Observational Study

Medicine® OPEN

Pulmonary resection in the treatment of multidrug-resistant tuberculosis

A case series

Lin Wang, BS[a], Fan Xia, MD[b], Feng Li, MD[c,*], Xueqin Qian, MS[d], Yijun Zhu, BS[a], Hui Chen, BS[a], Aoao Bian, MS[e], Jun Wang, MS[a], Min Zhang, MS[d], Hongwei Li, MS[a], Jiafu Han, MS[a], Nan Jiang, MS[f], Ning Xu, MS[g], Yanzheng Song, MS[a,*]

Abstract

Multidrug-resistant (MDR) and extensive drug-resistant (XDR) tuberculosis (TB) are significant health problems throughout the world. Although the main treatment is medical, adjunctive surgical resection may increase the chance of cure in selected patients with MDR-TB or XDR-TB. This study aimed to present a case series of patients who underwent surgical resection for MDR-TB.

Between March 2008 and November 2011, surgical resection was performed on 54 patients including 34 with MDR-TB and 20 with XDR-TB at the Departments of Surgery of Shanghai Public Health Clinical Center (Shanghai), Henan Chest Hospital (Henan), and Anhui Chest Hospital (Henan). Preoperative sputum smear samples were positive for 28 patients and sputum quantitative polymerase chain reaction was positive for 32. Patients were treated according to a standard therapy protocol for a mean of 4.2 months before the operation. The variables that affected treatment outcomes were identified through multivariate regression analysis.

Fifty-four patients were operated for MDR-TB with localized disease usually complicated by cavity formation or destroyed lung. Thirty-seven were males and 17 were females. Median age was 37.8 (range, 20–75) years. Lobectomy was performed in 46 patients and pneumonectomy in 8. Muscle flaps were used in 36 of the patients with lobectomy and 8 with pneumonectomy. Various complications occurred in 6 (11.1%) patients, including bronchopleural fistula in 1 patient, bleeding in 2 patients, and prolonged air leak in 2 patients. A favorable outcome was achieved in 47 patients (87%) who underwent surgical resection. Higher body mass index (BMI) was associated with better outcome (odds ratio = 0.537, 95% confidence interval: 0.310–0.928, $P = .026$).

Patients with MDR-TB had good treatment outcomes after adjunctive pulmonary resection, and with few complications. Higher BMI was related to a favorable outcome.

Abbreviations: AFB = acid–fast bacilli, BMI = body mass index, DST = drug susceptibility test, MDR-TB = multidrug-resistant tuberculosis, TB = tuberculosis, XDR = extensive drug-resistant, XDR-TB = extensively drug-resistant tuberculosis.

Keywords: multidrug resistant, operative, surgical procedures, therapeutic use, treatment outcome, tuberculosis

Editor: Ramon Teira Cobo.

LW and FX have contributed equally to this work.

This study was support by a grant: Clinical study of association between quantitative detection of Mycobacterium tuberculosis and surgical-assisted pulmonary resection for the treatment of MDR-TB patients (Project of Technology Commission of Shanghai Municipality KSF0546).

The authors have no conflicts of interest to disclose.

[a] Department of Thoracic Surgery, Shanghai Public Health Clinical Center, [b] Department of Tuberculosis, The Eighty-Fifth Hospital of PLA, [c] Scientific Research, Shanghai Public Health Clinical Center, [d] Department of Clinical Laboratory, Shanghai Public Health Clinical Center, Shanghai, [e] Department of Surgery, Suzhou Fifth People's Hospital, Suzhou, [f] Department of Surgery, Anhui Chest Hospital (Henan), Zhengzhou, [g] Department of Surgery, Anhui Chest Hospital (Anhui), Hefei, China.

[*] Correspondence: Yanzheng Song, Department of Thoracic Surgery, Shanghai Public Health Clinical Center Fudan University, Shanghai, China (e-mail: yanzhengsong@163.com).

