

## Original Article

# Efficacy analysis of bronchoscopic triple-drug delivery combined with chemotherapy for re-treatment of smear-positive cavitory pulmonary tuberculosis

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Received May 6, 2019; Accepted July 11, 2019; Epub September 15, 2019; Published September 30, 2019

**Abstract:** Objective: The aim of the current study was to analyze the clinical effects of bronchoscopic triple-drug delivery combined with chemotherapy for re-treatment of smear-positive cavitory pulmonary tuberculosis. Methods: A total of 144 patients, experiencing failed initial treatments for cavitory pulmonary tuberculosis, were enrolled in the study. All patients were smear-positive before receiving re-treatment. The patients were divided into the observation group and control group, according to a random number table, with 72 patients in each group. The control group received the routine chemotherapy regimen for 8 months. The observation group received bronchoscopic triple-drug delivery in combination with the routine chemotherapy regimen. Sputum conversion rates, cavity closure rates, and symptom improvement levels were compared between the groups. Immune function and pulmonary function were also compared between the two groups. Results: Sputum conversion rates and cavity closure rates in the observation group were 94.44% and 84.72%, respectively, significantly higher than those of the control group ( $P < 0.05$ ). After the consolidation phase, the observation group had lower scores concerning tuberculosis symptoms, including lower fevers, coughing and sputum production, chest pain, and loss of appetite ( $P < 0.05$ ).  $CD3^+$ ,  $CD4^+$  T-cells, and  $CD4^+/CD8^+$  ratios in the observation group were significantly higher at the end of 8 months. However,  $CD8^+$  T-cells were lower than those of the control group (all  $P < 0.05$ ). With the conclusion of treatment, pulmonary function in the observation group was better than that in the control group (all  $P < 0.05$ ). Conclusion: Bronchoscopic triple-drug delivery combined with chemotherapy for re-treatment of smear-positive cavitory pulmonary tuberculosis is more effective than chemotherapy alone. Therefore, this method is worthy of promotion in clinical practice.

**Keywords:** Bronchoscopy, chemotherapy, re-treatment of smear-positive cavitory pulmonary tuberculosis, pulmonary function, immune function

## Introduction

Tuberculosis is one of the most serious public health problems, worldwide. Current data indicates that about 1.8 million people die each year from tuberculosis [1]. At present, China is experiencing a serious tuberculosis epidemic. According to statistics, incidence and mortality rates of tuberculosis in China rank in the top 3 of Class A and Class B infectious diseases, making it a serious potential threat to the physical and mental health of the people [2]. Pulmonary tuberculosis is a lung disease caused by mycobacterium tuberculosis (MTB) infections. It is clinically characterized by coughing, sputum production, dyspnea, hemoptysis, low fever, loss of appetite, and chest pain. With the wide application of chemotherapy drugs in China, more than 95% of patients can be cured

with timely diagnosis and standardized treatment [3, 4]. However, in recent years, due to irrational and irregular drug use, the number of patients requiring re-treatment for tuberculosis has increased significantly. This is especially true for patients with smear-positive cavitory pulmonary tuberculosis. As the disease progresses and recurs, the cavity wall may appear thickened and fibrotic. Thus, it is difficult for orally-delivered chemotherapy drugs to penetrate the thickened cavity wall, reaching an inhibitory concentration. This factor is responsible for unsatisfactory therapeutic efficacy rates.

With the emergence and development of electronic bronchoscopy procedures, it is possible to re-treat smear-positive cavitory pulmonary tuberculosis with local anti-tuberculosis drug

## Bronchoscopic drug delivery for treatment of tuberculosis

delivery. This method can directly deliver chemotherapy drugs into lesions, improving local concentrations. This helps to avoid inefficiencies of oral deliveries, producing full therapeutic effects of the anti-tuberculosis drugs. In addition, bronchoscopy procedures can eliminate bronchial secretions and caseous necrosis, clearing the bronchial lumen. This is conducive to the formation of fresh granulation tissue and absorption of lesions [5, 6]. However, there are few reports concerning the method of bronchoscopic drug delivery for management of tuberculosis. The current study conducted a randomized controlled trial, analyzing the efficacy of bronchoscopic triple-drug delivery. The aim of the current study was to find a better alternative for re-treatment of smear-positive cavitory pulmonary tuberculosis.

