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Original Article

Risk factor analysis of postoperative complications after adjunctive pulmonary resection in patients with multidrug-resistant tuberculosis: A multi-institutional study

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KEYWORDS
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Abstract *Background and objective:* Multidrug-resistant tuberculosis (MDR-TB) requires extended treatment with regimens with multiple side effects, resulting in high treatment failure rates. Adjunctive lung resection combined with anti-tubercular agents improves outcomes. However, few studies have evaluated the potential harm from surgery and determined the optimal conditions for surgery. We aimed to analyze perioperative conditions to assess risk factors for postoperative complications in a multi-institutional setting.
Methods: This retrospective study included 44 patients with MDR-TB who underwent adjunctive lung resection at three management groups of the Taiwan MDR-TB consortium between January 2007 and December 2020. Demographic data, clinical characteristics, radiological findings, sputum culture status before surgery, primary or acquired drug resistance, surgical

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procedure, complications, and treatment outcomes were collected and analyzed. Multivariate logistic regression was used to identify risk factors for postoperative complications.
Results: Twenty-seven patients (61.4%) underwent lung resection using video-assisted thoracic surgery (VATS). The overall surgical complication rate was 20.5%, and the surgical mortality rate was 9.1%. Postsurgical hemothorax was the most common complication (11.4%). According to the univariate analysis, hilum involvement in images, positive preoperative sputum culture, and thoracotomy approach were unfavorable factors. VATS approach [adjusted OR, 0.088 (95% CI, 0.008—0.999)] was the only favorable factor identified by multivariate analysis.
Conclusion: The minimally invasive approach is a growing trend, and lobectomies and sublobar resections were the main procedures for MDR-TB. The VATS approach significantly reduced the surgical complication rate. Postsurgical hemothorax was noteworthy, and meticulous hemostasis of the chest wall and residual lung surface is critical for successful resections.

Introduction

Pulmonary tuberculosis (TB) is a public health threat. Most patients with TB are treated with a shorter course of combination therapy, including isoniazid, rifampicin, pyrazinamide, and ethambutol. However, multidrug-resistant tuberculosis (MDR-TB), defined as TB resistant to isoniazid and rifampicin, requires extended treatment and potentially toxic drug regimens, resulting in high rates of treatment failure and death.[1] The World Health Organization (WHO) estimated that 0.5 million people developed drug-resistant tuberculosis in 2019, of which 78% had MDR-TB. The success rate for treating drug-resistant TB is approximately 57%, in contrast to the 85% treatment success rate of newly diagnosed drug-susceptible TB.[2]

MDR-TB treatment regimens are costly, lengthy, and toxic, and outcomes are worse compared to drug-susceptible disease.[1] Thus, surgery has reemerged as a treatment for MDR-TB. Pomerantz et al. first reported improved outcomes using anti-tubercular agents combined with pulmonary resection for MDR-TB patients.[3] The goal of lung resection is to reduce bacterial loads via removing devitalized lungs, which act as a sanctuary for resistant organisms. A systemic review of 20 studies by Harris et al. demonstrated that adjunctive pulmonary resection combined with antituberculous chemotherapy improves outcomes, with a success rate of 81.9% in selected MDR-TB patients.[4] However, the selection criteria for lung resection are controversial, and surgeons' experience plays an important role in determining the timing and type of surgical intervention. Although the incidence of MDR-TB is increasing and lung resections are emphasized for cavitary or destroyed lungs, a paucity of robust clinical data has focused on surgical risks. Therefore, this study aimed to analyze perioperative conditions and determine risk factors for postoperative complications.

Methods

Patients and data

The Taiwan MDR-TB consortium (TMTC), which is funded by the Taiwan Centers for Disease Control, was established in 2007 to address the challenge of MDR-TB. The five DR-TB management groups each have lead hospitals. Senior TMTC clinicians with substantial experience in TB control and clinical management of MDR-TB ensure that treatment strategies are consistent with WHO recommendations and the results of drug susceptibility testing. A typical treatment regimen consists of a 6-drug intensive phase with ethambutol, pyrazinamide, kanamycin, either moxifloxacin or levofloxacin, prothionamide, and cycloserine, followed by a 5-drug continuation phase with ethambutol, pyrazinamide, either moxifloxacin or levofloxacin, prothionamide, and cycloserine. Regarding treatment duration, kanamycin used in the intensive phase should last for at least six months (or four months after sputum culture conversion), and the continuation phase will last at least 18 months after sputum culture conversion.

