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ORIGINAL RESEARCH

Risk Factors for Pulmonary Tuberculosis with Tracheobronchial Tuberculosis: Propensity Score Matching Analysis

Yinping Feng*, Jing Guo, Shuirong Luo, Guangnao Zhou*

Department of Tuberculosis, Lishui Hospital of traditional Chinese Medicine Affiliated to Zhejiang University of traditional Chinese Medicine, Lishui, 323000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Guangnao Zhou, Email zgn198615@163.com

Background: Pulmonary tuberculosis (PTB) with tracheobronchial tuberculosis (TBTB) can lead to tracheal stenosis and atelectasis, but the specific risk factors are currently unclear. Therefore, the goal of this retrospective study is to address this issue and help with the early diagnosis of TBTB.

Methods: Please include PTB hospitalized in our hospital from January 2021 to October 2023 in the study. After conducting bronchoscopy examinations, the patients were divided into two groups: the PTB group and the PTB&TBTB group. We used the propensity score matching (PSM) to align the baseline data of the two groups of patients, and then performed multiple logistic regression analysis to identify risk factors.

Results: 643 patients with PTB were included in the study, 227 of whom (35.30%) were diagnosed with TBTB. A total of 204 pairs of patients were successfully matched using the PSM. After matching, there were no statistically significant differences in basic information between the two groups of patients ($P>0.05$). Multivariate logistic regression analysis revealed that disease course ≥ 1 month (OR=1.85, 95% CI: 1.21–2.83), complicated with diabetes (OR=3.00, 95% CI: 1.91–4.70), and concomitant pulmonary cavity (OR=3.46, 95% CI: 2.23–5.36) were risk factors for PTB accompanied by TBTB (all $P<0.05$).

Conclusion: After adjusting for various influencing factors using PSM, the analysis demonstrated that disease course ≥ 1 month, complicated with diabetes, and concomitant pulmonary cavity are risk factors for PTB combined with TBTB. This emphasizes the significance of improving screening and implementing early intervention measures.

Keywords: pulmonary tuberculosis, tracheobronchial tuberculosis, propensity score matching, risk factors

Background

TBTB is a distinctive presentation of PTB that lacks specificity in clinical practice, the lesion is mainly located on the inner wall of the airway, with the vast majority secondary to pulmonary tuberculosis, and some patients may not necessarily have involvement in lung parenchyma. Without prompt treatment, it can cause narrowing, occlusion, and softening of the central airway, leading to inadequate airway drainage and atelectasis. It is often overlooked and misdiagnosed. Currently, bronchoscopy allows for direct observation of the bronchial mucosa and lumen, as well as the ability to conduct further pathogenic and pathological examinations through biopsy, brushing, and lavage, making it the most reliable method for diagnosing TBTB. By analyzing the risk factors of PTB accompanied by TBTB based on the results of bronchoscopy examinations, we can guide the clinical prediction of these patients, and improve bronchoscopy screening, early treatment, and long-term prognosis.

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Object and Methods

Research Object Selection

A retrospective analysis was conducted on clinical data from PTB who were hospitalized in our department from January 2020 to October 2023. This included the patients' age, gender, occupation, drinking history, smoking history, body mass index (BMI), serum albumin levels, disease course, presence of hemoptysis, diabetes status, presence of cavities, and presence of sputum bacteria. The study was approved by the hospital's Medical Ethics Committee (Approval number: LW-2024005).

Methods

Patients Inclusion and Exclusion Criteria

Inclusion criteria: (1) Patients who meet the diagnostic criteria for PTB;[1] (2) Patients who have undergone bronchoscopy examination; (3) The clinical data are complete. Exclusion criteria: (1) Patients with PTB who have not undergone bronchoscopy examination.; (2) Patients with significant MISSING clinical data.