Medicine (2017) 96:50(e9109)

Received: 14 April 2017 / Received in final form: 19 October 2017 / Accepted: 14 November 2017

http://dx.doi.org/10.1097/MD.0000000000009109

1. Introduction

Pulmonary tuberculosis (TB) remains a major challenge for healthcare authorities.[1] Multidrug-resistant TB (MDR-TB) poses a significant challenge to the control of TB worldwide, and is likely to be associated with the worst outcomes.[2–5] China is one of the world's 27 countries with the highest burden of MDR-TB and extensively drug-resistant TB (XDR-TB).[5] A recent meta-analysis suggested that MDR-TB cases have begun to decline with the implementation of MDR-TB treatment strategies, but the prevalence remains high, with 3% for XDR-TB.[6,7] These figures suggest that MDR-TB and XDR-TB are serious concerns in China.[8]

Current medical treatment for MDR-TB is usually not satisfactory, with toxicity, high expense, and an estimated mortality rate of 26%.[9–12] Therefore, the option to undergo pulmonary resection to remove a destroyed lung, lobe, or segment may be offered to remove a great number of TB cells that do not respond to chemotherapy. Although treatment guidelines for MDR- and XDR-TB have been published, the gold standard for the surgical management of pulmonary TB is controversial.[13,14] It has become clear that surgery should only be considered for carefully selected patients. But there remains some debate on the indications for surgery, the conditions for and timing of surgery, the types of operation that are suitable to treat

TB, and which are the contraindications for elective surgical treatment.[13,14]

Therefore, the aim of the current study was to evaluate the role of surgical pulmonary resection combined with chemotherapy for patients with MDR-TB and XDR-TB. We reviewed the outcomes of these patients who were treated with pulmonary resection for MDR-TB including XDR-TB.

2. Methods

2.1. Patients

This was a retrospective case series. All patients were treated in 1 of 3 centers in China. These were the Department of Thoracic Surgery, Shanghai Public Health Clinical Center, Shanghai; The Department of Surgery, Henan Chest Hospital, Henan; and the Department of Surgery, Anhui Chest Hospital, Anhui. The treatment was provided between October 2008 and February 2011. Most patients had previously been treated at other hospitals and were subsequently referred to the centers for further management.

The patients were included in the study according to the following inclusion criteria: their sputum culture was positive, and a drug sensitivity test confirmed rifampicin and isoniazid resistance; the disease could be resected with the expectation of adequate cardiopulmonary reserve postsurgery; and the patient had no serious heart, brain, or kidney disease; with one of the following: the disease was so severe or extensive that there was a high probability of failure or relapse with medical therapy alone; pulmonary complications (including pulmonary cavity, destroyed lung, bronchopleural fistula, and hemoptysis) were evident and had probably been caused by drug-resistant pulmonary TB, confirmed by bacteriological examination and drug susceptibility tests (DSTs) after 4 to 6 months of supervised anti-TB chemotherapy; and there were micronodular or calcified lesions.

Patients were excluded if they fulfilled any of the following criteria: anti-TB chemotherapy treatment had lasted <4 months (the World Health Organization [WHO] recommendations suggest 2–4 months); patients with anti-TB chemotherapy were followed up for 3 months, and X-ray and chest CT showed the lesion had changed; mental illness leading to the patient being unable to comply with the study; or poor compliance.

This study followed the principle of informed consent and was approved by the Shanghai Public Health Clinical Center's ethics committee.

2.2. Clinical data collection

All cultures and DST were performed at the TB laboratory of the Shanghai public health clinical center. Sputum cultures were performed monthly until 3 consecutive negative sputum culture results were achieved and then every 2 to 3 months until treatment completion. Decontaminated sputum samples were inoculated into both Lowenstein–Jensen media and the BACTEC MGIT 960 broth culture system (Becton, Dickinson and Company, Franklin Lakes, NJ). For all *Mycobacterium tuberculosis*-positive sputum cultures, first-line and second-line DSTs were performed using the absolute and proportion concentration methods, respectively, as previously described.[10] The drugs and concentrations (final concentration in MGIT tubes) were as follows: isoniazid 0.1 μg/mL, rifampicin 1.0 μg/mL, ethambutol 5.0 μg/mL, and streptomycin 1.0 μg/mL. Resistance was indicated by >100 growth units and susceptibility was determined by <100 growth units. Pyrazinamide testing was performed using the MGIT960 liquid broth system.

2.3. Surgery

All patients had received individualized multiple-drug chemotherapy, as determined by drug susceptibility studies. Treatment was directly observed during the hospitalization period, and drugs were self-administered after discharge. Preoperative evaluation included chest radiography and computed tomography for localizing the TB lesions, bronchoscopy for visualizing the airways and ruling out bronchial lesions, electrocardiogram, and spirometry for assessing lung function. Laboratory analyses included a complete blood count, chemistry panel, and HIV serologic testing.

