

Perioperative surgical outcome of video-assisted thoracic surgery for nontuberculous mycobacterial pulmonary disease

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Background: Surgical treatment is useful in some nontuberculous mycobacterial pulmonary disease (NTM-PD) cases. Cases such as those of localizing lesions and/or the presence of cavitation may have surgical indications; however, the evidence of surgical indications and/or the surgical approach is not always clear.

Objective: This study aimed to retrospectively analyze the results of surgical treatment for NTM-PD at the National Hospital Organization Fukuoka Higashi Medical Center and to investigate the appropriateness of video-assisted thoracoscopic surgery (VATS).

Methods: This study included 49 cases of NTM-PD resected from 2003 to 2021. The operative approaches were VATS and open thoracotomy (OT) in 28 and 21 cases, respectively.

Results: Univariate analysis revealed a significant difference in the operating time, blood loss, and drainage duration between the OT and VATS cases but not in the degree of adhesion. Multivariate analysis revealed that the surgical approach was the only independent factor for postoperative drainage duration.

Conclusion: Adhesion is frequently observed in NTM-PD surgeries, and achieving adequate pulmonary resection is difficult. However, VATS cases have a shorter operating time, blood loss, and drainage duration than do OT cases. Therefore, VATS is considered a useful approach for the surgical treatment of NTM-PD.

Keywords: nontuberculous mycobacterial pulmonary disease, video-assisted thoracic surgery, perioperative surgical outcome

Introduction

The number of operations for pulmonary tuberculosis is decreasing, whereas that for nontuberculous mycobacterial pulmonary disease (NTM-PD) is increasing in Japan.¹ The effectiveness of amikacin liposome inhalation suspension for NTM-PD has been proven as a new treatment,^{2–4} but that medical treatment alone cannot treat these lesions completely. In collaboration with Western-affiliated societies, including the European Respiratory Society (ERS), the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), and the Infectious Disease Society of America (IDSA), the American Thoracic Society (ATS), in 2020, published “Treatment

of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline” in terms of surgical indications for NTM-PD.⁵ The guidelines recommended surgical resection of the diseased lungs in selected patients with NTM-PD, such as those with failure of medical treatment, cavity disease, drug-resistant isolates, hemoptysis, and/or severe bronchiectasis. However, the guidelines did not specifically refer to the surgical approaches or methods. Furthermore, studies have reported increasing deaths from NTM-PD,⁶ although, to our knowledge, no evidence has indicated that surgical treatment reduces mortality. The usefulness of video-assisted thoracic surgery (VATS) for lung cancer is clear, whereas that

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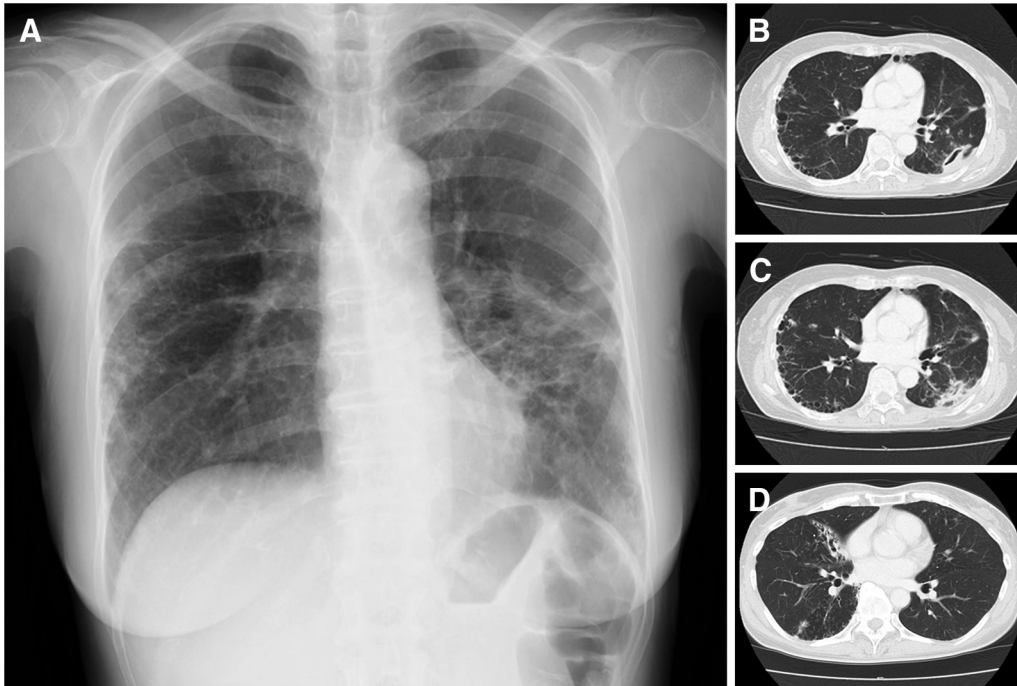


