## Adjuvant surgical resection for nontuberculous mycobacterial pulmonary disease: Effectiveness and complications

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## Abstract:

**BACKGROUND:** Standard antibiotic treatment for nontuberculous mycobacteria pulmonary disease (NTMPD) has unsatisfactory success rates. Pulmonary resection is considered adjunctive therapy for patients with refractory disease or severe complications, but surgical indications and extent of resection remain unclear. We present surgical treatment outcomes for NTMPD and analyzes risk factors for unfavorable outcomes.

**METHODS:** We conducted a retrospective investigation of medical records for patients diagnosed with NTMPD who underwent surgical treatment at Asan Medical Center between 2007 and 2021. We analyzed clinical data including microbiological and surgical outcomes.

**RESULTS:** A total of 71 NTMPD patients underwent thoracic surgery. Negative conversion of acid-fast bacillus (AFB) culture following pulmonary resection was observed in 51 (73.9%) patients. In terms of long-term outcomes, negative conversion was sustained in 38 cases (55.1%). Mortality occurred in 7 patients who underwent pulmonary resections for NTMPD. Statistically significant associations with factors for recurrence or non-negative conversion of AFB culture were found in older age (odds ratio [OR] =1.093, 95% confidence interval [CI]: 1.029–1.161, P=0.004), male sex (OR = 0.251, 95% CI: 0.071–0.892, P=0.033), and extensive NTMPD lesions involving three lobes or more (OR = 5.362, 95% CI: 1.315–21.857, P = 0.019). Interstitial lung disease (OR = 13.111, 95% CI: 1.554–110.585, P=0.018) and pneumonectomy (OR = 19.667, 95% CI: 2.017–191.797, P=0.018) were statistically significant risk factors for postoperative mortality.

**CONCLUSION:** Pulmonary resection can be an effective adjuvant treatment option for NTMPD patients, with post-operative antibiotic treatment as the primary treatment. Careful patient selection is crucial, considering the associated risk factors and resectability due to complications and recurrence.

#### Keywords:

Complication, nontuberculous mycobacteria pulmonary disease, pulmonary resection, recurrence

Non-tuberculous mycobacteria (NTM) are a group of acid-fast bacilli, excluding Mycobacterium tuberculosis and Mycobacterium leprae. These bacteria can cause infections in various organs, including pulmonary infections. Nontuberculous mycobacteria pulmonary disease (NTMPD) is the most frequent (65%–90%) among

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms. NTM-related infections.<sup>[1]</sup> Recently, the incidence of NTMPD has been increasing worldwide, likely due to increased awareness and accuracy of diagnostic methods, as well as an overall increase in its prevalence.<sup>[2]</sup> Standard treatment for NTMPD is based on macrolide-containing multiple antibiotics regimens proposed by international respiratory medicine and infectious diseases societies.<sup>[3]</sup> However,

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multiple antibiotic treatment has unsatisfactory success rates ranging from 34.0%–45.6% for MABC to 60.0%–65.7% for MAC.<sup>[4]</sup>

Given the unsatisfactory response to antibiotic treatment, surgical treatment has been considered a reasonable adjunctive therapy, especially for patients with refractory disease despite rigorous medical treatment, large cavitary lesions, or severe disease-related complications such as massive hemoptysis. However, in clinical practice guidelines, unclear recommendations for surgical indications are available, and the precise extent of pulmonary resection has not been defined.<sup>[3]</sup> Although previous studies have provided guidance and insight into the surgical outcomes of pulmonary resection of NTMPD, these findings vary considerably by institution, and long-term postoperative outcomes and predictors of recurrence or adverse events have been insufficiently evaluated.

In this study, we present the outcomes of surgical treatment of NTMPD at a single institution and analyze risk factors for unfavorable outcomes.