All patients received general anesthesia, they were intubated with a double lumen endotracheal tube, and had a chest tube placed. Resections were approached through a posterolateral thoracotomy. The type of resection was based on the extent of the pulmonary lesion. Most patients underwent placement of a muscle flap to buttress the bronchial stump. The technique of muscle flap construction used was initially described by Pairolero et al.[15] The serratus anterior muscle was initially used, but the latissimus dorsi muscle is now our muscle of choice. The latissimus dorsi is dissected from the chest wall, with the vascular supply left intact. A portion of either the 3rd or 4th rib is resected, through which the muscle is passed into the thoracic cavity. The muscle is then placed over the bronchial stump and secured with suture. A total of 44 muscle flaps were used. Muscle flaps were not used after lower lobectomies or segmental resections.

Patients were expected to remain on anti-TB drugs for 12 to 24 months after surgery, depending on when they achieved negative sputum culture conversion. Final treatment outcomes were determined by the WHO criteria.[16] Cure was considered when smears and cultures were negative throughout treatment for at least 18 months (or 24 months, in the absence of first-line drugs). A favorable outcome was defined as cure or treatment completion; a poor outcome was defined as treatment failure, death during treatment, or default with the exception of patients who defaulted treatment but had no evidence of TB disease by history or imaging, and had a negative follow-up sputum culture as they were considered to have a favorable outcome. Operative mortality was defined as any death occurring within 30 days after surgery in or out of the hospital, or after 30 days during the same hospitalization subsequent to the operation.

2.4. Data analysis and statistical analysis

Data were collected and managed using a REDCap (research electronic data capture) database.[12] Medical chart abstraction was performed to collect information on demographics, medical history, TB treatment history, chest imaging findings, surgical therapy, and TB treatment outcomes. Statistical analysis was performed using SPSS 22.0 (IBM SPSS Statistics for Windows; IBM Corp., Armonk, NY). Data were presented as mean ± standard deviation or percentage. Differences in categorical variables were tested using the chi-squared test. The 2-sample t test was used for continuous variables. Patients were assigned into the poor and good outcome subgroups according to their outcome. Logistic regression analysis was used to determine the factors that were related to a good outcome after the surgical procedure. A P value $<.05$ was considered statistically significant.

Table 1

Demographic and clinical characteristics of the 54 patients.

Demographics	n (% or range)
Mean age, y	38 (20–75)
Male	37 (69)
Female	17 (32)
Comorbidities (%)	
Diabetes	4 (7)
Cardiovascular disorders	2 (4)
Chronic liver diseases	8 (15)
COPD or other lung diseases	6 (11)
HIV infection	0
Smoking	3 (6)
Symptoms	
Cough and expectoration	28 (52)
Chest pain	2 (4)
Chest distress	5 (9)
Hemoptysis	15 (28)
Systemic symptoms	
Weight lost	38 (70)
Fever	8 (15)
Tuberculosis history and treatment case definition	
New	20 (37)
Previously treated with first-line drugs	19 (35)
Previously treated with second-line drugs	15 (28)
MDR	34 (63)
XDR	20 (37)
Mean months of TB treatment before surgery	21.4 (4–96)
Mean months of MDR/XDR-TB treatment before surgery	10 (4–36)
Median number of drugs received for MDR/XDR-TB treatment	5 (2–9)
Median known sensitive drugs received for MDR/XDR-TB treatment	3 (0–5)
Positive presurgery sputum AFB smear	28 (52)
Positive presurgery sputum PCR	32 (59)
Negative after-surgery sputum PCR	29 (91)
Radiologic results	
Multilobar disease	25 (40)
Bilateral disease	18 (33)
Cavitary disease	43 (80)
Bilateral cavitary disease	8 (15)
Totally destroyed lung	4 (7)
Surgical indication	
Medical treatment failure	16 (30)
High likelihood of treatment failure or disease relapse	32 (59)
Massive hemoptysis	6 (11)

AFB = acid–fast bacilli, COPD = chronic obstructive pulmonary disease, MDR = multidrug-resistant, PCR = polymerase chain reaction, TB = tuberculosis, XDR = extensive drug-resistant.

3. Results

3.1. Characteristics of the patients

A total of 54 patients with pulmonary XDR/MDR-TB underwent adjuvant surgical resection (Table 1). Their mean age was 38 years and 37 (69%) were males; 4 (7%) patients had diabetes, 2 (4%) had cardiovascular disorders, 8 (15%) had chronic liver diseases, and 6 (11%) had chronic obstructive pulmonary disease or other lung diseases. Major preoperative clinical manifestations included coughing in 28 patients, chest pain in 2, chest distress in 5, hemoptysis in 15, weight lost in 38, and fever in 8.