Figure 1. A typical chest X-ray of a patient with NTM-PD showing (A) infiltrative shadows in the lung field and a chest CT revealing (B) a cavity lesion, (C) a nodular lesion, and (D) bronchiectasis in the lung field. NTM-PD, nontuberculous mycobacterial pulmonary disease; CT, computed tomography

of VATS for NTM-PD is still unclear.⁷ Morino et al. revealed that preoperative rehabilitation reduces the risk of VATS for NTM-PD; however, there is still a higher risk using the open thoracotomy (OT) approach.⁸ The present study retrospectively compared the perioperative factors in VATS and OT cases of patients who underwent pulmonary resection for NTM-PD and investigated the efficacy of VATS.

Materials and Methods

Clinical data

The ethical committee of the National Hospital Organization Fukuoka Higashi Medical Center (Institutional Review Board [IRB] number: 2021-58) approved this study, which was conducted under the principles of the Declaration of Helsinki, seventh revision 2013. This study included 49 patients who underwent pulmonary resection for NTM-PD between January 2003 and April 2022. All patients received presurgical antibiotic treatment that included rifampicin, ethambutol, and clarithromycin. The preperiod included operations performed from 2003 to 2014, whereas the postperiod were those from 2015 to 2022. The NTM-PD diagnostic methods included sputum culture, tissue culture, and pathological findings, such as Ziehl-Neelsen staining,

fluorescence staining, and/or clinical examinations. Cases were diagnosed according to the diagnostic criteria of the Japanese Society for Tuberculosis and Nontuberculous Mycobacteria as NTM if they had a typical finding on computed tomography (CT), such as a nodular lesion, cavity lesion, and/or bronchial ectasia, and were positive for sputum culture tests more than twice or the bronchial lavage test more than once. Clinical examination included chest X-ray and CT. Typical chest X-ray results revealed an infiltrative shadow in the lung field (Figure 1A) and chest CT shows a cavity lesion (Figure 1B), nodular lesion (Figure 1C), and bronchiectasis (Figure 1D). Surgical indications included cases in which lesions were localized, cavity lesions, antibiotic treatment resistance, and hemoptysis. The clinical parameters, including age at surgery, sex, bacterial species, and perioperative factors, such as operating time, bleeding volume, adhesion score, and drainage duration, were compared between VATS and OT cases. The VATS method used 3 ports and 1 mini-incision port (Figure 2A), while the OT approach used a posterolateral incision (Figure 2B). Intrathoracic findings of pulmonary resection for NMT-PD frequently revealed adhesions (Figure 3). The adhesion scores were 0, 1, 2, and 3 for those with no adhesion, mild adhesion (within a single-lobe range), moderate adhesion