### Materials and methods

#### Patients

A total of 144 patients, experiencing failed initial treatments for cavitory pulmonary tuberculosis, admitted to Lanling County People's Hospital. From June 2017 to July 2018, were enrolled in the study. All patients were smear-positive before re-treatment. The patients were divided into the observation group and control group, according to a random number table, with 72 patients in each group. The control group received routine chemotherapy for 8 months. The observation group received bronchoscopic triple-drug delivery in combination with routine chemotherapy. All patients provided informed consent. The study was approved by the Ethics Committee of Lanling County People's Hospital.

**Inclusion criteria:** Patients met the diagnostic criteria for cavitory tuberculosis according to the *Guidelines for Diagnosis and Treatment of Tuberculosis* developed by the Chinese Tuberculosis Society of the China Medical Association in 2013 [7]; Chest X-rays showed lesions confined in one lobe and there was only one tuberculosis cavity; Sputum smear was positive; Aged between 18 and 65 years old.

**Exclusion criteria:** Patients with multiple tuberculosis cavities, autoimmune diseases, diabetes, extrapulmonary tuberculosis, or lung cancer; Patients with respiratory failure or hemoptysis; Patients with major organ dysfunction; Under immunosuppressive treatment or diagnosed with HIV infection; History of cognitive or

mental disorders; Allergic to any of the drugs used in this study.

#### Methods

The control group received the conventional standard chemotherapy regimen 2HRZES/6-HRE: H: Isoniazid (Guangdong Huanan Pharmaceutical Group Co., Ltd., China) 0.30 g/day orally once a day; R: Rifampicin (Hainan Pharmaceutical Factory Co., Ltd., China) 0.60 g/day orally once a day; Z: Pyrazinamide (Shenyang Hongqi Pharmaceutical Co., Ltd., China) 1.50 g/day orally once a day; E: Ethambutol (Guangzhou Baiyunshan Mingxing Pharmaceutical Co., Ltd., China) 0.75 g/day orally once a day; S: Streptomycin (Huabei Pharmaceutical Co., Ltd., China) 0.75 g/day by intramuscular injections, once a day. After 2 months of the intensive phase, pyrazinamide and streptomycin were discontinued. The other drugs were continued for another 6 months, including the consolidation phase. The observation group was treated with bronchoscopic-delivered triple-drugs, based on the above regimen. Patients in the observation group underwent electronic bronchoscopy procedures, aiming to determine the distribution of lesions in the bronchus. Purulent secretions, caseous necrosis, and granulation tissue were then removed, clearing the bronchial lumen. A catheter was inserted 8 mm distal to the tip of the bronchoscope, delivering the triple anti-tuberculosis drug mixture. This included 5 mL 0.90% sodium chloride solution, 0.10 g isoniazid (Shanghai Xinya Pharmaceutical Co., Ltd., China), 0.10 g levofloxacin injections (Shandong Qidu Pharmaceutical Co., Ltd., China), and 0.20 g amikacin injections (Shanghai Fuda Pharmaceutical Co., Ltd., China). Dosages were adjusted based on patient conditions, ensuring that the volume was no more than 10 mL. The drug mixture was aspirated and sprayed several times, achieving uniform drug distribution. After the catheter and the bronchoscope were withdrawn, patients maintained the lateral decubitus position for no less than 30 minutes. Bronchoscopic treatment was administered once a week for 8 months.

