remained. Lung function further declined, with FEV_{1%} pred of

26.20%, FEV₁/FVC ratio of 45.08% (E-F).

DISCUSSION

This prospective cohort study represents the first long-term follow-up of TB patients in China over 5-year period, using post-TB treatment lung function at the 5-year mark as the primary outcome^[4]. At baseline, during active TB, 13.2% (7/53) of patients exhibited airflow obstruction, a proportion comparable to the 14.2% (52/365) reported in Malawi^[11]. However, at the 5-year follow-up, the proportion of patients with airflow obstruction increased to 17.0% (9/53). This study highlights that, even after receiving standardized, full-course anti-TB treatment, TB patients showed no significant improvement in lung function over the long-term. Furthermore, among the nine patients presenting with airflow obstruction at the 5-year follow-up, seven met the clinical criteria for TB-COPD^[8,15,17]. Notably, four of these patients were under 60 years old, and exhibited persistent airflow obstruction throughout the 5-year period, warranting heightened clinical attention.

Studies have indicated that up to 50% of TB patients continue to exhibit some form of persistent lung dysfunction after completing treatment^[26]. A recent retrospective cohort study from South Korea in 2025 evaluated lung function in 351 individuals with prior pulmonary TB, demonstrating that 20.2% developed COPD during follow-up, a progression rate comparable to our observed results^[27]. Small

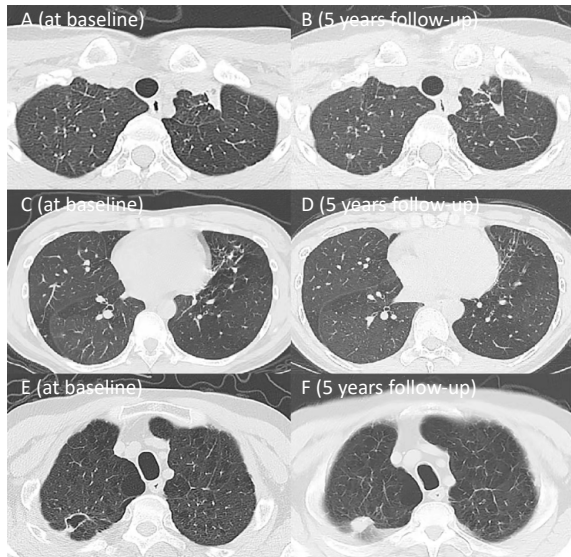


Figure 4. Two representative cases of airflow obstruction: non-smoker and smoker. (A–D) Comparison of chest CT at initial test and the 5-year follow-up in the non-smoker. (E–F) Comparison of chest CT at initial test and the 5-year follow-up in the smoker.

Table 5. Baseline characteristics and clinical features of 9 patients with airflow obstruction

Number of patients	Sex	Age (years)	Pack-years of smoking	Previous TB	FEV ₁ (L) (Initial test /5-year follow-up)	FVC (L) (Initial test /5-year follow-up)	FEV ₁ /FVC (%) (Initial test /5-year follow-up)	DLCO% pred (%) (Initial test /5-year follow-up)	Radiological score (Initial test /Treatment completion/5-year follow-up)	TB-COPD (Yes/No)
Case 1	Female	37	0	No	1.44/1.26	2.42/2.39	59.50/52.63	69.90/73.50	5.0/3.5/3.0	Yes
Case 2	Female	39	0	No	2.77/2.44	3.66/3.59	75.68/67.96	45.40/110.10	0.5/0.7/0.7	Yes
Case 3	Male	47	0	No	2.39/2.41	3.66/3.78	65.30/63.81	75.80/66.40	8.0/3.0/1.0	Yes
Case 4	Male	63	70	No	0.94/0.84	1.74/1.87	54.02/45.08	22.90/26.40	4.0/3.0/3.6	Yes
Case 5	Male	75	25	No	2.39/2.25	3.38/3.25	70.71/69.15	57.90/83.30	10.0/7.5/8.0	Yes
Case 6	Male	69	40	No	3.35/2.53	4.54/4.35	73.78/58.19	70.70/68.40	3.5/0.5/0.5	Yes
Case 7	Male	63	30	No	2.59/1.38	3.78/2.85	68.51/48.45	60.20/84.80	16.5/11.0/11.0	Yes
Case 8	Female	46	0	Yes	0.81/0.63	1.68/1.39	48.21/45.40	49.10/—	12.0/10.0/10.0	No
Case 9	Male	53	0	No	1.52/1.14	2.44/2.06	62.29/55.64	77.60/86.30	16.5/18.0/19.0	No

Note. TB, tuberculosis; TB-COPD, tuberculosis-associated chronic obstructive pulmonary disease; The definition of lung function parameters are consistent with the above mentioned; Case 8 had missing DLCO.