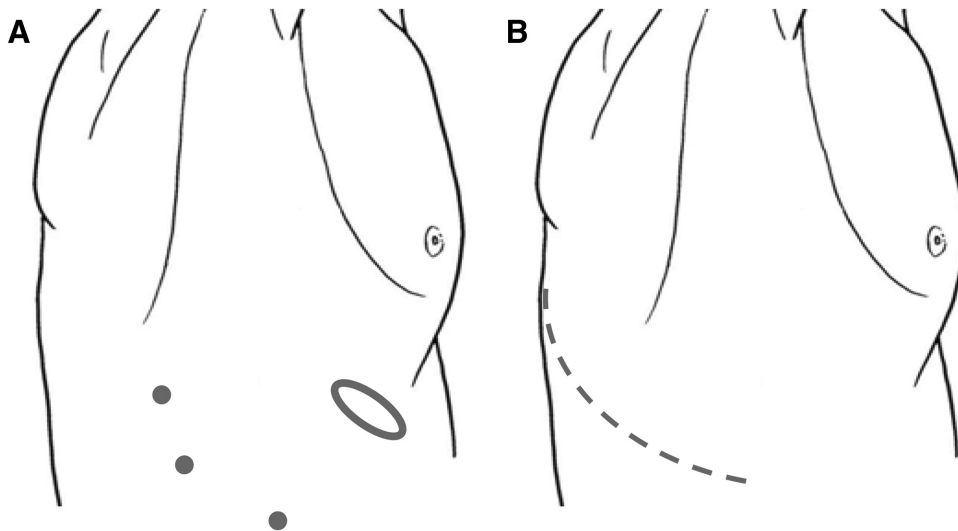


Figure 2. (A) VATS approach using 3 ports in the 4th, 6th, and 8th intercostal spaces and only one 4-cm mini-incision port. (B) OT approach using a posterolateral incision. VATS, video-assisted thoracoscopic surgery; OT, open thoracotomy

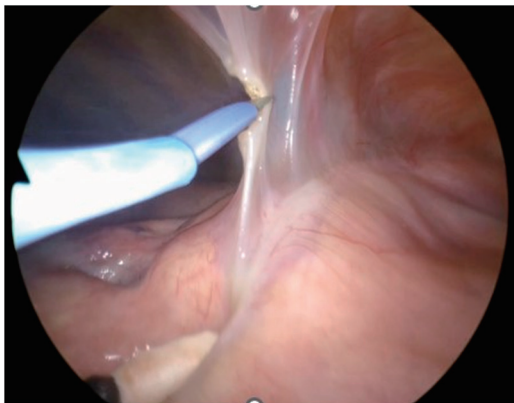


Figure 3. Intrathoracic findings of pulmonary resection for NTM-PD frequently revealed adhesions. A mild adhesion was observed within the single-lobe range. NTM-PD, nontuberculous mycobacterial pulmonary disease

(within a bilobar range), and severe adhesion (more than moderate adhesion), respectively.

Statistical analyses

All statistical analyses were performed using the JMP version 14.0 statistical software package for Windows (SAS Institute, Cary, NC, USA). Student's *t*-test or the χ^2 test was used to evaluate significant differences in patient parameters between the groups. Statistical significance was set at $P < 0.05$.

Results

Surgical approaches for pulmonary resections of NTM-PD

This study included 28 (57.1%) VATS and 21 (42.9%) OT cases.

Comparison of patient clinical characteristics

Table 1 summarizes the clinical characteristics of the NTM-PD surgical treatment. Significant differences in age, bacterial species, or localization of the main lesion were not observed; however, the large number of females, partial resection, segmentectomy and postperiod, and the small number of lobectomies and pneumonectomy in VATS cases were significant ($P = 0.0004$).

Comparison of the perioperative factors

Table 2 summarizes the perioperative factors of the cases of surgical treatment for NTM-PD. No significant differences in the degree of adhesion were found; however, significant differences in the short operating time, less blood loss, and shorter drainage duration were observed in the VATS cases ($P = 0.04$, $P = 0.0002$, and $P = 0.03$, respectively).