We retrospectively reviewed all registered MDR-TB patients who underwent adjunctive lung resection between January 2007 and December 2020 from three TMTC management groups, including Tainan Chest Hospital/National Cheng Kung University Hospital (Southern Taiwan, n = 26), Wan Fang Hospital (Northern Taiwan, n = 10), and Buddhist Tzu Chi General Hospital (Eastern Taiwan, n = 8). This study was approved by the National Cheng Kung University Hospital Institutional Review Board (A-ER-109-035), Wan Fang Hospital (N202009027), and Buddhist Tzu Chi General Hospital (IRB109-271-B). Informed consent was waived due to the retrospective design. All patients were monitored until December 2021 or death. Exclusion criteria were patient age of 18 years or less, unavailable patient or surgical characteristics, or extrapulmonary TB. All subjects were non-HIV-immunocompromised patients.

Definitions

Resistance types were classified based on WHO definitions.[5] MDR-TB patients without prior TB treatment were classified as having primary resistance. Patients with a history of previous TB treatment or non-compliance with treatment were classified as having acquired resistance. Treatment outcomes were classified as cured, treatment completed, treatment failed, died, or lost to follow-up based on international recommendations. Treatment outcomes were assessed 30 months after the initiation of MDR-TB treatment, and postoperative chemotherapy was continued for 12—24 months after converting to a negative sputum culture.

The location and extent of the disease were determined, and the areas of lung resection were evaluated using chest computed tomography. Hilum involvement was defined as lesions involving the central bronchovascular bundle, leading to deformity of lobar bronchi and volume reduction of target lobes.

Surgical indications

Individually tailored treatment regimens were selected at multidisciplinary staff conferences after reviewing patient histories and drug susceptibilities. Lack of sputum conversion after three months of medical treatment indicated refractory to medical treatment, and these cases were referred for surgery consultation during the multidisciplinary conferences. Surgical indications included failure of medical therapy, need to limit disease progression (persistent cavity lesions with possible relapses), localized (e.g., an isolated cavity) or extensive pulmonary disease, and symptom control (massive hemoptysis). Patients had to be fit to undergo surgery.[6,7] Patients who underwent emergency surgery for hemoptysis were excluded.

Choice of surgical procedure

The choice of video-assisted thoracic surgery (VATS) or thoracotomy depended on the lesion extent and the surgeon's experience. If unexpected situations during VATS required conversion, a mini-thoracotomy or conventional thoracotomy was performed. Sublobar resections (segmentectomy and wedge) were preferred for peripheral lesions, such as a simple cavity and tuberculoma, whereas lobectomies were chosen for large cavitary lesions, especially with hilum involvement, and destroyed lobes. Pneumonectomy was reserved for cases with total lung destruction. When multiple unilateral cavities were encountered, all cavitary lesions were resected without compromising postoperative pulmonary function. In contrast, only major cavitary lesions were resected when compromised postoperative pulmonary function was predicted. If bilateral lungs with unilateral predominance were involved, the most affected lung areas were resected.

Surgical complication grading

The Clavien-Dindo classification system is a widely used method to grade surgical complications.[8] It has five grades, from I to V, based on the severity and the type of intervention needed. Grade I complications are minor and do not require any intervention other than observation. Grade II complications are moderate and can be managed with medication, blood transfusion, or parenteral nutrition. Grade III complications are severe and need surgical, endoscopic, or radiological intervention. Grade IIIa complications do not require general anesthesia, while grade IIIb complications do. Grade IV complications are critical and involve organ failure that requires intensive care. Grade IVa complications affect one organ system, while grade IVb complications affect multiple organ systems. Grade V complications are fatal and result in the death of the patient.