Most patients (34, 63%) were retreatment TB cases who had been previously treated with either first- (26, 48%) or second-line drugs (8, 15%); 20 (37%) had XDR-TB. Patients received a median of 5 anti-TB drugs and had received XDR/MDR-TB treatment for an average of 10 months prior to surgery. Twenty-eight (52%) had a positive presurgery sputum acid–fast bacilli (AFB) smear for *M tuberculosis*. Real-time quantitative polymerase chain reaction (qPCR) analysis for presurgery sputum shows a similar positive rate with presurgery sputum AFB smear (32% vs. 29%). The frequency of drug resistance is shown in Table 2.

Table 2

Frequency of drug resistance among patients with XDR-TB and MDR-TB.

TB drugs	XDR (n = 20), N (%)	MDR (n = 34), N (%)	Total (n = 54), N (%)
Isoniazid	20 (100)	34 (100)	54 (100)
Rifampin	20 (100)	34 (100)	54 (100)
Streptomycin	17 (85)	21 (66)	38 (70)
Ethambutol	14 (70)	19 (59)	33 (61)
Pyrazinamide	12 (60)	20 (63)	32 (59)
Ofloxacin	9 (45)	11 (34)	20 (37)
Levofloxacin	6 (30)	8 (25)	14 (26)
Moxifloxacin	5 (25)	6 (19)	11 (20)
Amikacin	13 (65)	3 (9.4)	16 (30)
Capreomycin	16 (80)	5 (16)	21 (39)

MDR = multidrug-resistant, TB = tuberculosis, XDR = extensive drug-resistant.

Imaging revealed cavitary disease in 43 (80%) patients, bilateral disease in 18 (33%), presence of cavities in 41 (76%), presence of bilateral cavitary disease in 8 (15%), and totally destroyed lung in 4 (7%).

3.2. Surgery

The most common indication for surgery was a high likelihood of treatment failure or disease relapse (59%) followed by medical treatment failure (29%) and massive hemoptysis (11%). All patients had surgical resection performed including 8 pneumonectomies (15%), 46 lobectomies (85%), and 9 lobectomies with wedge reception (17%). The patient who underwent multiple wedge resections had previous contralateral pneumonectomy for a destroyed lung owing to TB: he did not have sufficient pulmonary function for anatomic resection.

3.3. Treatment outcomes

Sputum AFB smear and sputum qPCR were undertaken for all patients at the time of the operation. Surgical operations were carried out according to general procedures in our hospitals. Table 3 shows the surgical complications that occurred according to whether the patients had positive sputum PCR prior to surgery. No spillage of the contents of cavities into the operative field occurred in any patient. There was no operative mortality. Postoperative complications occurred in 6 patients (11%): 1 patient (2%) had major complication of a bronchopleural fistula, 2 patients (4%) had bleeding, and 3 patients (6%) had a prolonged air leak (Table 3).

The treatment stratagem for postsurgical empyema with bronchopleural fistula was as follows. In early postpneumonectomy empyema with bronchopleural fistula, balanced chest tube drainage was used, and in late postpneumonectomy empyema with bronchopleural fistula the tube was connected to a standard water seal. Immediate surgery was performed to repair the bronchial stump and provide Eloesser flaps for long-term open drainage and irrigation. After surgery, all patients received a multidrug regimen postoperatively that was generally the same as their preoperative regimen.

Table 3

Treatment outcomes and complications grouped by positive or negative presurgery sputum PCR.

	Positive presurgery sputum qPCR (n=32)	Negative presurgery sputum qPCR (n=22)
Favorable treatment outcomes	27 (84%)	20 (91%)
Cure	22	18
Completed	4	2
Default	1	0
Unfavorable treatment outcomes	5 (16%)	2 (9%)
Failure	4	2
Default	1	0
Death	0	0
Patients with major complication		
Bronchopleural fistula	1	0
Intrathoracic bleeding necessitating reoperation	1	1
Prolonged air leak	1	2

PCR=polymerase chain reaction, qPCR=quantitative polymerase chain reaction.