Discussion

In Japan, the number of operations for pulmonary tuberculosis is decreasing, whereas that for NTM-PD is increasing.¹ Pulmonary tuberculosis is highly infectious, and surgical treatment is necessary to avoid the spread of infection. Conversely, studies have reported increasing deaths from NTM-PD⁶; however, to our knowledge, no evidence has indicated that surgical treatment reduces mortality.

NTM-PD does not spread infection and slow progress; therefore, determining surgical indications is often difficult. The ATS, in collaboration with other Western-affiliated societies, including the ERS, the ESCMID,

Table 1. Comparison of the characteristics between VATS and OT

Characteristics	VATS (n = 28)	OT (n = 21)	P value
Age (years)			
<65	21	16	
≥65	7	5	0.92
Gender			
Male	5	14	
Female	23	7	0.0004
Bacterial species			
<i>M. avium</i>	19	11	
<i>M. intracellulare</i>	2	7	
<i>M. abscessus</i>	3	0	
<i>M. kansasii</i>	1	1	
Unknown	3	2	0.07
Localization			
Right upper lobe	9	10	
Right middle lobe	9	8	
Right lower lobe	2	0	
Left upper lobe	6	2	
Left lower lobe	2	1	0.365
Surgical method			
Partial resection	8	1	
Segmentectomy	4	0	
Lobectomy	16	14	
Bilobectomy	0	3	
Pneumonectomy	0	3	0.005
Surgical period			
Preperiod	7	17	
Postperiod	21	4	0.0001

VATS, video-assisted thoracoscopic surgery; OT, open thoracotomy; *M. avium*, *Mycobacterium avium*; *M. intracellulare*, *Mycobacterium intracellulare*; *M. abscessus*, *Mycobacterium abscessus*; *M. kansasii*, *Mycobacterium kansasii*

and the IDSA, first developed a guideline for NTM-PD in 1990⁹ and 20 years later, after 3 revisions, in 2020, published “Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline.”²⁵ This guideline recommended surgical resection as an additional treatment after consulting a specialist for NTM-PD. Furthermore, surgical resection should be considered for refractory and complicated cases in which medical treatment is unsuccessful in patients with cavitary pulmonary lesions, drug-resistant bacteria, hemoptysis, and/or severe bronchiectasis. As many as 14 guideline-based articles were published.^{10–23} The British Thoracic Society (BTS) also published the BTS guidelines for the management of NTM-PD in 2017.²⁴ Among those, evidence statements

resulted in high sputum culture negative conversion rates and low relapse rates after pulmonary resections in selected patients with NTM-PD.

Pneumonectomy for NTM-PD is associated with considerable complication rates, and more extensive resection and pneumonectomy are associated with higher complication rates. Postoperative morbidity and mortality have decreased as surgeons and institutions become more experienced in performing pulmonary resections for NTM-PD. Among the recommendations, the role of pulmonary resection for NTM-PD should be considered in cases of difficult diagnoses and for drug-resistant cases, and pulmonary resection for NTM-PD may be indicated in those with localized severe disease, which should be performed after multiprofessional

Table 2. Comparison of perioperative factors between VATS and OT

Perioperative factor	VATS (n = 28)	OT (n = 21)	P value
Operating time (minutes)	198.1 ± 95.3	268.8 ± 143.1	0.04
Amount of bleeding (g)	51.9 ± 24.5	303.5 ± 118.1	0.0002
Adhesion score (0–3)	1.03 ± 0.72	1.42 ± 0.76	0.12
Drainage duration (day)	3.01 ± 1.46	4.72 ± 2.17	0.03

VATS, video-assisted thoracoscopic surgery; OT, open thoracotomy

assessment in centers familiar with treating patients with NTM-PD. Those patients should receive antibiotic treatment before pneumonectomy, which should be continued for 12 months after negative conversion. Noteworthy, antibiotic treatment is usually not required after resection of a solitary NTM nodule in patients without other pulmonary NTM involvement.