Statistical analysis

Patient demographic and perioperative characteristics were assessed with descriptive statistics. Continuous data were expressed as medians with interquartile ranges (IQRs), whereas categorical data were expressed as numbers (percentages). To identify predictors of surgical complications, multivariate logistic regression models were constructed using characteristics with p-values <0.100 in univariate analyses. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics for Windows, version 19 (IBM Corp., Armonk, N.Y).

Results

Forty-four patients with MDR-TB who underwent adjunctive lung resection were included in the analysis. Table 1 shows patient characteristics. Most patients were male (68.2%) and less than 65 years old (88.6%). Twenty-eight (63.6%) patients had comorbidities, and diabetes was the most common comorbidity (41.7%). Twenty-three patients (52.3%) were new (primary resistance), and 21 (47.7%) patients were re-treated (acquired resistance). Cavitary

Table 1 Clinical characteristics of patients with multi-drug resistance treated with adjunctive surgery.

	Overall N = 44
Sex, Male, n (%)	30 (68.2)
Age, years, median (IQR)	46 (36.0–59.5)
Comorbidity, n (%)	
Diabetes mellitus	21 (47.7)
Cardiovascular disease	9 (20.5)
Chronic HBV or HCV infection	3 (6.8)
Disease type at the case registration	
Primary resistance (new)	23 (52.3)
Acquired resistance (re-treated)	21 (47.7)
Radiographic characteristics, n (%)	
Laterality	
Unilateral	41 (93.2)
Bilateral	3 (6.8)
Resection lesion classification	
Cavity ± tuberculoma(s)	34 (77.3)
Destroyed lobe/lung ± scattered tuberculomas	5 (11.4)
Destroyed lobe + ipsilateral cavity	1 (2.3)
Tuberculoma only	4 (9.1)
Hilar involvement	20 (45.5)
Preoperative chemotherapy, months, median (IQR)	9.9 (6.55–17.1)
Preoperative sputum culture, n (%)	
Positive	10 (22.7)
Negative	34 (77.3)
Treatment outcomes	
Cured/treatment completed	37 (84.1)
Died	7 (15.9)

IQR: interquartile range.

Table 2 Perioperative treatment duration of the 37 cured patients with adjunctive surgery.

Treatment duration, months, median (IQR)	Overall	Positive preoperative sputum culture N = 7	Negative preoperative sputum culture N = 30	P-value
Pre-conversion chemotherapy	7.2 (3.9–11.8)	16.6 (6.4–20.1)	6.2 (3.7–9.4)	0.0627
Post-conversion chemotherapy	18.3 (18.2–19.2)	18.3 (18.2–18.3)	18.4 (18.2–19.7)	0.0952
Preoperative chemotherapy	11.1 (6.4–17.6)	14.3 (5.1–19.2)	10.7 (8.4–17.5)	0.8920
Postoperative chemotherapy	16.2 (11.3–18.4)	18.8 (18.5–20.6)	15.3 (9.9–16.8)	**0.0013**
Total medication duration	25.9 (22.8–30.2)	30.0 (24.6–38.4)	25.9 (22.6–29.3)	0.1406

Statistical significance was defined as a P-value < 0.05.

lesions were the most common indication for surgery (79.5%). Destroyed lobes or lungs were detected in 6 patients (13.6%), including one patient with RUL destroyed lobe and RLL cavity, which were both resected. Preoperative sputum bacteriologic conversion was achieved in 34 patients (77.3%). Patients received anti-TB drugs during a median of 9.9 months before surgery (7.3 months in patients with primary resistance and 14.4 months in patients with acquired resistance).

The treatment success rate was 84.1%, and the major cause of unfavorable outcomes was death, including treatment-related deaths of 5 patients and non-treatment-related deaths of 2 patients (suicide and traffic accident). One treatment-related death was due to pneumonia seven months after surgery; the others were surgical mortalities. No treatment failures or loss to follow-up occurred during definitive medical treatment.

Table 2 shows the duration of drug treatment in the 37 patients who completed treatment. The median durations of preoperative and postoperative chemotherapy were 11.1 months and 16.2 months, respectively. The median overall treatment duration was 25.9 months. The duration of postoperative chemotherapy in the primary and acquired resistance groups were similar (16.3 and 16.0 months, respectively). The median follow-up time was 79.2 months (IQR: 46.8–109.2 months); 2 patients (5.4%) relapsed in 14.4 and 19.2 months after completing treatment. The median pre-conversion drug duration was 16.6 months (IQR: 6.4–20.1 months) for the 7 patients with positive preoperative sputum culture; after surgery, the patients all achieved sputum conversion within three months (median: 1.3 months, IQR: 0.4–2.3 months).