#### Observational indices

##### *Sputum negative conversion rates*

Sputum smear tests were performed once per month. Sputum negative conversion is defined

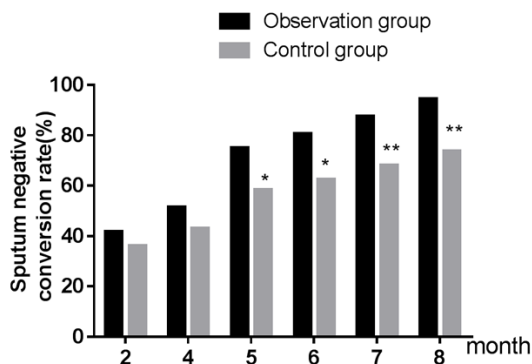
## Bronchoscopic drug delivery for treatment of tuberculosis

**Table 1.** Comparison of general conditions ( $\bar{x} \pm sd$ , n, %)

Group	Observation group (n = 72)	Control group (n = 72)	$\chi^2/t$	P
Gender			0.117	0.732
Male	43	45		
Female	29	27		
Age (year)	38.60 $\pm$ 7.50	37.30 $\pm$ 8.10	1.057	0.293
Course of disease (year)	3.05 $\pm$ 0.54	3.10 $\pm$ 0.56	0.545	0.586
Cavity type			0.417	0.812
Fibrous cavity	43	42		
Caseous cavity	27	29		
Others	2	1		

**Table 2.** Comparison of sputum conversion rates (n, %)

Group	Observation group (n = 72)	Control group (n = 72)	$\chi^2$	P
At the end of 2 <sup>nd</sup> month	30 (41.67)	26 (36.11)	0.468	0.494
At the end of 4 <sup>th</sup> month	37 (51.39)	31 (43.06)	1.003	0.317
At the end of 5 <sup>th</sup> month	54 (75.00)	42 (58.33)	4.500	0.034
At the end of 6 <sup>th</sup> month	58 (80.56)	45 (62.50)	5.763	0.016
At the end of 7 <sup>th</sup> month	63 (87.50)	49 (68.06)	7.875	0.005
At the end of 8 <sup>th</sup> month	68 (94.44)	53 (73.61)	11.642	0.001



**Figure 1.** Comparison of sputum negative conversion rates. \*P < 0.05, \*\*P < 0.01, compared with the observation group.

as two consecutive negative smear tests, with the smear tests remaining negative until the end of treatment [8].

### Cavity changes

Chest X-rays were obtained after the intensive phase and consolidation phase, observing changes of the cavities. Cavity changes were assessed as follows: 1) Closed: Cavity disappeared; 2) Shrunken: Reduction of the cavity

diameter was more than half of the original cavity; 3) Unchanged: Reduction or expansion of the cavity was less than half the diameter of the original cavity; and 4) Expanded: Expansion of the cavity was more than half the diameter of the original cavity [9].

### Symptom improvements

Before and immediately after the 8 months of treatment, patient symptoms, including low fever (37.20-37.80°C), coughing and sputum production, chest pain, and loss of appetite, were assessed based on 4-scale scoring criteria: 0 points: No symptoms; 1 point: Mild; 2 points: Moderate; 3 points: Severe.

Low fever: 0 points: No symptoms; 1 point: Occasional low fever in the afternoon; 2 points: Frequent low fever in the afternoon; 3 points: Persistent low fever in the afternoon.

Coughing and sputum production: 0 points: No symptoms; 1 point: Occasional coughing with no sputum; 2 points: Frequent coughing with small amounts of sputum that moderately affected patient daily life; 3 points: Frequent coughing with large amounts of sputum, severely affecting patient daily life. Chest pain: 0 points: No symptoms; 1 point: Mild pain and tolerable; 2 points: Moderate pain that affected patient sleep, barely tolerable; 3 points: Severe pain and intolerable. Loss of appetite: 0 points: No symptoms; 1 point: Decreased appetite; 2 points: No appetite; 3 points: Anorexia accompanied by fat aversion, fatigue, nausea, and vomiting.