Patients Data Collection

Patients with significant missing clinical data, such as age, gender, occupation, history of alcohol consumption, history of smoking, BMI, presence of diabetes, serum albumin levels, hemoptysis, and presence of cavity, were collected for the patients through the inpatient management information system.

Case Grouping

Based on the findings of fiberoptic bronchoscopy examination, the study participants were classified into two groups: PTB group and PTB&TBTB group.

TBTB

We previously classified forms of tracheobronchial tuberculosis (TBTB) into seven subtypes by bronchoscopic finding: actively caseating, edematous-hyperemic, fibrostenotic, tumorous, granular, ulcerative, and nonspecific bronchitic.[2]

Statistical Analysis

All data were analyzed using SPSS 26.0 software. Count data are expressed as percentages (%), and differences between groups are compared using chi-square (χ^2) test. Measurement data that conforms to a normal distribution are represented by the mean ± standard deviation ($\bar{x} \pm s$) and *t*-test is used. Measurement data that do not conform to a normal distribution are represented by the median (M) and interquartile range (P25, P75). Inter-group comparisons are performed using the Mann–Whitney *U*-test. The PSM extension program was utilized to perform propensity score matching between two groups of patients using the 1:1 nearest neighbor matching method, and the quality of the matching results was ensured by defining clamp values. Multiple logistic regression analysis was utilized to examine the factors influencing pulmonary tuberculosis with tracheal and bronchial tuberculosis, and a statistically significant difference was found ($P<0.05$).

Results

Case Screening

A total of 895 patients with PTB were included in the study; however, 35 had incomplete clinical data and 217 did not undergo bronchoscopy examination. As a result, 643 patients were ultimately included and categorized into PTB group (416 cases), PTB&TBTB group (227 cases) based on the presence of tracheal and bronchial tuberculosis. Following propensity score matching (PSM), a total of 204 pairs of patients were successfully matched (Figure 1).

Comparison of Clinical Features Between Two Groups of Patients Before PSM

There were no statistically significant differences in age and occupation between the two groups of patients ($P>0.05$). However, there were statistically significant differences in BMI, alcohol consumption, smoking, and the occurrence of hemoptysis ($P<0.05$; Table 1).

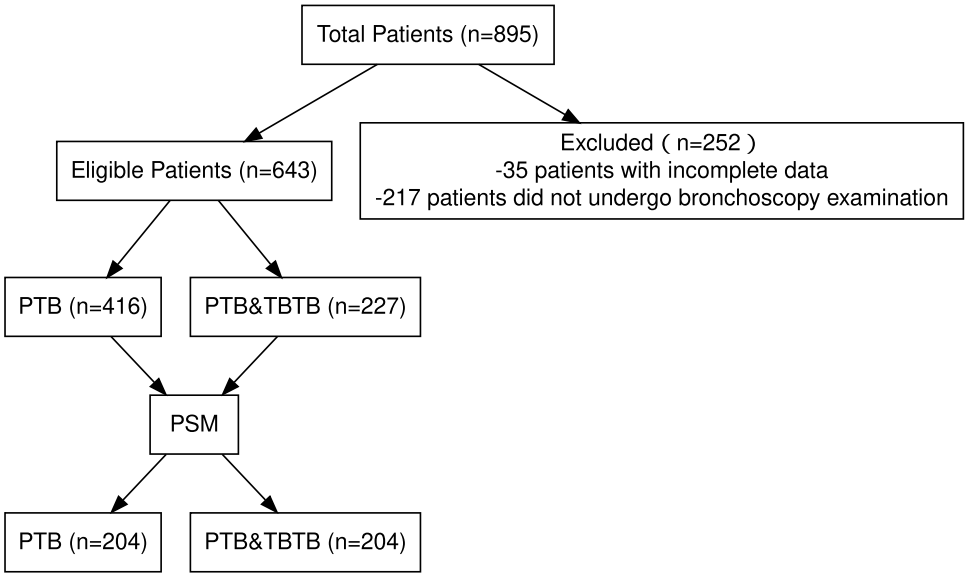

Figure 1 A flow chart for screening eligible studies.