Table 3 Surgical procedure and postoperative surgical complications.

	Overall N = 44
Approach type, n (%)	
Video-assisted thoracoscopic surgery	27 (61.4)
Thoracotomy	17 (38.6)
Laterality of resected lesion, n (%)	
Right side	19 (43.2)
Left side	25 (56.8)
Procedure type, n (%)	
Lobectomy	23 (52.3)
Lobectomy + ipsilateral segmentectomy	2 (4.5)
Segmentectomy	9 (20.5)
Pneumonectomy	2 (4.5)
Wedge	8 (18.2)
Operation time, min, median (IQR)	175.0 (145.0–227.3)
Intraoperative blood loss, mL, median (IQR)	100.0 (0–375.0)
ICU stay, days, median (IQR)	1.0 (0–1.0)
Chest tube duration, days, median (IQR)	3.0 (2.0–5.3)
Overall surgical complication, n (%)	9 (20.5)
Grade I/II	2 (4.5)
Grade III/IV	3 (6.8)
Grade V	4 (9.1)
Death during hospitalization, n (%)	4 (9.1)

Table 3 shows surgical procedure details and perioperative outcomes. Twenty-seven patients (61.4%) underwent lung resections by VATS, including 4 (14.8%) who required thoracotomy conversion for adhesiolysis or bleeding control. Thirty-six (81.8%) patients underwent anatomic resection, and 8 (18.2%) patients underwent wedge resection (Supplementary Table 1). Two patients underwent pneumonectomy, with one on each side. No simultaneous or sequential bilateral lung resection surgeries were performed. All patients with primary resistance (n = 23) had unilateral disease, and 6 patients (26.1%) had hilar involvement. Most (73.9%) of these patients underwent VATS; however, 3 (14.3%) patients of acquired resistance (n = 21) had bilateral lung disease, and 14 (66.7%) patients had hilum involvement. Eleven of these patients (52.4%) were managed by a thoracotomy approach. The median operation time and intraoperative blood loss were 175 min (IQR: 145–227) and 100 ml (IQR: 0–375), respectively.

The overall surgical complication rate was 20.5%, and the surgical mortality rate was 9.1% (Supplementary Table 2). Complication details are listed in Table 4. Seven patients (15.9%) had major complications (Grade III or higher). Postsurgical hemothorax was the most common complication (11.4%). Four patients with hemothorax required emergency reoperation, and 2 of these patients suffered from multiple organ failures caused by refractory hemorrhagic shock. Among the four surgical mortalities, three underwent thoracotomy for RUL lobectomy, and one underwent thoracotomy for LUL lobectomy. When surgical mortality was calculated by treatment year, the mortality

Table 4 Postoperative complications in nine patients were classified using the Clavien-Dindo grading system.

Complication	N (%)	Management
Postsurgical hemothorax	5 (11.4)	
Grade II	1	Blood transfusion
Grade III	1	Re-exploration
Grade IV	1	Re-exploration
Grade V	2	Re-exploration
Pneumonia	3 (6.8)	
Grade IV	1	Intubation/antibiotic treatment
Grade V	2	Intubation/antibiotic treatment
Prolonged air leakage, Grade I	1 (2.3)	Conservative treatment
BPF, Grade III	1 (2.3)	Bronchoscopic embolization
Postsurgical empyema without BPF, Grade III	1 (2.3)	Tube drainage only due to severe pneumonia

BPF: bronchopleural fistula.

rate was 21.4% (3/14) from 2007 to 2010 but decreased to 3.3% (1/30) from 2011 to 2020.

The logistic regression analysis of factors associated with overall complications is shown in Table 5. Hilum involvement [crude OR, 5.923 (95% CI, 1.067–32.898)], positive preoperative sputum culture [crude OR, 7.500 (95% CI, 1.484–37.906)], and thoracotomy approach [crude OR, 23.111 (95% CI, 2.528–211.261)] were identified as unfavorable factors in the univariate analysis. VATS approach was the only favorable factor identified in the multivariate analysis [adjusted OR, 0.088 (95% CI, 0.008–0.999), p-value = 0.0499].