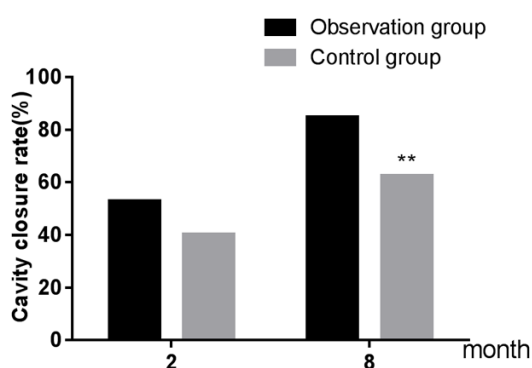
### Immune function

Before and immediately after treatment, 5 mL of peripheral blood was collected from each patient. ZS-AD6 flow cytometry (Suzhou Zhongsheng Medical Technology Co., Ltd., China) was used to measure CD3<sup>+</sup>, CD4<sup>+</sup>, and CD8<sup>+</sup> T-cells in peripheral blood via monoclonal antibody immunofluorescence. CD4<sup>+</sup>/CD8<sup>+</sup> ratios were calculated based on obtained values.

## Bronchoscopic drug delivery for treatment of tuberculosis

**Table 3.** Comparison of cavity changes (n, %)

Group	Observation group (n = 72)	Control group (n = 72)	u	P	$\chi^2$	P
At the end of 2 <sup>nd</sup> month			1.879	0.060		
Closed	38 (52.78)	29 (40.28)			2.261	0.133
Shrunken	24 (33.33)	25 (37.72)				
Unchanged	10 (13.89)	14 (19.44)				
Expanded	0 (0.00)	4 (5.56)				
At the end of 8 <sup>th</sup> month			3.045	0.002		
Closed	61 (84.72)	45 (62.50)			9.152	0.003
Shrunken	7 (9.72)	16 (22.22)				
Unchanged	4 (5.56)	8 (11.11)				
Expanded	0 (0.00)	3 (4.17)				



**Figure 2.** Comparison of cavity closure rates. \*\*P < 0.01, compared with the observation group.

### Pulmonary function

All patients were subject to pulmonary function tests, before and after treatment, using the BH9CMS-2 lung function machine (Beijing Zhongxi Yuanda Technology Co., Ltd., China). Pulmonary function parameters, including forced vital capacity (FVC), forced expiratory volume in 1 s (FEV<sub>1</sub>), and inspiratory capacity (IC), were collected for comparisons.

### Statistical analysis

Data were analyzed with SPSS 19.0 statistical package. Quantitative values are expressed as mean  $\pm$  standard deviation ( $\bar{x} \pm sd$ ) and differences between groups were evaluated using t-tests. Enumeration data are expressed as number/percentages (n/%) and were compared by  $\chi^2$  tests. Overall cavity changes between the two groups were compared using Mann-Whitney U-tests. P < 0.05 indicates statistical significance.

## Results

### Comparison of general conditions

There were no significant difference in general conditions between the two groups (all P > 0.05), as shown in **Table 1**.

### Comparison of sputum negative conversion rates

Sputum negative conversion rates of the observation group at the 5<sup>th</sup>, 6<sup>th</sup>, 7<sup>th</sup>, and 8<sup>th</sup> month after treatment were significantly higher than those of the control group (all P < 0.05). See **Table 2** and **Figure 1**.

### Comparison of cavity changes

When the intensive phase was completed at the end of 2<sup>nd</sup> month, although the cavity closure rate of the observation group was higher than that of the control group, differences were not significant (P > 0.05). When the consolidation phase was completed, at the end of 8<sup>th</sup> month, the cavity closure rate was significantly higher in the observation group than in the control group. Overall cavity changes in the observation group were better than those of the control group, according to Mann-Whitney U-testing (P < 0.05). See **Table 3** and **Figure 2**.

### Comparison of improvement of symptoms

At the end of 8<sup>th</sup> month, the observation group showed lower scores concerning tuberculosis symptoms, including low fever, coughing and sputum production, chest pain, and loss of appetite (all P < 0.05). See **Table 4** and **Figure 3**.