airway dysfunction, characterized by premature airway closure, air trapping, airflow limitation, and regional ventilation heterogeneity, is considered a key pathophysiological feature of TB-COPD^[28]. A prior case report documented a 23-year-old non-smoking male TB patient who developed severe chronic airflow limitation. Pathological examination revealed only residual TB lesions in the bilateral upper lobes, but pathological examination confirmed granulomatous inflammation in multiple lung areas, predominantly around small bronchovascular bundles, along with significant perilesional fibrosis^[29]. The aforementioned cross-sectional study from China found that 48.9% of patients with a TB history had small airway dysfunction—significantly higher than those without prior TB—further supporting the link between TB and small airway disease^[16]. A 2023 study from South Korea reported that 13.4% of TB patients exhibited airflow obstruction on spirometry post-treatment, despite no detectable residual lesions on CXR, suggesting that small airway and microvascular pathology are often undetectable by CXR, and may underlie functional impairment^[30]. Thus, while imaging is important for evaluating PTLD, lung function provides essential complementary information that imaging alone cannot capture^[31].

Previous studies have shown that TB patients who are older, long-term smokers, have severe/extensive lesions, receive irregular treatment, or experience recurrent infections are more prone to lung function decline^[21,31-33]. In our study, the nine patients with airflow obstruction were older and had greater smoking exposure than those with normal airflow function, which suggests that age and smoking are significant contributing factors to airflow obstruction^[34]. Although Multivariable analysis did not identify age, smoking history, or radiological score as independent risk factors, this may be related to the small sample size. A recent meta-analysis reported that drug-sensitive TB patients had significantly higher FVC and FEV₁ post-treatment compared to drug-resistant TB^[15]. In our cohort, only 3 patients had drug-resistant TB, yet their lung function remained normal throughout treatment and follow-up. This may be attributed to their younger age (< 50 years), male sex, limited lesion extent, absence of cavitary lesions, and the small sample size of drug-resistant cases, which may limit the conclusions of this observation. Additionally, 64.2% of patients in our study exhibited reduced diffusing capacity during the stable phase of anti-TB treatment, aligning with prior reports

(62.2%)^[35]. Mechanistically, TB infection triggers granulomatous inflammation and fibrotic repair. Post-TB pulmonary fibrosis can thicken alveolar walls, disrupt alveolar structure, and reduce the effective surface area for gas-exchange, thereby impairing diffusing capacity. Vascular inflammation or alveolar destruction may further contribute to the loss of diffusion surface area, exacerbating the dysfunction^[35,36].

STUDY LIMITATIONS

This study has several limitations: First, the study has a relatively high loss to follow-up over the 5-year period. Due to the COVID-19 pandemic, many patients were unable to undergo pulmonary function testing as scheduled, which also affected follow-up in the later stages of the study, potentially compromising statistical power. Nevertheless, there were no significant differences in baseline characteristics—including sex, age, radiological score, and lung function—between the 53 patients who completed follow-up and those lost to follow-up, suggesting that the follow-up group remained representative of the overall cohort. Second, the study enrolled outpatients with relatively mild TB. We speculate that hospitalized TB patients might exhibit a higher prevalence of airflow obstruction, which may not reflect the higher prevalence in hospitalized cohorts of airflow obstruction compared to hospitalized patients. Third, as a single-center study, these results may lack generalizability.

CONCLUSION

In summary, this study demonstrates that pulmonary TB patients show no significant improvement in overall lung function during 5-year follow-up following the completion of anti-TB treatment. The initial test revealed that 13.2% of patients presented with airflow obstruction. By the 5-year follow-up, this proportion had increased to 17.0%, with most cases attributable to TB-COPD. Notably, the development of airflow obstruction in young-to-middle-aged individuals highlights the need for greater clinical awareness. These findings underscore the importance of long-term monitoring for TB patients and support the routine assessment of lung function to enable early detection and intervention of pulmonary impairment. Future studies with expanded sample sizes will be conducted to further validate these findings.

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Competing Interests There are no conflicts of interest to declare.

Ethics This study was approved by the Medical Ethics Committee of Peking University Third Hospital (Ethical approval number: M2022296).

Authors' Contributions Full access to all study data and responsibility for data integrity and analytical accuracy were held by Zikang Sheng and Xiaoyan Gai. The study was jointly directed by Xiaoyan Gai and Yongchang Sun, who contributed equally as corresponding authors. Patient recruitment was conducted by Wenli Cao. Follow-up was performed by Zikang Sheng and Wenli Cao. Patient data collection, data analysis, and manuscript preparation were conducted by Zikang Sheng, Hongling Chu, Yanqing Le, Junfeng Wu, Yafei Rao and Brian Allwood. All authors critically reviewed the manuscript, approved the final version, and agreed to be accountable for all aspects of the work.

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