Three randomized controlled trials have recommended VATS in terms of the surgical approach and the usefulness of thoracoscopic surgery for primary lung cancer.^{25–29} However, to our knowledge, no evidence has indicated which of the VATS or OT methods is optimal for pulmonary resection of NTM-PD. It generally remains a case-by-case decision for surgeons in Japan. Similar randomized controlled trials are warranted to investigate NTM-PD. The present study revealed a significantly shorter drainage duration in VATS cases than that in OT cases in terms of perioperative factors in the univariate analysis. Moreover, multivariable analysis revealed that the surgical approach was the only independent factor for postoperative drainage duration. The short drainage duration of the VATS cases is thought to be caused by less damage to the chest wall and hemostasis that could be sufficiently achieved by closely monitoring the intrathoracic findings. Therefore, these results indicated that VATS is an acceptable method for pulmonary resection of NTM-PD.

The limitations of this study included its retrospective design and small sample size. Furthermore, a bias was found in the VATS and OT cases in the surgical methods and periods, i.e., pre- and/or postperiods. Further randomized controlled trials are warranted to investigate the efficacy of various surgical approaches for NTM-PD. Additionally, the patients' prognoses and mortality rates were not mentioned because the patients' outcomes were lost to follow-up. Therefore, we used drainage duration to evaluate short-term perioperative factors.

Conclusion

VATS is a useful and minimally invasive approach for the surgical treatment of NTM-PD.

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Conflicts of Interest: None

References

- Shiraishi Y. Current status of nontuberculous mycobacterial surgery in Japan: analysis of data from the annual survey by the Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg* 2016; 64: 14–7.
- Griffith DE, Eagle G, Thomson R, et al. CONVERT Study Group. Amikacin liposome inhalation suspension for treatment-refractory lung disease caused by Mycobacterium avium complex (CONVERT) a prospective, open-label, randomized study. *Am J Respir Crit Care Med* 2018; 198: 1559–69.
- Golia A, Mahmood BR, Fundora Y, et al. Amikacin liposome inhalation suspension for Mycobacterium avium complex lung disease. *Sr Care Pharm* 2020; 35: 162–70.
- Hoy SM. Amikacin liposome inhalation suspension in refractory Mycobacterium avium complex lung disease: a profile of its use. *Clin Drug Investig* 2021; 41: 405–12.
- Daley CL, Iaccarino JM, Lange C, et al. Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline. *Clin Infect Dis* 2020; 71: e1–36.
- Morimoto K, Iwai K, Uchimura K, et al. A steady increase in nontuberculous mycobacteriosis mortality and estimated prevalence in Japan. *Ann Am Thorac Soc* 2014; 11: 1–8.
- Tseng YT, Pan CT, Yang SM, et al. Recent advances and controversies in surgical intervention of nontuberculous mycobacterial lung disease: A literature review. *J Formos Med Assoc* 2020; 119(Suppl 1): S76–83.
- Morino A, Murase K, Yamada K. Complications after video-assisted thoracic surgery in patients