## Bronchoscopic drug delivery for treatment of tuberculosis

**Table 4.** Comparison of symptom improvement ( $\bar{x} \pm sd$ )

Group	Observation group (n = 72)	Control group (n = 72)	t	P
Low fever				
Before treatment	2.36 ± 0.42	2.40 ± 0.40	0.585	0.559
At the end of treatment	0.58 ± 0.10	1.05 ± 0.15	22.122	< 0.001
Cough and sputum production				
Before treatment	2.38 ± 0.43	2.36 ± 0.40	0.289	0.773
At the end of treatment	0.60 ± 0.12	1.09 ± 0.18	19.219	< 0.001
Chest pain				
Before treatment	2.20 ± 0.35	2.18 ± 0.34	0.348	0.729
At the end of treatment	0.48 ± 0.08	0.76 ± 0.15	13.976	< 0.001
Loss of appetite				
Before treatment	2.20 ± 0.37	2.19 ± 0.38	0.160	0.873
At the end of treatment	0.46 ± 0.07	0.75 ± 0.10	20.159	< 0.001

### Comparison of immune function

At the end of 8<sup>th</sup> month, CD3<sup>+</sup>, CD4<sup>+</sup> T-cells, and CD4<sup>+</sup>/CD8<sup>+</sup> ratios increased in both groups, compared with before treatment. However, CD8<sup>+</sup> T-cells decreased (all P < 0.05). CD3<sup>+</sup>, CD4<sup>+</sup> T-cells, and CD4<sup>+</sup>/CD8<sup>+</sup> ratios in the observation group were significantly higher than those in the control group. CD8<sup>+</sup> T-cells were lower in the observation group than in the control group (all P < 0.05). See **Table 5** and **Figure 4**.

### Comparison of pulmonary function

When treatment was completed, pulmonary function indices, including FVC, FEV<sub>1</sub>, and IC, in both groups increased significantly, compared with before treatment (all P < 0.05). Furthermore, increases in the observation group were more pronounced than those in the control group (all P < 0.05). See **Table 6** and **Figure 5**.

### Discussion

Smear-positive re-treatment pulmonary tuberculosis is a special type of tuberculosis, characterized by a long course, severity, and difficulty in management [10, 11]. Statistics indicate that the incidence rate of chronic fibrous cavity in patients with smear-positive re-treatment pulmonary tuberculosis is 55%. The number of MTB in the cavity wall could reach 10<sup>7</sup>-10<sup>9</sup> due to vigorous proliferation of MTB in the caseous necrosis [12]. Additionally, thickening and fibrosis of the cavity wall can hinder drug penetra-

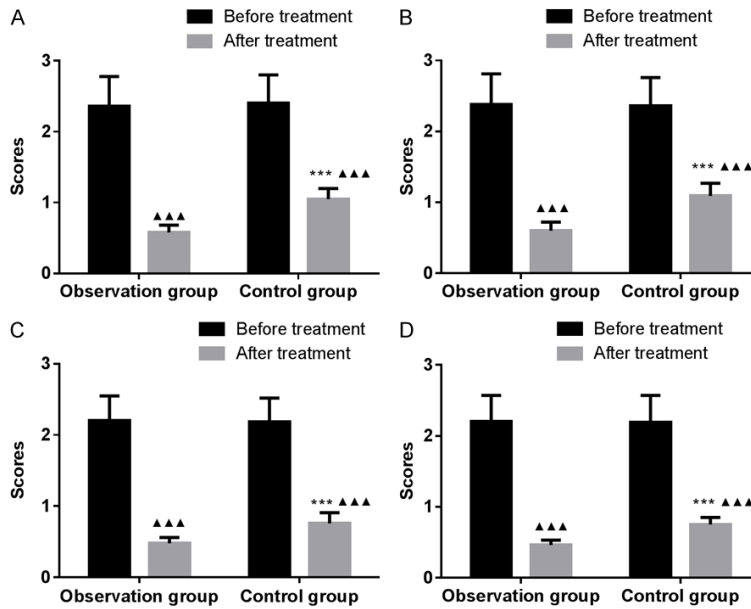
tion, making local drug concentrations lower than the inhibitory concentration. As a result, MTB cannot be eradicated. Cavities cannot be healed. Thus, sometimes multi-drug resistant tuberculosis may occur [13, 14]. Gillespie et al. found that cavitary tuberculosis mainly occurs in patients with positive sputum smears. In those patients, the therapeutic effects of anti-tuberculosis drugs are often compromised because the thick-

ened cavity wall has poor blood circulation. This makes drug penetration more difficult [15]. Therefore, the search for more effective treatment options has become a hot spot in clinical research.