Clinical Characteristics of Two Groups of Patients After PSM

A 1:1 propensity score matching was performed using age, gender, occupation, BMI, alcohol consumption, smoking, and hemoptysis as matching variables. A total of 204 pairs of patients were successfully matched, and no statistically significant differences were observed in each variable after matching ($P>0.05$; Table 2).

Single Factor Analysis After PSM

After performing PSM to balance the covariates of the two groups, we subsequently compared the disparities in other factors among the two patient groups. Our analysis revealed statistically significant variances between the two groups in terms of disease course≥1 month, complicated with diabetes, and concomitant pulmonary cavity (all $P<0.05$; Table 3).

Table 1 Comparison of Clinical Features Between Two Groups of Patients Before PSM

Variable	Total (n = 643)	PTB (n = 416)	PTB&TBTB (n = 227)	Statistic	*P*
Age, Mean ± SD	58.75 ± 17.86	59.53 ± 17.91	57.31 ± 17.72	t=1.507	0.132
BMI, M (Q_1, Q_3)	20.43 (18.97, 22.22)	20.76 (19.15, 22.43)	19.83 (18.73, 22.05)	Z=2.565	0.010
Gender, n (%)				χ^2=33.820	<0.001
Female	182 (28.3)	86 (20.67)	96 (42.29)		
Male	461 (71.7)	330 (79.33)	131 (57.71)		
Work, n (%)				χ^2=0.030	0.863
Non-peasants	87 (13.53)	57 (13.70)	30 (13.22)		
Peasants	556 (86.47)	359 (86.30)	197 (86.78)		
Smoking, n (%)				χ^2=4.757	0.029
No	397 (61.74)	244 (58.65)	153 (67.40)		
Yes	246 (38.26)	172 (41.35)	74 (32.60)		
Drinking, n (%)				χ^2=8.568	0.003
No	318 (49.46)	188 (45.19)	130 (57.27)		
Yes	325 (50.54)	228 (54.81)	97 (42.73)		
Hemoptysis, n (%)				χ^2=24.788	<0.001
No	452 (70.3)	320 (76.92)	132 (58.15)		
Yes	191 (29.7)	96 (23.08)	95 (41.85)		

Table 2 Clinical Characteristics of Two Groups of Patients After PSM

Variable	Total (n = 408)	PTB (n = 204)	PTB&TBTB (n = 204)	Statistic	*P*
Age, Mean ± SD	58.63 ± 17.67	58.36 ± 18.59	58.91 ± 16.74	t=0.311	0.756
BMI, M (Q_1, Q_3)	20.07 (18.94, 22.03)	20.43 (19.10, 22.03)	19.84 (18.73, 22.04)	Z=0.874	0.382
Gender, n (%)				χ^2=0.042	0.839
Female	156 (38.24)	79 (38.73)	77 (37.75)		
Male	252 (61.76)	125 (61.27)	127 (62.25)		
Work, n (%)				χ^2=0.189	0.664
Non-peasants	55 (13.48)	26 (12.75)	29 (14.22)		
Peasants	353 (86.52)	178 (87.25)	175 (85.78)		
Smoking, n (%)				χ^2=0.277	0.599
No	273 (66.91)	139 (68.14)	134 (65.69)		
Yes	135 (33.09)	65 (31.86)	70 (34.31)		
Drinking, n (%)				χ^2=0.355	0.551
No	220 (53.92)	107 (52.45)	113 (55.39)		
Yes	188 (46.08)	97 (47.55)	91 (44.61)		
Hemoptysis, n (%)				χ^2=0.010	0.919
No	247 (60.54)	124 (60.78)	123 (60.29)		
Yes	161 (39.46)	80 (39.22)	81 (39.71)		