## Methods

## Patient selection and data collection

We reviewed the medical records of all patients who underwent surgical treatment and were diagnosed with NTMPD at Asan Medical Center between April 2007 and July 2021. Diagnoses were made using the diagnostic criteria of the American Thoracic Society/Infectious Disease Society (ATS/IDSA) guidelines.<sup>[5]</sup> The inclusion criteria for the study were patients diagnosed with NTMPD who underwent pulmonary resection having a minimum of 12 months of postoperative follow-up duration. Patients who underwent thoracic surgery for differential diagnosis of nodules, empyema drainage, or concomitant tuberculosis treatment were excluded.

Data including patient age, sex, body mass index (BMI), underlying diseases, treatment durations, antibiotic treatment for NTMPD, pre- and postoperative acid-fast bacillus (AFB) culture and smear results, preoperative pulmonary function test (PFT), and chest computed tomography (CT) findings were collected.

AFB smears and cultures were performed according to the standard guidelines. Sputum was cultured using a solid medium (Ogawa medium, Korean Institute of Tuberculosis, South Korea) and liquid medium (BACTEC 960 Mycobacterial Growth Indicator Tube, Becton Dickinson, Sparks, MD, USA). NTM species were identified using reverse-blot hybridization of the rpoB gene (GenoType Mycobacterium CM/AS; HAIN Life Science, Germany). The NTM diagnostic techniques of our institution are described in detail elsewhere.<sup>[6]</sup>

Pulmonology specialists and surgeons at our institution determined patient selection and the extent of surgery. All patients diagnosed with NTMPD received standard combination antibiotic therapy based on the clinical practice guidelines of the ATS/IDSA. Preoperative antibiotic treatment was continued for at least 12 months after pulmonary resection unless patients had side effects or issues of compliance. The indication for pulmonary resection of NTMPD included severe complications such as massive hemoptysis and refractory infection despite treatment with multidrug chemotherapy regimens with cavitary lesions or severe bronchiectasis.

Negative conversion of AFB culture was defined as three consecutive negatives in AFB sputum cultures. Recurrence was defined as microbiological re-identification with two consecutive positives in AFB sputum cultures with NTM species identification. In cases wherein NTM species were not identified, recurrence was determined based on definite progression of radiographic findings. The postoperative residual lesion was identified by comparing preoperative and postoperative image findings.

## **Ethics statement**

The Institutional Review Board of Asan Medical Center approved this study (IRB No. 2022–1704) for the review and publication of patient record information. Informed consent was not required to use patient medical data, and before analysis, patient information was anonymized and de-identified.

## **Statistical analysis**

Continuous variables are reported as medians and interquartile ranges, while categorical variables are presented as counts and percentages. Risk factors associated with recurrence or non-negative conversion of AFB culture and mortality following pulmonary resection were initially identified as significant using univariate logistic regression analysis. Subsequently, these risk factors were further evaluated using a multivariate logistic regression model. Statistical analysis was performed using SPSS Statistics 26 software (IBM Corp., Armonk, NY, USA). P < 0.05 was considered statistically significant.

## Results

## **Patients characteristics**

During the study period, 79 patients with NTMPD underwent thoracic surgery. Five cases were excluded from the study cohort. Among them, two patients underwent pulmonary resection for multidrug-resistant tuberculosis treatment, one patient for differential diagnosis of the nodule, and two cases were for empyema drainage. Three cases with a lack of medical records were also excluded. Finally, 71 patients were included in the study [Figure 1].

The median age of the study population was 55 years (49–64), and the BMI was  $20.7 \text{ kg/m}^2$  (19.7–22.0). Forty-three (60.5%) patients were female. The main comorbidity was a history of tuberculosis, which was present in 51 (71.8%) patients, and 5 (7.0%) patients had interstitial lung disease (ILD). Detailed information on other comorbidities and PFT results can be found in Table 1.

The major species were *avium complex*, accounting for 48 (67.6%) patients, followed by *M. abscessus* in 20 (28%) patients. Among all patients, 51 (71.8%) had positive AFB cultures before surgery. The median duration of preoperative chemotherapy was 9 months (3–15), and the duration of postoperative chemotherapy was 5 months (0–11). Cavitary lesions were observed in 50 (71.4%) patients on chest CT, followed by bronchiectatic lesions in 21 (29.6%). The extent of NTMPD involvement showed that single lobe lesions were the most common, observed in 36 (50.7%) patients, while extensive involvement, with lesions in three or more lobes, was found in 26 (36.6%) patients. Further information on the microbiologic and radiologic characteristics of the included patients is presented in Table 2.