3.4. PCR results

Among 32 qPCR-positive MDR TB patients, 22 patients (69%) were cured, 4 patients (13%) completed therapy, 4 patients (13%) failed treatment, 2 patients defaulted but 1 was considered cured (3%) and the other patient had an unfavorable outcome (3%), and no patient died. Among 22 qPCR-negative MDR-TB patients, 18 patients (82%) were cured, 2 patients (9%) completed therapy, 1 patient (5%) failed treatment, and 1 patient (5%) defaulted. The favorable outcome rates did not differ significantly between patients with qPCR-positive and those with qPCR-negative results (84% vs. 91%; $P=.286$; Table 3).

In all, 52 patients of the total 54 patients completed follow up (2 cases with positive PCR results had lost contact). One of these patients had persistent positive sputum culture results 12 months after surgery, so this patient was considered as having treatment failure, the other patient had negative sputum culture results 1 month after surgery, this patient was lost to follow up at 11 months after surgery, and this case was considered as good prognosis. The mean follow up after surgery was 385 days for the 52 patients who completed follow up. Favorable outcomes were achieved in 47 (87%) patients, including one of the patients who was lost to follow-up; 27 (84%) in those with qPCR-positive and 20 (91%) in qPCR-negative patients. Six patients (9%) completed treatment. The patients received a mean of 421 days of M/XDR-TB treatment before surgery and 252 days after surgery. Of the 7 (13%) patients with unfavorable outcomes, including 1 who was lost to follow-up, 6 (11%) experienced treatment failure, and 2 (4%) defaulted on their treatment (1 patient remained sputum culture positive 12 months after default and 1 was the patient who was lost to follow up). Among the 32 qPCR-positive MDR TB patients, 31 had negative qPCR results postsurgery; however, in 4 patients their sputum culture tested positive again within 4 months and so they subsequently experienced treatment failure, and one of the patient's sputum culture continued to test positive at 12 months of follow up, which was also considered as treatment failure.

3.5. Factors related to treatment outcome

Univariate analysis suggested that the only factor which exerted an influence on the prognosis was body mass index (BMI). The multivariate logistic regression analysis also showed that BMI was related to a successful treatment outcome. The result showed an odds ratio=0.537 with a 95% confidence interval: (0.310, 0.928), $P=.026$. The results indicated that per unit increase in BMI, the risk of a poor prognosis decreased by 46% (Table 4).

4. Discussion

The aim of this study was to provide information on a series of patients who were selected to undergo surgical resection as an adjunctive intervention to drug treatment for MDR-TB. The results show that patients undergoing this procedure had a favorable outcome in 87% of cases. Complications occurred in 11% of cases, but these were not related to the positive or negative results of preoperative sputum culture or the qPCR result. The only factor that influenced outcome was BMI. Currently, MDR-TB remains a serious health and economic problem, particularly in developing countries.[14] In the present study, the indications for surgery[14,16–18] were sputum positivity in 28 cases and a high risk of relapse in 25 cases. Surgery is controversial for sputum negative cases, but it has been shown that surgical resection is essential for a cavitary lesion or destroyed lung or lobe because of the difficulty of antibiotic penetration and the high number of organisms contained within the cavity. It is necessary to resect all cavitary disease and destroyed lung, and leave no grossly diseased lung behind.

Anatomically, this study reveals several intriguing observations. Left lung destruction was found in more than 88% of the patients who underwent a pneumonectomy. The predilection for left lung destruction in patients with pulmonary TB has been reported by others.[19] The reason for this is not clear. It is possible that the anatomic differences between the left and right main stem bronchi and the location of the lobar bronchi may account for this discrepancy. When there is isolated infection without total lung destruction, the right upper lobe is the most common site of infection.[20]

The timing of surgery is crucial for postoperative mortality, morbidity, and the chance of cure. The best time for surgery should be the period with the least number of bacilli, which may occur 3 months after the start of a new regimen. When no highly effective anti-TB agents are available, and symptoms are progressive, lung resection should be considered to prevent further damage to the lungs. Lalloo et al[21] also pointed out that timely surgical intervention was necessary in order to prevent the spread of MDR-TB and to protect the remaining normal lung.[22]

Surgical complications for TB patients will continue to represent a challenge to practicing thoracic surgeons. The postoperative complication rate reported in the recent studies of surgical treatment for MDR TB was 5% to 26%. Complications associated with surgical resection mainly include bronchopleural fistula, prolonged air leaks, and postoperative bleeding. In our series, major complications occurred in 11% (6/54 patients).