Table 3 Single Factor Analysis After PSM

Variable	Total (n = 408)	PTB (n = 204)	PTB&TBTB (n = 204)	Statistic	*P*
Disease course, n (%)				χ^2=7.155	0.007
<1 month	197 (48.28)	112 (54.90)	85 (41.67)		
≥1 month	211 (51.72)	92 (45.10)	119 (58.33)		
DM, n (%)				χ^2=23.940	<0.001
No	267 (65.44)	157 (76.96)	110 (53.92)		
Yes	141 (34.56)	47 (23.04)	94 (46.08)		
Hypoalbuminemia, n (%)				χ^2=3.347	0.067
No	250 (61.27)	134 (65.69)	116 (56.86)		
Yes	158 (38.73)	70 (34.31)	88 (43.14)		
Cavity, n (%)				χ^2=31.319	<0.001
No	251 (61.52)	153 (75.00)	98 (48.04)		
Yes	157 (38.48)	51 (25.00)	106 (51.96)		
Pathogen positive, n (%)				χ^2=1.428	0.232
No	182 (44.61)	97 (47.55)	85 (41.67)		
Yes	226 (55.39)	107 (52.45)	119 (58.33)		

Multivariate Logistic Regression Analysis After PSM

The variables that demonstrated statistical significance (P<0.05) in the aforementioned univariate analysis were considered as independent variables, while the presence or absence of tracheobronchial tuberculosis was considered the dependent variable for binary logistic regression analysis. The results indicated that disease course≥1 month (OR=1.85, 95% CI: 1.21–2.83), complicated with diabetes (OR=3.00, 95% CI: 1.91–4.70), and concomitant pulmonary cavity (OR=3.46, 95% CI: 2.23–5.36) were identified as risk factors for PTB accompanied by TBTB (P<0.05; Table 4).

Table 4 Multivariate Logistic Regression Analysis After PSM

Variable	*β*	*S.E*	*Z*	*P*	OR (95% CI)
Disease course≥1 month	0.62	0.22	2.85	0.004	1.85 (1.21–2.83)
Complicated with diabetes	1.10	0.23	4.79	<0.001	3.00 (1.91–4.70)
Concomitant pulmonary cavity	1.24	0.22	5.53	<0.001	3.46 (2.23–5.36)

Discussion

According to the latest global tuberculosis report from the World Health Organization in 2023, there were 10.6 million tuberculosis patients worldwide in the previous year, with 1.3 million deaths attributed to tuberculosis.[3] TBTB is a distinct form of tuberculosis that infects the trachea and bronchial mucosa, and can involve any layer of the tracheobronchial wall.[4] It is a prevalent subtype of PTB, primarily affecting the mucosa, submucosa, smooth muscle, cartilage, and even the outer membrane of the trachea or bronchi.[5] The majority of TBTB cases are secondary to PTB, and some patients with TBTB may not necessarily have lung parenchyma involvement.[6] According to reports, TBTB is observed in 10% to 39% of patients with PTB.[7,8] TBTB can result in thickening of the tube wall, narrowing of the tube lumen, bronchial dissemination, bronchiectasis, and may also contribute to airway stenosis.[9] Sme of the clinical manifestations of TBTB lack specificity, so vigilance is necessary. Combined with imaging, timely improvement of bronchoscopy examination, and early treatment, these manifestations can also lead to tracheal and bronchial stenosis.[10] According to reports, during the healing process of TBTB, it can lead to tracheal and bronchial fibrosis and result in airway stenosis in 11% to 42% of patients.[8] A study in South Korea also showed that TBTB is one of the main causes of benign airway stenosis, which can lead to progressive dyspnea and hypoxemia.[11] TBTB is often misdiagnosed or delayed in clinical practice, primarily due to insufficient imaging and bronchoscopy evaluation.[12] Currently, bronchoscopy is an essential diagnostic method for TBTB, allowing for direct observation of tracheal lesions and determination of their type, location, range, and severity. The study of risk factors for PTB accompanied by TBTB can effectively guide clinical practice, and conducting bronchoscopy on high-risk patients can lead to accurate diagnosis and treatment.