Wedge resection was the most common type of pulmonary resection, performed in 32 cases (54.1%). Lobectomy was performed in 25 cases (35.2%), and pneumonectomy in four cases (5.6%). The approaches of pulmonary resection were thoracotomy in 32 (45.1%) patients and video-assisted thoracoscopic surgery (VATS) in 37 (52%) patients, with a similar distribution. Two cases required approach conversion due to severe adhesions. Detailed information on the extent of pulmonary resection is provided in Table 3.



Figure 1: Flow chart of study cohort. NTMPD = Nontuberculous mycobacterial pulmonary disease, MDR-TB = Multidrug-resistant tuberculosis

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#### **Treatment outcomes**

The median follow-up period after surgical treatment of NTMPD was 44 months (22–96). Negative conversion of AFB culture after pulmonary resection, excluding only hemostasis, was observed in 51 (73.9%) patients. Among the patients with the negative conversion of

#### Table 1: Baseline characteristics of study cohort

Variable	No. (%)
Age (years)	55 (49–64)
Female (sex)	43 (60.5)
BMI (kg/m <sup>2</sup> )	20.7 (19.7–22.0)
Underlying disease	
DM	5 (7.0)
CRF	2 (2.8)
History of TB	51 (71.8)
ILD	5 (7.0)
Predicted FVC	83 (71.2–91.0)
Predicted FEV <sub>1</sub>	70 (61.5–85.0)

Data are presented as median (IQR) or, n (%) of patients. BMI=Body mass index, DM=Diabetic mellitus, CRF=Chronic renal failure, TB=Tuberculosis, ILD=Interstitial lung disease, FEV<sub>1</sub>=Forced expiratory volume 1 s, FVC=Forced vital capacity, IQR=Interquartile range

#### Table 2: Microbiologic and radiologic characteristics of study cohort

Variable	No. (%)
Mycobacterium species	
<i>M. avium</i> complex	48 (67.6)
M. avium	19 (26.8)
M. intracellulare	22 (31.0)
Coinfection of M. avium and M. intracellulare	7 (9.9)
M. abscessus	20 (28.2)
M. kansasii	1 (1.4)
M. fortuitum	1 (1.4)
M. kumamotonense	1 (1.4)
Clarithromycin resistance in M. abscessus	2 (2.8)
Positive preoperative sputum AFB culture	51 (71.8)
Identified AFB stain in pathology	45 (63.4)
Duration of preoperative antibiotic therapy (months)	9 (3–15)
Duration of postoperative antibiotic therapy (months)	5 (0–11)
Regimen of multiple antibiotics therapy	
No medication	9 (12.6)
Macrolide based	5 (7.0)
Macrolide based + IV antibiotics	54 (76.1)
Others	3 (42)
Chest CT pattern	
Cavitary lesion	50 (71.4)
Bronchiectatic lesion	21 (29.6)
Extent of involved pulmonary lesion	
Single lobe	36 (50.7)
Two lobes	19 (26.8)
>3 lobes	26 (36.6)

Data are presented as median (IQR) or *n* (%) of patients. AFB=Acid-fast bacillus, CT=Computed tomography, IQR: Interquartile range, M. avium=Mycobacterium avium, *M. fortuitum=Mycobacterium fortuitum, M. intracellulare=Mycobacterium intracellulare, M. abscessus=Mycobacterium abscessus, M. avium=Mycobacterium avium, M. kansasii=Mycobacterium kansasii, M. kumamotonense=Mycobacterium kumamotonense,* IV=Intravenous AFB culture, 10 (19.6%) experienced recurrence during follow-up. Regarding long-term outcomes, negative conversion was sustained in 38 cases (55.1%). A total of 24 (34.7%) patients experienced recurrence or persistent positive of AFB culture, among whom 15 required antibiotic treatment or reoperation. Mortality occurred in seven patients among all pulmonary resections of NTMPD [Figure 2].