Bronchoscopic therapy is a new treatment method that combines lesion removal and drug delivery. It can eliminate secretions and debris, clearing the bronchial lumen and cavities. It can also deliver isoniazid, levofloxacin, amikacin, and other drugs directly into the lesions, increasing local concentrations. This is a major advantage over oral administration. Increased local drug concentrations inhibit the proliferation of MTB in the cavity and improve sputum negative conversion rates. As a result, bronchoscopic therapy has been gradually recognized and promoted. Satisfactory outcomes have been obtained [16, 17]. Yuan et al. found that the sputum negative conversion rates increased by 25% after 6 months of bronchoscopic therapy [18]. Fu et al. confirmed that cavity closure rates in the initial treatment for cavitary pulmonary tuberculosis reached 60% after 6 months of bronchoscopic lavage and drug delivery. This rate was significantly higher than that of 30% in the control group [19]. The above results indicate that bronchoscopic therapy can effectively improve the prognosis of patients with pulmonary tuberculosis. However, studies concerning bronchoscopic therapy for treatment of more complicated cases of tuberculosis, including re-treatment smear-positive cavitary pulmonary tuberculosis, are scarce. In the current study, sputum negative conversion



## Bronchoscopic drug delivery for treatment of tuberculosis



**Figure 3.** Comparison of symptom improvement. A: Low fever; B: Cough and sputum production; C: Chest pain; D: Loss of appetite. ▲▲▲P < 0.001, compared with before treatment. \*\*\*P < 0.001, compared with the observation group.

**Table 5.** Comparison of immune function ( $\bar{x} \pm sd$ )

Group	Observation group (n = 72)	Control group (n = 72)	$\chi^2/t$	P
CD3 <sup>+</sup> (%)				
Before treatment	58.45 ± 4.86	58.38 ± 4.80	0.087	0.931
At the end of treatment	69.62 ± 5.84	61.75 ± 5.27	8.489	< 0.001
CD4 <sup>+</sup> (%)				
Before treatment	24.68 ± 3.87	24.73 ± 4.02	0.076	0.940
At the end of treatment	43.84 ± 5.05	27.86 ± 4.76	19.539	< 0.001
CD8 <sup>+</sup> (%)				
Before treatment	27.80 ± 4.62	27.74 ± 4.57	0.078	0.938
At the end of treatment	19.30 ± 2.28	25.04 ± 3.12	12.604	< 0.001
CD4 <sup>+</sup> /CD8 <sup>+</sup>				
Before treatment	0.76 ± 0.21	0.77 ± 0.20	0.293	0.770
At the end of treatment	1.72 ± 0.28	1.08 ± 0.23	14.987	< 0.001

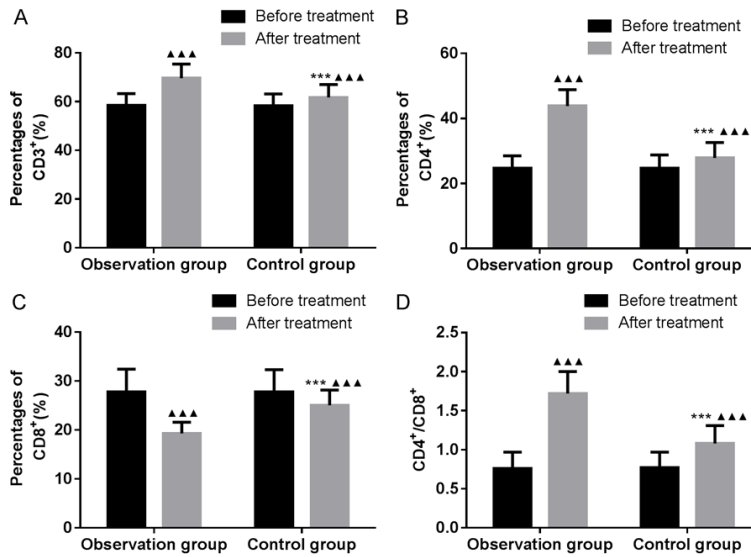
and cavity closure rates of the observation group after the consolidation phase were 94.44% and 84.72%, respectively, significantly higher than those in the control group. In addition, the observation group showed lower scores for tuberculosis symptoms, including low fever, coughing and sputum production, chest pain, and loss of appetite. Results suggest that the combination of routine chemotherapy with bronchoscopic triple-drug delivery can improve therapeutic outcomes, alleviate

