

**Risk factors and biomarkers for post-tuberculosis lung damage
in a Chinese cohort: protocol for a prospective observational
study**

ABSTRACT

Introduction: Post-tuberculosis lung damage (PTLD) refers to the residual pulmonary impairment following the completion of tuberculosis (TB) treatment, characterized by persistent respiratory symptoms and abnormal pulmonary function. The risk factors and biomarkers for PTLD have been scarcely investigated. Additionally, it remains unclear whether and to what extent cigarette smoking affects PTLD in patients with TB.

Methods and analysis: This prospective observational study will enroll 400 adult male ever-smoker or never-smoker patients aged 25–60 years, with newly confirmed active TB between 2022 and 2024 from the Department of Respiratory and Critical Care Medicine at Peking University Third Hospital and the Tuberculosis Department at Beijing Geriatric Hospital. Baseline data (age, smoking history, and smoking pack-years), clinical symptoms, lung functions, and chest CT (computed tomography) findings will be prospectively collected. Respiratory questionnaires, lung function measurements, and chest CT examinations will be completed during follow-up visits 6 months after the initiation of TB treatment, immediately after the completion of TB treatment, and 1 year, 2 years, and 3 years after the completion of TB treatment. Peripheral blood samples will be obtained at baseline, and a Luminex xMAP-based multiplex immunoassay will be used to measure 40 inflammatory mediators and cytokines in serum. The collected data will be analyzed to determine the incidence and factors/biomarkers of PTLD after TB treatment.

Ethics and dissemination: The study was approved by the Ethics Committee of Peking University Third Hospital (approval number: (2022)271-03; approval date: June 8, 2022). The research results will be disseminated through scientific and medical conferences and will be published in an academic journal.

Keywords: tuberculosis; post-tuberculosis lung damage; clinical epidemiology; cigarette smoking; respiratory infection

Objectives

This prospective study aims to determine the incidence of PTLD, examine trends in the changes in lung function, and investigate the impact of smoking and other factors on respiratory symptoms, lung function, and chest CT findings, which will aid in the development of prognostic and therapeutic strategies for PTLD.

METHODS AND ANALYSIS

Study participants

This prospective observational study will enroll male patients who were newly diagnosed with active TB from the Department of Respiratory and Critical Care Medicine at Peking University Third Hospital and the Tuberculosis Department at Beijing Geriatric Hospital between 2022 and 2024. The study team will screen patients who were newly diagnosed with active TB in an outpatient setting.

Inclusion criteria

Male patients aged 25–60 years newly diagnosed with pulmonary TB—based on the 2018 diagnostic criteria for TB released by the National Health and Family Planning Commission of the People’s Republic of China—will be included in the study. Sputum smear microscopy and TB culture tests will be performed for patients exhibiting persistent respiratory symptoms until 6 months after treatment initiation or until the completion of treatment.

Exclusion criteria

The following patients will be excluded from analysis: (1) patients with positive sputum smear or TB culture results; (2) human immunodeficiency virus-positive patients; (3) patients infected with multidrug-resistant TB; (4) patients with malignant neoplasms (e.g., lung cancer) or severe cardiovascular and cerebrovascular diseases; (5) non-compliant patients who were unable to complete the lung function tests; and (6) patients without lung parenchymal destruction (such as tuberculous pleurisy).

All study participants provided written informed consent. The study flowchart is presented in Figure 1.

Study content

This study will be conducted at Peking University Third Hospital, and Beijing Geriatric Hospital 6 months after the initiation of TB treatment, immediately after the completion of the treatment, and 1 year, 2 years, and 3 years after the completion of treatment.

The following general data obtained from the study participants will be recorded: age, socioeconomic status (employment and income), number of years of smoking, smoking index (smoking index = number of cigarettes smoked per day × years of smoking), symptoms, St. George's Respiratory Questionnaire (SGRQ) scores, COPD Assessment Test (CAT) scores, blood test results (complete blood count, CD4 lymphocyte count, plasma glucose, glycated hemoglobin). Peripheral blood samples will be obtained at baseline for the measurement of inflammatory mediators and cytokines will be detected. A symptom questionnaire survey, chest CT, and lung function tests will be performed according to standard procedures (Table 1).

Prior to enrollment, patients will be informed of the study as well as of the relevant examinations that will be performed.

Primary outcome measures

Trends in the changes in lung function, including forced expiratory volume (FEV₁), forced vital capacity (FVC), and FEV₁/FVC.^a

Secondary outcome measures

Absorption of TB lesions on lung CT scans after TB treatment

Chest CT images will be interpreted by a respiratory physician and a radiologist.

Parenchymal and airway lesions detected on CT scans will be recorded.^[14, 15]

Quality of life and respiratory symptoms

The CAT (self-administered), SGRQ, and UK Medical Research Council (MRC) Dyspnea Scale will be utilized.

Serum inflammatory markers and their correlation with airflow limitation
Serum cytokines will be detected at baseline prior to TB treatment.