The postoperative mortality and morbidity rate for pulmonary TB is decreasing. This is largely owing to proper selection of the patient, development of the anesthesia technique, stapling devices, and the effective use of anti-TB agents postoperatively.[23,24] The mortality rate of MDR-TB after surgery ranged from 0% to 3%.[25–29] We did not register any mortality in our study. The low complication rate (lack of bronchopleural fistula, operative mortality, or major complications) might be due to the >5 preoperative anti-TB drugs administered for >3 months. However, when we assessed the number of complications

Table 4

Univariate and multivariate analyses of factors related to a favorable treatment outcome.

					Multivariate analysis			
	Total	**Favorable outcome (n=47)**	**Unfavorable outcome (n=7)**	***P***	**OR**	**95% CI**		***P***
Age	38±13	37±13.5	41±12	.518	1.019	0.962	1.080	.512
BMI	21±1.97	21±1.96	19±1.12	.016	0.537	0.310	0.928	.026
Bilateral X-ray lesions				.203	2.844	0.564	14.340	.205
Unilateral	35 (65%)	32 (68%)	3 (43%)					
Bilateral	19 (35%)	15 (32%)	4 (57%)					
DR				1.000	1.324	0.264	6.627	.733
MDR	34 (63%)	30 (64%)	4 (57%)					
XDR	20 (37%)	17 (36%)	3 (43%)					
New				1.000	1.324	0.264	6.627	.733
Yes	20 (37%)	17 (36%)	3 (43%)					
No	34 (63%)	30 (64%)	4 (57%)					
Prior first-line treatment				.687	1.453	0.289	7.299	.650
Yes	19 (35%)	16 (34%)	3 (43%)					
No	35 (65%)	31 (66%)	4 (57%)					
Prior second-line treatment				.366	0.393	0.043	3.572	.407
Yes	15 (28%)	14 (30%)	1 (14%)					
No	39 (72%)	33 (70%)	6 (86%)					
Total number of resistant drugs	4 (2.9)	4 (2.8)	6 (3.9)	.275	1.437	0.884	2.337	.144
	4.7±1.6	4.6±1.5	5.6±2.1					
Four-month culture conversion				1.000	1.105	0.222	5.509	.903
Yes	22 (41%)	19 (40%)	3 (43%)					
No	32 (59%)	28 (60%)	4 (57%)					
Presurgery sputum PCR				.687	1.852	0.325	10.538	.487
Positive	32 (59%)	27 (57%)	5 (71%)					
Negative	22 (41%)	20 (43%)	2 (29%)					

BMI=body mass index, CI = confidence interval, DR=drug resistance, MDR=multidrug-resistant, OR=odds ratio, PCR=polymerase chain reaction, XDR=extensive drug-resistant.

according to whether the patients had a positive PCR result or not we found no differences between the groups. The role of routine muscle flap reinforcement in patients with MDR-TB is debatable. Other authors provide 4 indications for the use of a muscle flap: positive sputum at the time of surgery, pre-existing bronchopleural fistula, polymicrobial contamination of the thoracic cavity, and anticipated space problems after lobectomy.[20] In our study, it was used to prevent the postoperative development of bronchopleural fistulae, especially in patients with a positive sputum at the time of the operation. All our patients had positive sputum cultures or smears.

The successful treatment of any infectious disease involves a delicate balance of host and pathogen processes. Surgery for MDR-TB can best be considered as a neoadjuvant "debulking" procedure to remove a major, focal burden of TB bacilli contained within necrotic and nonviable lung tissue. In one study, resected tissue culture demonstrated mycobacterial growth even from patients who were sputum AFB smear-negative preoperatively.[30] In the present study, we also performed tissue culture for 9 subjects with sputum culture-negativity before surgery, and all of them had tissue that was both smear- and culture-positive. Incomplete resection of TB lesions, especially cavities, but also nodules, bullae, microcavities, or fibrotic areas, is one of the risk factors for disease relapse.[31] These prior studies and the excellent outcome in our study exemplify the benefit of complete or radical removal of all tuberculous lesions for cure in both MDR-TB patients.

The only risk factor associated with poor outcome in univariate and multivariate analyses was BMI. This suggests that patients with a higher BMI were more likely to have a favorable outcome. Unfortunately, there is very limited literature on risk factors for poor outcome among MDR-TB surgical patients. A study from Latvia found that less drug resistance was associated with favorable outcomes,[26] another study from Korea[27] found that low BMI, increasing drug resistance, and bilateral disease were associated with poor outcomes. In a study of retreatment cases from the United States,[32] XDR-TB, bilateral disease, and low BMI were associated with poor outcomes. An issue with all reported MDR/XDR-TB surgery studies including ours is limited sample size, making it difficult to conduct a meaningful multivariate analysis, fully evaluating risk factors for a poor outcome.