This study aims to investigate the risk factors for PTB accompanied by TBTB. The findings indicate that PTB with disease course≥1 month are more likely to develop TBTB (OR=1.85, 95% CI: 1.21–2.83). Delayed treatment, defined as a disease course≥ 1 month, is associated with a higher likelihood of Mycobacterium tuberculosis spreading. Several studies have identified patients with symptoms lasting for more than 4 weeks before treatment as independent risk factors for PTB with concomitant TBTB.[8] If the disease course is prolonged, the patient's body remains in a state of high metabolism and high consumption for an extended period of time, making them more susceptible to nutritional risks and disrupting the patient's defense mechanisms. Patients with PTB and diabetes have a higher likelihood of being associated with TBTB (OR=3.00, 95% CI: 1.91–4.70). In China, the prevalence of diabetes is as high as that of tuberculosis. It is essential to conduct simultaneous screening for both diseases to enhance the diagnosis and management of patients with dual impact, particularly to reduce the risk of tuberculosis cavities.[13] Diabetes is recognized as a risk factor for PTB. A systematic review comparing 13 studies investigating the association between diabetes and tuberculosis revealed that the risk of tuberculosis in patients with diabetes was approximately three times higher.[14] The T lymphocyte count and function are reduced in patients with diabetes.[15] Some published comparative studies indicate that cavitary diseases are more common in patients with diabetes than in non-diabetic patients.[16] It is worth considering that diabetes patients may have immune dysfunction, which makes them more susceptible to cavitations.[13] Patients with cavities are significantly more likely to have TBTB (OR=3.46, 95% CI: 2.23–5.36). Cavity formation is one of the most frequent imaging manifestations of PTB, with studies indicating that approximately 29% to 87% of patients diagnosed with PTB exhibit cavity-like changes.[17] The treatment outcomes for PTB are suboptimal, with high levels of infectivity and drug resistance. There is also a correlation between treatment recurrence and the presence of cavities.[18] The formation of TBTB is generally believed to be caused by tuberculosis through four pathways: direct dissemination, lymphatic drainage, hematogenous dissemination, and invasion of adjacent lymph node tuberculosis into the bronchi. Among these pathways, pulmonary tuberculosis is most commonly spread through the trachea. Pulmonary cavities are caused by

liquefaction and necrosis of lung lesions after infection with Mycobacterium tuberculosis, which are discharged through the bronchi and introduced into the air, making TBTB more likely to occur. There is currently a widespread belief that the development of pulmonary tuberculosis cavities is linked to the immune and nutritional status of the patient's body. Immune function is associated with the predominance of T helper (Th2) CD4+ cells in the alveoli, and a decrease in CD4+ cells can lead to increased susceptibility in the body.[19] Several studies have demonstrated that patients with cavities exhibit higher sputum bacterial positivity and higher concentrations of sputum bacteria.[20]

To conclude, the PSM method effectively balanced the bias of confounding, revealing that course≥1 month, complicated with diabetes, concomitant pulmonary cavity were significant risk factors for PTB with TBTB. However, TBTB are associated with a poor prognosis, often leading to tracheal stenosis and breathing difficulties. As a result, early bronchoscopy screening should be conducted in clinical practice for PTB with these identified risk factors, enabling prompt diagnosis and treatment. It should be noted that this study has certain limitations, and it is recommended that future research includes more prospective studies with larger sample sizes to further delineate the risk factors for patients with PTB accompanied by TBTB.

Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval and Consent to Participate

I confirm that I have read the Editorial Policy pages. This study was conducted with approval from the Ethics Committee of Lishui Hospital of Traditional Chi- nese Medicine. This study was conducted in accordance with the declaration of Helsinki. Written informed consent was obtained from all participants.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests in this work.

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