- with pulmonary nontuberculous mycobacterial lung disease who underwent preoperative pulmonary rehabilitation. *J Phys Ther Sci* 2015; 27: 2541–4.
9. Wallace RJ Jr, O'Brien R, Glassroth J, et al. Diagnosis and treatment of disease caused by nontuberculous mycobacteria. *Am Rev Respir Dis* 1990; 142: 940–53.
 10. Shiraishi Y, Fukushima K, Komatsu H, et al. Early pulmonary resection for localized Mycobacterium avium complex disease. *Ann Thorac Surg* 1998; 66: 183–6.
 11. Shiraishi Y, Nakajima Y, Takasuna K, et al. Surgery for Mycobacterium avium complex lung disease in the clarithromycin era. *Eur J Cardiothorac Surg* 2002; 21: 314–8.
 12. Nelson KG, Griffith DE, Brown BA, et al. Results of operation in Mycobacterium avium-intracellulare lung disease. *Ann Thorac Surg* 1998; 66: 325–30.
 13. Pezzia W, Raleigh JW, Bailey MC, et al. Treatment of pulmonary disease due to Mycobacterium kansasii: recent experience with rifampin. *Rev Infect Dis* 1981; 3: 1035–9.
 14. Jeon K, Kwon OJ, Lee NY, et al. Antibiotic treatment of Mycobacterium abscessus lung disease: a retrospective analysis of 65 patients. *Am J Respir Crit Care Med* 2009; 180: 896–902.
 15. Mitchell JD, Bishop A, Cafaro A, et al. Anatomic lung resection for nontuberculous mycobacterial disease. *Ann Thorac Surg* 2008; 85: 1887–93.
 16. Jarand J, Levin A, Zhang L, et al. Clinical and microbiologic outcomes in patients receiving treatment for Mycobacterium abscessus pulmonary disease. *Clin Infect Dis* 2011; 52: 565–71.
 17. Koh WJ, Kim YH, Kwon OJ, et al. Surgical treatment of pulmonary diseases due to nontuberculous mycobacteria. *J Korean Med Sci* 2008; 23: 397–401.
 18. Yu JA, Pomerantz M, Bishop A, et al. Lady Windermere revisited: treatment with thoracoscopic lobectomy/segmentectomy for right middle lobe and lingular bronchiectasis associated with non-tuberculous mycobacterial disease. *Eur J Cardiothorac Surg* 2011; 40: 671–5.
 19. Kang HK, Park HY, Kim D, et al. Treatment outcomes of adjuvant resectional surgery for nontuberculous mycobacterial lung disease. *BMC Infect Dis* 2015; 15: 76.
 20. Shiraishi Y, Nakajima Y, Katsuragi N, et al. Pneumonectomy for nontuberculous mycobacterial infections. *Ann Thorac Surg* 2004; 78: 399–403.
 21. Lang-Lazdunski L, Offredo C, Le Pimpec-Barthes F, et al. Pulmonary resection for Mycobacterium xenopi pulmonary infection. *Ann Thorac Surg* 2001; 72: 1877–82.
 22. Watanabe M, Hasegawa N, Ishizaka A, et al. Early pulmonary resection for Mycobacterium avium complex lung disease treated with macrolides and quinolones. *Ann Thorac Surg* 2006; 81: 2026–30.
 23. van Ingen J, Verhagen AF, Dekhuijzen PN, et al. Surgical treatment of non-tuberculous mycobacterial lung disease: strike in time. *Int J Tuberc Lung Dis* 2010; 14: 99–105.
 24. Haworth CS, Banks J, Capstick T, et al. British Thoracic Society guidelines for the management of non-tuberculous mycobacterial pulmonary disease (NTM-PD). *Thorax* 2017; 72(Suppl 2): ii1–64.
 25. Kirby TJ, Mack MJ, Landreneau RJ, et al. Lobectomy–video-assisted thoracic surgery versus muscle-sparing thoracotomy: a randomized trial. *J Thorac Cardiovasc Surg* 1995; 109: 997–1002.
 26. Sugi K, Kaneda Y, Esato K. Video assisted thoracoscopic lobectomy achieves a satisfactory long-term prognosis in patients with clinical stage IA lung cancer. *World J Surg* 2000; 24: 27–31.
 27. Long H, Tan Q, Luo Q, et al. Thoracoscopic surgery versus thoracotomy for lung cancer: short-term outcomes of a randomized trial. *Ann Thorac Surg* 2018; 105: 386–92.
 28. Yan TD, Black D, Bannon PG, et al. Systematic review and meta-analysis of randomized and nonrandomized trials on safety and efficacy of video-assisted thoracic surgery lobectomy for early-stage non-small cell lung cancer. *J Clin Oncol* 2009; 27: 2553–62.
 29. Cai YX, Fu XN, Xu QZ, et al. Thoracoscopic lobectomy versus open lobectomy in stage I non-small cell lung cancer: a meta-analysis. *PLoS One* 2013; 8: e82366.