As mentioned above a major limitation of this study is the small sample size. In addition, this study has other limitations including the retrospective nature of the analysis, the limited follow-up time, and the lack of a control group. Other factors that need to be considered are the large time span for patient inclusion and the fact that some patients were transferred from other hospitals, meaning that they did not have a unified standard premedication strategy, which made it difficult to obtain more instructive clinical conclusions.

Our findings are similar to previous reports suggesting that surgical resection may improve MDR-TB outcomes.[28,29,32–38] Our findings support the important role of adjunctive surgical resection in the management of pulmonary MDR-TB patients who meet the criteria for surgery. Preoperative sputum smear positive or negative MDR-TB is not an absolute indication for surgery, it is only a preoperative reference. The optimal timing of adjunctive surgery remains unknown and has not been adequately addressed in treatment guidelines or clinical studies.

The results of this study show that a series of patients with MDR-TB had good treatment outcomes after adjunctive pulmonary resection. Higher BMI was related to a favorable outcome. Our study suggests that proper patient selection and the timing of operations are crucial to achieve a high success rate of pulmonary MDR-TB with well-localized pulmonary cavities.

References

[1] Orenstein EW, Basu S, Shah NS, et al. Treatment outcomes among patients with multidrug-resistant tuberculosis: systematic review and meta-analysis. Lancet Infect Dis 2009;9:153–61.

[2] Problems of multidrug- and extensively drug-resistant TB. Drug Ther Bull 2012;50:21–4.

[3] Sotgiu G, Ferrara G, Matteelli A, et al. Epidemiology and clinical management of XDR-TB: a systematic review by TBNET. Eur Respir J 2009;33:871–81.

[4] Chiang CY, Yew WW. Multidrug-resistant and extensively drug-resistant tuberculosis. Int J Tuberc Lung Dis 2009;13:304–11.

[5] Jassal M, Bishai WR. Extensively drug-resistant tuberculosis. Lancet Infect Dis 2009;9:19–30.

[6] Zhang J, Gou H, Hu X, et al. Status of drug-resistant tuberculosis in China: a systematic review and meta-analysis. Am J Infect Control 2016;44:671–6.

[7] Duan Q, Chen Z, Chen C, et al. The prevalence of drug-resistant tuberculosis in mainland china: an updated systematic review and meta-analysis. PLoS ONE 2016;11:e0148041.

[8] Zhao Y, Xu S, Wang L, et al. National survey of drug-resistant tuberculosis in China. N Engl J Med 2012;366:2161–70.

[9] Torun T, Tahaoglu K, Ozmen I, et al. The role of surgery and fluoroquinolones in the treatment of multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 2007;11:979–85.

[10] Somocurcio JG, Sotomayor A, Shin S, et al. Surgery for patients with drug-resistant tuberculosis: report of 121 cases receiving community-based treatment in Lima. Peru Thorax 2007;62:416–21.

[11] Chan ED, Laurel V, Strand MJ, et al. Treatment and outcome analysis of 205 patients with multidrug-resistant tuberculosis. Am J Respir Crit Care Med 2004;169:1103–9.

[12] Yew WW, Leung CC. Update in tuberculosis 2007. Am J Respir Crit Care Med 2008;177:479–85.

[13] Olcmen A, Gunluoglu MZ, Demir A, et al. Role and outcome of surgery for pulmonary tuberculosis. Asian Cardiovasc Thorac Ann 2006;14:363–6.

[14] Mohsen T, Zeid AA, Haj-Yahia S. Lobectomy or pneumonectomy for multidrug-resistant pulmonary tuberculosis can be performed with acceptable morbidity and mortality: a seven-year review of a single institution's experience. J Thorac Cardiovasc Surg 2007;134:194–8.

[15] Pairolero PC, Arnold PG, Piehler JM. Intrathoracic transposition of extrathoracic skeletal muscle. J Thorac Cardiovasc Surg 1983;86:809–17.

[16] World Health OrganizationManagement of MDR-TB: a field guide: a companion document to Guidelines for Programmatic Management of Drug-Resistant Tuberculosis: Integrated Management of Adolescent and Adult Illness (IMAI). Pearson Schweiz Ag 2009;63:307–19.