symptoms, and improve patient prognosis.

Under stimulation of MTB, the immune system is often compromised. This is manifested as the suppression of T-cell-mediated cellular immunity. T-cell subsets usually show that CD3<sup>+</sup> and CD4<sup>+</sup> T-cells are decreased and CD8<sup>+</sup> T-cells are increased. Additionally, CD4<sup>+</sup>/CD8<sup>+</sup> ratios decrease, indicating that the host's immune system is impaired [20]. Previous studies have found that CD4<sup>+</sup> and CD8<sup>+</sup> T-cells synergistically mediate immune system to protect against MTB. CD4<sup>+</sup> T-cells play a key role in orchestrating adaptive immune response by activating CD8<sup>+</sup> T-cells and stimulating macrophage proliferation and phagocytosis. CD8<sup>+</sup> T-cells are responsible for dissolving macrophages that have phagocytized MTB [21]. Altered CD4<sup>+</sup>/CD8<sup>+</sup> ratios can lead to activation of MTB proliferation, even the emergence of drug-resistant and mutant strains. Results showed that CD3<sup>+</sup>, CD4<sup>+</sup> T-cells, and CD4<sup>+</sup>/CD8<sup>+</sup> ratios in the observation group were higher than those in the control group after the consolidation phase. Moreover, CD8<sup>+</sup> T-cells were lower than those of the control group. Results further suggest that chemotherapy combined with bronchoscopic triple-drug

delivery can effectively enhance immune function, compared to chemotherapy alone. Li et al. treated 63 patients with smear-positive retreatment cavitary pulmonary tuberculosis using bronchoscopic drug delivery. At the end of the 2<sup>nd</sup> and 6<sup>th</sup> month, CD3<sup>+</sup>, CD4<sup>+</sup> T-cells, and CD4<sup>+</sup>/CD8<sup>+</sup> ratios increased and CD8<sup>+</sup> T-cells decreased, compared with before treatment. Their results indicated that patient immune function was improved, in accord with present results [22].

## Bronchoscopic drug delivery for treatment of tuberculosis



**Figure 4.** Comparison of immune function. A: CD3<sup>+</sup>; B: CD4<sup>+</sup>; C: CD8<sup>+</sup>; D: CD4<sup>+</sup>/CD8<sup>+</sup> ratios. ▲▲▲P < 0.001, compared with before treatment. \*\*\*P < 0.001, compared with the observation group.

**Table 6.** Comparison of pulmonary function ( $\bar{x} \pm sd$ )

Group	Observation group (n = 72)	Control group (n = 72)	$\chi^2/t$	P
<b>FVC (L)</b>				
Before treatment	3.40 ± 0.75	3.42 ± 0.74	0.161	0.872
At the end of treatment	4.32 ± 0.92	3.78 ± 0.85	3.658	< 0.001
<b>FEV<sub>1</sub> (L)</b>				
Before treatment	3.04 ± 0.68	3.05 ± 0.70	0.087	0.931
At the end of treatment	3.91 ± 0.75	3.31 ± 0.73	4.864	< 0.001
<b>IC (L)</b>				
Before treatment	1.86 ± 0.38	1.88 ± 0.39	0.317	0.756
At the end of treatment	2.82 ± 0.45	2.34 ± 0.40	6.765	< 0.001

Note: FVC: Forced vital capacity; FEV<sub>1</sub>: Forced expiratory volume in 1s; IC: Inspiratory capacity.