Discussion

Multidisciplinary team working should be the standard of care for MDR-TB management. Although antituberculous chemotherapy is the gold standard, lung resection plays an important role as an adjuvant treatment. A systemic review by Xu et al. showed that the treatment success rate for patients who underwent a combination approach could be improved to approximately 84%.[9]

Although adjunctive lung resection for MDR-TB treatment has been well investigated, MDR-TB surgery is still challenging and usually requires thoracotomy rather than VATS despite technical advances in minimally invasive surgery. Only 6% of patients reported by Kang et al. and 22.8% of patients reported by Marfina et al. underwent lung resections via VATS for MDR-TB.[10,11] In the present study, up to 61.4% of patients underwent VATS approach. Three risk factors for postoperative complications were identified by univariate analysis, including hilum involvement, positive preoperative sputum culture, and thoracotomy approach. However, only VATS significantly reduced surgical complications based on the multivariate analysis. Minimally invasive surgery may minimize chest trauma and decrease the influence on postoperative respiratory rehabilitation, which results in faster recovery and better pulmonary function.

Table 5 The logistic regression analysis for risk of overall postoperative complication.

	Event, N (%)	Overall complication			
		Crude OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Sex					
Female	1/14 (7.1)	Ref.			
Male	8/30 (26.7)	4.727 (0.530–42.199)	0.1643		
Comorbidity					
No	5/18 (27.8)	Ref.			
DM or HTN or Chronic HBV or HCV infection	4/26 (15.4)	0.473 (0.107–2.083)	0.3220		
Disease type					
Primary resistance	2/23 (8.7)	Ref.		Ref.	
Acquired resistance	7/21 (33.3)	5.250 (0.949–29.051)	0.0575	2.587 (0.265–25.223)	0.4132
Hilum involvement					
No	2/24 (8.3)	Ref.		Ref.	
Yes	7/20 (35.0)	5.923 (1.067–32.898)	**0.0420**	4.460 (0.386–51.533)	0.2312
Preoperative sputum culture					
Negative	4/34 (11.8)	Ref.		Ref.	
Positive	5/10 (50.0)	7.500 (1.484–37.906)	**0.0148**	5.075 (0.483–53.315)	0.1758
Pre-surgical chemotherapy (mon)	–	0.980 (0.879–1.092)	0.2468		
Approach Type					
Thoracotomy	8/17 (47.1)	Ref.		Ref.	
VATS	1/27 (3.7))	0.043 (0.005–0.396)	**0.0054**	0.088 (0.008–0.999)	**0.0499**
Surgical procedure					
S/W	1/17 (5.9)	Ref.		Ref.	
L/P	8/27 (29.6)	6.737 (0.760–59.756)	0.0867	1.7273 (0.0986–30.259)	0.7083

S/W: segmentectomy/wedge; L/P: lobectomy/pneumonectomy.
Statistical significance was defined as a P-value < 0.05.

Table 6 Literature review of MDR-TB patients with adjunctive lung resection.