Complications related to pulmonary resection occurred in 22 (30%) patients. The most common was air leak lasting more than 7 days and was observed in 13 (18.3%) patients. Bronchopleural fistula (BPF) was confirmed in five cases (7.1%), and acute exacerbation of ILD was observed in two cases (1.4%) [Table 4]. Table 5

#### Table 3: Extent of pulmonary resection for nontuberculous mycobacterial pulmonary disease and approach

Variable	n (%)
Type of pulmonary resection	
Wedge resection	32 (54.1)
Single	24
Multiple	8
Segmentectomy	7 (9.9)
With wedge resection	2
Without wedge resection	4
Bisegmentectomy	1
Lobectomy	25 (35.2)
With wedge resection	5
With segmentectomy	4
Without sublobar resection	16
Bilobectomy	3 (4.2)
Pneumonectomy	4 (5.6)
Right	3
Left	1
Approach	
Thoracotomy	32 (45.1)
VATS	39 (54.9)
Conversion from VATS to thoracotomy	2

Data are presented as *n* (%) of patients. VATS=Video-assisted thoracoscopic surgery

# Table 4: Complication of pulmonary resection fornontuberculous mycobacterial pulmonary disease

Variable	n (%)
Number of patients with complications	23 (32.4)
Prolonged air leak (>7 days)	13 (18.3)
Treatment required	2
BPF	5 (7.1)
Acute exacerbation of ILD	2 (2.8)
Postoperative bleeding-required reoperation	2 (2.8)
ARDS	1 (1.4)
Mortality	7 (9.9)
Before discharge	4
After discharge	3

Data are presented as, *n* (%) of patients. BPF=Bronchopleural fistula, ILD=Interstitial lung disease, ARDS=Acute respiratory distress syndrome

provides an overview of the seven mortality cases. The primary cause of mortality was BPF in five of the seven cases (71.4%), and the purpose of surgery, excluding one case, was for the negative conversion of NTMPD. Among the four cases of pneumonectomy patients, two resulted in mortality.

### **Risk factor analysis**

The univariate logistic analysis revealed statistically significant risk factors for recurrence or non-negative conversion of AFB culture, including older age (odds ratio [OR] = 1.071,95% confidence interval [CI]: 1.018-1.127, P = 0.008), surgical approach (OR = 0.311, 95%) CI: 0.112–0.878, P = 0.027), extensive NTMPD lesions involving three lobes or more (OR = 3.500, 95% CI: 1.021-12.001, P = 0.046), and the presence of remaining NTMPD lesion after pulmonary resection (OR = 3.500, 95% CI: 1.021–12.001, P = 0.046). In the multivariate logistic analysis model, older age (OR = 1.093, 95% CI: 1.029–1.161, P = 0.004), male sex (OR = 0.251, 95% CI: 0.071-0.892, P = 0.033), and extensive NTMPD lesions involving three lobes or more (OR = 5.362, 95% CI: 1.315–21.857, P = 0.019) showed statistically significant associations. Detailed information on the risk factor analysis for recurrence or nonnegative conversion of AFB culture, including undisclosed factors, can be found in Table 6.

For the risk factors related to postoperative mortality, the univariate logistic analysis indicated that female sex (OR = 4.457, 95% CI: 0.800–12.001, P = 0.046), ILD as a comorbidity (OR = 8.133, 95% CI: 1.092–60.587, P = 0.041), and pneumonectomy (OR = 12.4, 95% CI:



Figure 2: Treatment outcomes of pulmonary resection of nontuberculous mycobacterial pulmonary disease. Data are presented as number (%) of patients: (a) Excluded two cases of pulmonary resection for hemostasis only, total number of patients was 69. (b) Including all patients of study cohort, total number of patients was 71. NTMPD = Nontuberculous mycobacterial pulmonary disease, MDR-TB = Multidrug-resistant tuberculosis