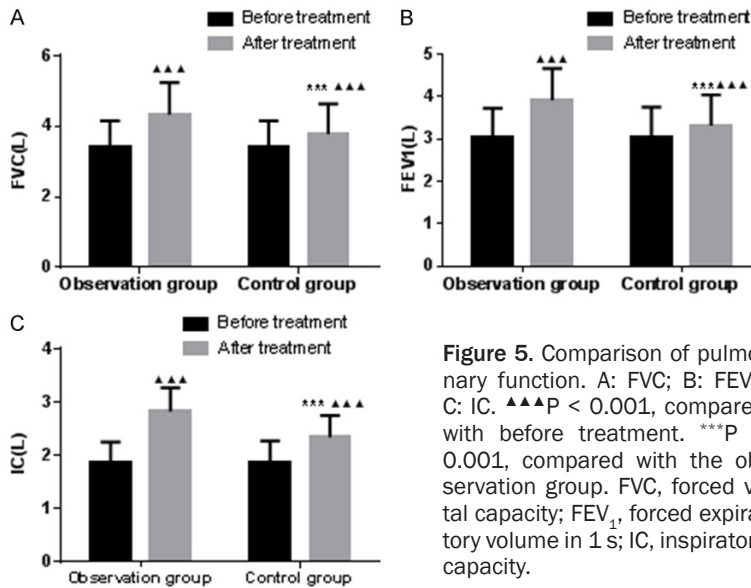
Cavitary pulmonary tuberculosis can cause progressive fibrosis in lung tissues, resulting in mucociliary dysfunction and accumulation of bronchial secretion. Patients cannot effectively cough up sputum due to reduced ventilation and airway blockage. In addition, fibrosis can lead to poor local blood circulation, which has been associated with a continuous decline in lung function [23]. Hypoxia, in turn, aggravates fibrosis in the lung tissues and impedes healing of tuberculosis cavities. This often results in a rapid decline in the quality of life of patients. In the current study, after 8 months of treatment, FVC, FEV<sub>1</sub>, and IC levels in the observation group were higher than those in the control

group. Results suggest that the combination of chemotherapy with bronchoscopic therapy can improve the lung function of patients, accelerate the healing process, and improve prognosis. Zhao et al. showed that, in patients treated with bronchoscopic drug delivery, serum levels of inflammatory factors decreased, while lysozyme activity was upregulated. Macrophage phagocytosis was enhanced, while T-cell numbers were increased, reflecting improved immune function. Furthermore, the histology structure of the lungs was improved, as well as lung function. Therefore, patients treated with bronchoscopic therapy can expect faster recovery times [24]. Although electronic bronchoscopy may cause some complications, it is safe and tolerable. However, patients should be closely monitored and indications and contraindications should be strictly followed [25]. However, it is worth noting that, due to the emergence of drug-resistant strains of MTB, there is still a certain failure rate in patients with smear-positive re-treatment cavitary pulmonary tuberculosis [26, 27].

One limitation of the current study was the relatively small number of subjects from a single center. This factor may have impeded in-depth statistical analyses of the outcomes. Further research is necessary, investigating the underlying mechanisms, aiming to find better alternatives for treatment of cavitary pulmonary tuberculosis.

In summary, bronchoscopic triple-drug delivery combined with chemotherapy for re-treatment of smear-positive cavitary pulmonary tuberculosis is more effective than chemotherapy alone. Therefore, it is highly recommended for clinical practice.

## Bronchoscopic drug delivery for treatment of tuberculosis



**Figure 5.** Comparison of pulmonary function. A: FVC; B: FEV<sub>1</sub>; C: IC. ▲▲▲▲ P < 0.001, compared with before treatment. \*\*\*P < 0.001, compared with the observation group. FVC, forced vital capacity; FEV<sub>1</sub>, forced expiratory volume in 1 s; IC, inspiratory capacity.

### Disclosure of conflict of interest

None.

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## Bronchoscopic drug delivery for treatment of tuberculosis

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