First author, year	Country	Years	Cohort size, MDR (n)	Age (years)	Thoracotomy (%)/VATS (%)	Pneumonectomy (%)/Lobectomy (%)/Sublobar resection (%)	Perioperative complications (%)	Perioperative mortality (%)	Treatment outcome (%)
Chiang,[8] 2001	Taiwan	1990–1999	27	44	100/0	37.0/48.1/14.9	11.0	4.0	89
Park,[9] 2002	South Korea	1995–1999	49	35	100/0	24.5/71.4/4.1	16.3	0	90
Naidoo,[10] 2005	South Africa	1996–2000	23	30	100/0	73.9/26.1/0	17.4	0	96
Dewan,[11] 2006	Indian	1999–2003	74	20–40	100/0	50.0/40.5/9.5	32.4	6.8	84
Kir,[12] 2006	Turkey	1993–2005	79	38	100/0	53.1/45.7/1.2	39.0	2.5	95
Mohsen,[13] 2007	Egypt	1995–2005	23	24	100/0	48.0/52.0/0	34.7	4.3	91
Wang,[14] 2008	China	1995–2006	56	39	100/0	44.6/55.4/0	25.0	0	75
Shiraishi,[15] 2009	Japan	2000–2007	56	46	100/0	36.1/54.1/9.8	16.0	0	98
Orki,[16] 2009	Turkey	1997–2005	55	34	100/0	30.9/69.1/0	29.1	1.8	95
Kang,[5] 2010	South Korea	1996–2008	46 MDR + 26 XDR	31	94/6	31.5/53.4/15.1	15.3	1.4	Overall: 90 MDR: 93
Yaldiz,[17] 2011	Turkey	2003–2006	13	44	100/0	38.5/61.5/0	23.0	7.6	92
Man,[18] 2012	Romania	1995–2005	45	55	100/0	0/76.9/23.1	13.3	0	NR
Xie,[19] 2013	China	1992–2011	43	45	100/0	18.6/81.4/0	11.6	0	93
Vashakidze,[20] 2013	USA	2008–2011	51 MDR + 24 XDR	30	100/0	10.6/54.7/34.7	9.0	0	MDR: 90 XDR: 67
Wang,[21] 2017	China	2008–2011	34 MDR + 20 XDR	38	100/0	14.8/85.2/0	11.1	0	87
Ma Y,[22] 2017	China	1992–2012	14 MDR + 7 XDR	37	100/0	9.5/90.5/0	33.3	0	Overall: 38 MDR: 50
Marfina,[6] 2018	Russia	2012–2015	22 MDR + 35 XDR	33	73.5/26.5	57.1/20.4/22.4	17.5	0	MDR: 95.5 XDR: 65.7
Huang (current study)	Taiwan	2007–2020	44	46	38.6/61.4	4.5/56.8/38.7	20.5	9.1	84

NR: non-reported; MDR: multidrug-resistant; XDR: extensively drug-resistant; VATS: video-assisted thoracoscopic surgery.

Minimally invasive surgery for MDR-TB is feasible when surgeons are familiar with VATS techniques and instruments.[12–17] From our experience, patients with single cavitary lesions and primary resistance are good candidates for VATS, but patients with acquired resistance may not be absolutely contraindicated. In our study, 17 (73.9%) patients with primary resistance underwent VATS; in contrast, 11 (52.4%) patients with acquired resistance needed thoracotomies. Theoretically, the patients with acquired resistance had extensive lung disease with more hilum involvement caused by long-term inflammation compared to the patients with primary resistance. Long-term pulmonary inflammation in re-treated patients may induce more severe pleural adhesions and fibrocalcified lymph nodes, leading to increasing surgical difficulty, more intraoperative blood loss, and longer operation time.

Few studies compared surgical complications after VATS and thoracotomy in MDR-TB patients. The reported surgical complication rates ranged from 9.0% to 39.0%, and the perioperative mortality ranged from 0 to 7.6%.[10,11,18–32] Naidoo et al. reported that postsurgical hemothorax occurred in 8.7% of the study population, and Xie et al. indicated that postsurgical hemothorax was the most common complication (5.6%).[20,29] Consistent with previous reports, postoperative hemothorax was the most common complication in our cohort and aggressive management with blood transfusion or re-exploration was required. Extrapleural dissection at the beginning of pneumolysis is a good alternative approach because intrapleural dissection commonly causes more extensive injury to the lung parenchyma, leading to significant blood loss. Most importantly, meticulous hemostasis, combined with electrocautery and gauze packing, should be performed for small perforating vessels in the internal intercostal muscles after lung resection to decrease the incidence of postsurgical hemothorax.

The overall surgical mortality was relatively high in the present study, possibly due to insufficient surgical experience or inappropriate patient selection in the early period. However, with more experience in MDR-TB surgery, the mortality rate decreased to 3.3% in the last decade (Supplementary Table 2). Two patients suffered from catastrophic bleeding and coagulopathy following massive blood transfusions. Severe pulmonary infection and septic shock occurred in the other patients. All cases of surgical mortality had extensive lung disease or critical hilum involvement. Therefore, careful preoperative assessments, including resectable lesions and operable patients, are crucial. In addition, early intervention before severe lung destruction is important and depends on good cooperation between pulmonologists and thoracic surgeons. Patients with failure to achieve sputum conversion after 3–6 months of medication treatment should be referred for surgical evaluation.