	Table 5: Profile of	mortality cases o	f pulmonary	resection for	r nontuberculous	mycobacterial	pulmonary (	disease
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Age/sex	Species of NTM	Purpose of surgery	Extent of surgery	Negative conversion	Period to mortality	Complications and cause of mortality
69/male	M. avium	Curative	Lobectomy	-	35 days	ILD aggravation, prolonged air leak, ECMO apply
70/male	M. fortuitum	Hemostasis	Pneumonectomy	-	2 days	Shock, ARDS
57/male	M. intracellulare	Curative	Lobectomy	-	2 months	BPF, pneumonia empyemectomy (POD 20 days)
68/male	M. abscessus	Curative	Wedge resection	-	3 months	BPF, pneumonia, empyema
64/male	M. avium	Curative	Lobectomy	Yes	15 months	BPF, pneumonia, ILD aggravation
53/female	M. abscessus	Curative	Bilobectomy	Yes	55 months	Recurrence of NTM (POD 28 months), BPF, pneumonia
55/female	M. abscessus	Curative	Pneumonectomy	No	110 months	BPF, pneumonia

BPF=Bronchopleural fistula, ILD=Interstitial lung disease, ARDS=Acute respiratory distress syndrome, ECMO=Extracorporeal membrane oxygenation, POD=Postoperative day, NTM=Nontuberculous mycobacteria, *M. avium=Mycobacterium avium, M. fortuitum=Mycobacterium fortuitum, M. intracellulare=Mycobacterium intracellulare, M. abscessus=Mycobacterium abscessus* 

Table 6: Univariable	and multivariable	logistic analysis	s of risk factor	s for recurrence	or nonnegative	conversion
of acid-fast bacillus	culture					

Variables	Uı	nivariable analys	sis	Multivariable analysis		
-	OR	95% CI	Р	OR	95% CI	Р
Age (years)	1.071	1.018-1.127	0.008*	1.093	1.1029-1.161	0.004*
Male	0.349	0.116-1.05	0.061	0.251	0.071-0.892	0.033*
Predicted FEV <sub>1</sub> <80%	1.256	0.471-3.352	0.649			
BMI <18.5	0.720	0.122-4.297	0.716			
DM	2.375	0.269-15.268	0.362			
CRF			0.999			
ТВ	0.729	0.259-2.047	0.548			
ILD			0.999			
M. abscessus	0.293	0.193–1.824	0.362			
Wedge resection	1.615	0.603-4.325	0.340			
Thoracotomy	0.311	0.112-0.878	0.027*			
Cavitary pattern	0.952	0.311–2.917	0.932			
Extent of lesion ( $\geq$ 3 lobes)	3.500	1.021-12.001	0.046*	5.362	1.315–21.857	0.019*
Remnant lesion	3.500	1.021-12.001	0.046*			
Postoperative antibiotic treatment duration ( $\geq$ 12 months)	0.875	0.265-2.885	0.826			
Positive in intraoperative AFB culture	1.714	0.586-5.011	0.325			
Positive in preoperative AFB culture	1.685	0.548-5.18	0.362			

BMI=Body mass index, DM=Diabetes mellitus, CRF=Chronic renal failure, TB=Tuberculosis, ILD=Interstitial lung disease, FEV<sub>1</sub>=Forced expiratory volume 1 s, AFB=Acid-fast bacillus, OR=Odds ratio, CI=Confidence interval, *M. abscessus=Mycobacterium abscessus* 

1.428–107.674, P = 0.022) were statistically significant. ILD (OR = 13.111, 95% CI: 1.554–110.585, P = 0.018) and pneumonectomy (OR = 19.667, 95% CI: 2.017–191.797, P = 0.018) remained as statistically significant risk factors in the multivariate logistic analysis model. Sex, older age, comorbidity other than ILD, approach, chest CT pattern, extent of NTMPD, and remnant lesions did not have a statistically significant relationship with mortality [Table 7].