[17] Takeda S, Maeda H, Hayakawa M, et al. Current surgical intervention for pulmonary tuberculosis. Ann Thorac Surg 2005;79:959–63.

[18] Naidoo R. Active pulmonary tuberculosis: experience with resection in 106 cases. Asian Cardiovasc Thorac Ann 2007;15:134–8.

[19] Ashour M. Pneumonectomy for tuberculosis. Eur J Cardiothorac Surg 1997;12:209–13.

[20] Pomerantz BJ, Cleveland JCJr, Olson HK, et al. Pulmonary resection for multi-drug resistant tuberculosis. J Thorac Cardiovasc Surg 2001;121:448–53.

[21] Lalloo UG, Naidoo R, Ambaram A. Recent advances in the medical and surgical treatment of multi-drug resistant tuberculosis. Curr Opin Pulm Med 2006;12:179–85.

[22] Iseman MD, Madsen L, Goble M, et al. Surgical intervention in the treatment of pulmonary disease caused by drug-resistant *Mycobacterium tuberculosis*. Am Rev Respir Dis 1990;141:623–5.

[23] Moran GJ, Fuchs MA, Jarvis WR, et al. Tuberculosis infection-control practices in United States emergency departments. Ann Emerg Med 1995;26:283–9.

[24] Moran GJ, McCabe F, Morgan MT, et al. Delayed recognition and infection control for tuberculosis patients in the emergency department. Ann Emerg Med 1995;26:290–5.

[25] Pomerantz M, Mault JR. History of resectional surgery for tuberculosis and other mycobacterial infections. Chest Surg Clin N Am 2000;10:131–3.

[26] Dravniece G, Cain KP, Holtz TH, et al. Adjunctive resectional lung surgery for extensively drug-resistant tuberculosis. Eur Respir J 2009;34:180–3.

[27] Kim HJ, Kang CH, Kim YT, et al. Prognostic factors for surgical resection in patients with multidrug-resistant tuberculosis. Eur Respir J 2006;28:576–80.

[28] Michael JS, John TJ. Extensively drug-resistant tuberculosis in India: a review. Indian J Med Res 2012;136:599–604.

[29] Morris MI, Daly JS, Blumberg E, et al. Diagnosis and management of tuberculosis in transplant donors: a donor-derived infections consensus conference report. Am J Transplant 2012;12:2288–300.

[30] Pomerantz M, Brown J. The surgical management of tuberculosis. Semin Thorac Cardiovasc Surg 1995;7:108–11.

[31] van Leuven M, De Groot M, Shean KP, et al. Pulmonary resection as an adjunct in the treatment of multiple drug-resistant tuberculosis. Ann Thorac Surg 1997;63:1368–72.

[32] Gegia M, Kalandadze I, Kempker RR, et al. Adjunctive surgery improves treatment outcomes among patients with multidrug-resistant and extensively drug-resistant tuberculosis. Int J Infect Dis 2012;16:e391–6.

[33] Park SK, Kim JH, Kang H, et al. Pulmonary resection combined with isoniazid- and rifampin-based drug therapy for patients with multidrug-resistant and extensively drug-resistant tuberculosis. Int J Infect Dis 2009;13:170–5.

[34] Man MA, Nicolau D. Surgical treatment to increase the success rate of multidrug-resistant tuberculosis. Eur J Cardiothorac Surg 2012;42:e9–12.

[35] Xie B, Yang Y, He W, et al. Pulmonary resection in the treatment of 43 patients with well-localized, cavitary pulmonary multidrug-resistant tuberculosis in Shanghai. Interact Cardiovasc Thorac Surg 2013;17:455–9.

[36] Vashakidze S, Gogishvili S, Nikolaishvili K, et al. Favorable outcomes for multidrug and extensively drug resistant tuberculosis patients undergoing surgery. Ann Thorac Surg 2013;95:1892–8.

[37] Shiraishi Y, Nakajima Y, Katsuragi N, et al. Resectional surgery combined with chemotherapy remains the treatment of choice for multidrug-resistant tuberculosis. J Thorac Cardiovasc Surg 2004;128:523–8.

[38] Orki A, Kosar A, Demirhan R, et al. The value of surgical resection in patients with multidrug resistant tuberculosis. Thorac Cardiovasc Surg 2009;57:222–5.