Of note, is pneumonectomy beginning to wane? Pneumonectomy is sometimes necessary for MDR-TB with lung destruction. In the past, pneumonectomies were more common (Table 6). Chiang et al. reported the treatment results in Taiwan from 1990 to 1999, and 37% of MDR-TB patients underwent pneumonectomies.[18] However, from 2007 to 2020, only 2 patients (4.5%) underwent pneumonectomy in the present study. More effective medications may have resulted in decreasing lung destruction. Fox et al. analyzed 26 cohorts and concluded that partial lung resection, except pneumonectomy, was associated with improved treatment success.[33] Wang et al. indicated that disease-free survival was 60% after pneumonectomy and 87.1% after lobectomy (n = 56).[24] Therefore, following the minimally invasive trend, lobectomy or sublobar resections seem to be more common as adjunctive surgery for MDR-TB.

Our study is limited by its retrospective design, relatively small case numbers, and lack of XDR-TB patients, although this study consisted of three major TMTC groups. We did not routinely perform preoperative pulmonary function tests due to concerns of air spreading; alternatively, we used performance status or 6-min walking tests to ensure adequate pulmonary reserve.[34] In addition, even though drug information was not analyzed, treatment strategies were consistent with WHO recommendations, and patients were reviewed regularly by the expert TMTC committee to assess drug regimen efficacy. Despite these limitations, our results may help establish surgical indications, guide patient selection, and determine operation risks to improve surgical outcomes in MDR-TB patients.

The details of adjunctive pulmonary resection for MDR-TB, such as optimal surgical timing, are still debated. The potential risk of air-borne transmission during surgery before negative sputum conversion is a concern; however, prolonged medical treatment may cause chronic inflammation and intraoperative complications. Our limited results indicate that early surgical resection can accelerate sputum conversion and reduce treatment duration. However, any conclusions about surgical timing cannot be made based on the present study, and future investigations are needed to shape evolving management guidelines.

In conclusion, multidisciplinary team working is the standard of care for MDR-TB management, and adjunctive lung resection is important for improving treatment outcomes. A minimally invasive approach is the trend, and early referral for surgical consultation makes the VATS approach more feasible. In addition, lobectomy or sublobar resection is becoming the main procedure. The VATS approach results in fewer postoperative complications, according to the multivariate analysis. Postsurgical hemothorax is a common complication, and meticulous hemostasis of the chest wall and lung parenchyma is critical.

Author contributions

Wei-Li Huang: Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); writing – original draft (equal); writing – review and editing (equal).
Shun-Tien Chien: Data curation (equal); funding acquisition (equal); investigation (equal); methodology (equal); resources (equal); supervision (equal); writing – original draft (equal); writing – review and editing (equal).
Ming-Chih Yu: Data curation (equal); funding acquisition (equal); investigation (equal); resources (equal); supervision (equal); writing – review and editing (equal).

Bee-Song Chang: Data curation (equal); funding acquisition (equal); investigation (equal); resources (equal); supervision (equal); writing — review and editing (equal).
Yi-Ting Yen: Data curation (equal); investigation (equal); methodology (equal); resources (equal) writing — review and editing (equal).
Ming-Ho Wu: Investigation (equal); resources (equal); writing — review and editing (equal).
Yau-Lin Tseng: Conceptualization (equal); data curation (equal); formal analysis (equal); funding acquisition (equal); methodology (equal); project administration (equal); supervision (equal); writing — review and editing (equal).

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Human ethics approval declaration

This study was performed in accordance with the Declaration of Helsinki. This human study was approved by National Cheng Kung University Hospital Institutional Review Board, Wan Fang Hospital Institutional Review Board, and Buddhist Tzu Chi General Hospital Institutional Review Board - approval: A-ER-109-035, N202009027, and IRB109-271-B. Informed consent was waived due to the retrospective design.

Conflicts of interest

None declared.

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Appendix A. Supplementary data

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