#### Discussion

In this study, we analyzed the long-term outcomes and factors related to unfavorable outcomes after pulmonary resection in patients with NTMPD. The initial negative conversion rate of AFB culture after surgical treatment was 75%, with a long-term rate of approximately 55%. Although these rates may seem insufficient, considering that the study cohort comprised patients who responded poorly to antibiotic pulmonary resection as adjuvant therapy for NTMPD. However, compared with previous studies that reported negative conversion rates of 80%-100%, the overall negative conversion rate in our study was comparatively lower.<sup>[7-11]</sup> Given that the majority of previous studies have a medication maintenance period of over 12 months after surgery, the possible reason for this lower conversion rate could be attributed to the shorter duration of the postoperative medication period of our study due to drug side effects or poor patient compliance. The guidelines suggest that patients with NTMPD should maintain antibiotic treatment for at least 12 months after culture conversion.<sup>[12]</sup> This recommendation also indicates the duration of antibiotic treatment after surgery is at least 12 months. However, such recommendations from ATS/IDSA are considered conditional, and the optimal duration of antibiotic therapy after surgery remains unclear.<sup>[7,8,13]</sup> According to Yotsumoto T., preoperative sputum smear ( $\geq 2+$ ) is an

treatment, these results support the effectiveness of

Variables		Univariable analysis			Multivariable analysis			
	OR	95% CI	Р	OR	95% CI	Р		
Age (years)	1.061	0.980-1.149	0.142					
Male	4.457	0.800-12.001	0.046*					
Predicted FEV <sub>1</sub> <80%	3.214	0.580-17.818	0.181					
BMI<18.5	1.917	0.390-9.427	0.423					
DM	2.500	0.239-26.122	0.334					
CRF			0.999					
ТВ	2.930	0.331-25.931	0.334					
ILD	8.133	1.092-60.587	0.041*	13.111	1.554-110.585	0.018*		
M. abscessus	2.074	0.042-10.234	0.371					
Pneumonectomy	12.400	1.428-107.674	0.022*	19.667	2.017-191.797	0.018*		
Thoracotomy	3.017	0.545-16.717	0.206					
Cavitary pattern			0.999					
Extent of lesion ( $\geq$ 3 lobes)	2.942	0.585-14.809	0.191					
Remnant lesion	1.680	0.186–15.138	0.644					

Table 7: Univariable and multivariable logistic analysis of risk	factors for mortality
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BMI=Body mass index, DM=Diabetes mellitus, CRF=Chronic renal failure, TB=Tuberculosis, ILD=Interstitial lung disease, FEV<sub>1</sub>=Forced expiratory volume 1 s, AFB=Acid-fast bacillus, OR=Odds ratio, CI=Confidence interval, *M. abscessus=Mycobacterium abscessus* 

independent risk factor for recurrence after pulmonary resection for NTMPD (P = 0.024).<sup>[11]</sup> On this basis, they suggest the importance of reducing bacterial burden through preoperative antibiotics therapy. However, in this study, the duration of medication intake for over 12 months was not significantly associated with AFB culture conversion. The few patients who have maintained antibiotic treatment for more than 12 months might have influenced this result. In line with the results of previous studies, including that by Takuma *et al.*, and our lower negative conversion rate, maintaining antibiotic therapy during a specific period after pulmonary resection should be necessary.

Female sex and older age were statistically significant risk factors associated with recurrence and non-negative conversion. These findings are consistent with previous research conducted by Kim *et al*. and may be influenced by treatment compliance, genetic factors, and hormonal differences.<sup>[14]</sup> In particular, the unfavorable outcomes observed in female patients can be attributed to their higher susceptibility to NTM, which could lead to increased recurrence rates or intractability.<sup>[15-17]</sup> However, the underlying mechanisms of this difference and the contribution of sex hormones are still not fully understood. In an experimental model, Tsuyuguchi et al. demonstrated that estrogen can influence host defense and susceptibility to NTM, suggesting a potential role of hormonal effects in sex disparities in treatment, including surgical interventions.<sup>[18]</sup>

Recent studies identified residual lesions as a significant risk factor for recurrence.<sup>[9,14,19]</sup> In our study, remnant NTMPD lesions were significantly associated with recurrence or non-negative conversion of AFB culture in the univariable analysis but not in the multivariable analysis. Instead, extensive NTMPD lesions were a statistically significant risk factor in the multivariable analysis. As the extent of the lesion increases, the possibility of resectability decreases, suggesting a close relationship between these two factors. However, we could not identify a statistically significant correlation between them because in the case of patients without chest CT for measuring residual lesions after pulmonary resection, residual lesions may not be accurately reflected due to indirect measurement through postoperative chest X-ray or the extent of the resected pulmonary lesion. Complete resection and resectable extent of NTMPD lesions are important factors in achieving negative conversion of AFB culture.

Comorbidities of ILD were statistically associated with postoperative mortality. Acute exacerbation of ILD following pulmonary resection for lung cancer has been reported at a rate of 4%–32%.<sup>[20]</sup> In the case of NTMPD pulmonary resection, adhesiolysis is often required, resulting in a higher possibility of lung injury and longer operation time than pulmonary resection for lung cancer. Careful selection and postoperative close observation are mandatory for NTMPD pulmonary resection in patients with ILD.

The reported mortality rate for NTMPD pulmonary resection ranges from 0% to 18%.<sup>[13]</sup> In our study, the mortality rate was approximately 10%. The primary cause of mortality was BPF – all patients who developed BPF died, and one case was associated with pneumonectomy. Previous studies on BPF in pulmonary resection of NTMPD have primarily focused on its association with pneumonectomy.<sup>[21,22]</sup> A notable finding of our study is the occurrence of BPF in various extents of pulmonary resection. Further research is needed to identify risk factors beyond pneumonectomy, and active prevention strategies, such as bronchial reinforcement

using muscle or omental flap, must be considered, given the catastrophic consequences of BPF.

### In inflammatory pulmonary diseases such as NTMPD, dense pleural adhesions and calcified lymph nodes can create difficulty in performing minimally invasive surgery. Therefore, in the past, many surgeons preferred thoracotomy to VATS for inflammatory lung diseases.<sup>[23]</sup> With the development of surgical techniques and instruments, VATS has been widely utilized, including for inflammatory lung diseases. Many studies have demonstrated the feasibility of VATS lung resection for pulmonary tuberculosis, including that VATS can achieve similar results to conventional pulmonary resection via thoracotomy.<sup>[24-26]</sup> In our study, VATS was used in 52.1% of cases, and the conversion rate was only 5.4%. In our study, similar to the result of studies according to tuberculosis, the surgical approach did not have a statistically significant impact on treatment outcomes or complications. These results suggest that the VATS approach can be considered a primary approach for the pulmonary resection of NTMPD.

Our study has several limitations. This retrospective cohort study was conducted at a single institution with a small patient population. NTMPD is highly heterogeneous, with clinical manifestations varying widely depending on the causative species, and symptoms and progression vary widely from patient to patient. It is difficult to quantitatively evaluate these diverse clinical manifestations, and subgroup analysis by species was limited due to the small sample size. Well-designed randomized controlled trials or establishing a national database are needed to overcome these issues.

## Conclusion

Pulmonary resection can be an effective adjuvant treatment option for patients with NTMPD who are refractory to antibiotic therapy and experience complications such as hemoptysis. Older age, female sex, and extensive involvement of more than three lung lobes were associated with non-negative conversion in AFB and recurrence of NTM. Notably, ILD and pneumonectomy were identified as risk factors for postoperative mortality. Given the relatively high long-term recurrence rate, surgical resection for NTMPD should be considered an adjuvant treatment, accompanied by stringent post-operative medication as primary treatment. Moreover, careful patient selection is crucial, considering the associated risk factors and resectability due to the potential occurrence of catastrophic complications such as BPF or acute exacerbation of ILD.

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#### **Conflicts of interest**

There are no conflicts of interest.

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