Review

Surgical Treatment of Complications of Pulmonary Tuberculosis, including Drug-Resistant Tuberculosis

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SUMMARY

Surgery for drug-resistant tuberculosis has been shown to be safe and effective, with similar level of mortalities associated with surgical intervention observed with that for lung cancer. While surgery has been an option to treat TB in the pre-antibiotic era, it is now increasingly used to treat complications of pulmonary TB, particularly in patients with drug-resistant TB who do not respond to medical treatment. The two most frequent indications for lung resection in drug-resistant TB, are i) failed medical treatment with persistent sputum positivity or ii) patients who have had medical treatment and are sputum negative, but with persistent localized cavitary disease or bronchiectasis. Massive hemothorax is a potentially life-threatening complication of TB. Lung resection is potentially curative in patients with massive hemothorax or cavitary or bronchiectatic disease. Bronchial artery embolization in these patients has a high success rate but bears also the risk of recurrence. Lung resection can be safely undertaken in selected patients with HIV co-infection and pulmonary complications of TB. Ambulatory drainage is a novel, safe, affordable and effective method of draining a chronic TB associated empyema thoracis. We review here the current surgical treatment of the complications of pulmonary TB and discuss the experience from the Durban Cardiothoracic Surgery Unit for the surgical treatment of patients with complicated pulmonary TB.

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1. Introduction

Prior to the availability of anti-tuberculosis (TB) drugs, surgery was the only treatment option for the treatment of TB. However, with the advent of anti-tuberculosis drugs, antibiotic treatment became the standard therapy for TB. Yet the battle against TB and the progress of the past several decades in TB treatment is at risk to be lost with the emergence of drug-resistant TB (DR-TB). Lung resection is increasingly being explored as a treatment option for patients with DR-TB who exhibit poor results in the antibiotic treatment regimens, or are in need for prolonged treatment with second line drugs or injectable drugs. This is particularly true for patients with extensively drug resistant TB (XDR-TB). Patients with DR-TB exhibiting lung destruction exhibit similar risks of surgery as compared to patients undergoing lung resection for bronchial carcinoma. 1,2 It is also recommended that lung resection should be the primary modality of treatment and not bronchial artery

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embolization for patients with life-threatening massive hemoptysis with localized cavitary lung disease. We discuss in this review the current literature in the field of surgical treatment for TB and discuss our experience (i.e., the Durban Cardiothoracic surgical team) concerning the management of patients undergoing lung resection. We also discuss a novel method of managing chronic TB associated empyema, not suitable for decortication.

The results of medical treatment particularly for XDR-TB are dismal with cure rates of 7% at 2 years and 5% at 5 years and mortality of 46% at 2 years and 73% at 5 years. Surgery for pulmonary TB gave rise to the discipline of Thoracic Surgery. It is now more increasingly being investigated as treatment for drug-resistant tuberculosis in the presence of lung destruction. Thoracic surgery has evolved from drainage of empyema through bronze cannula and ‘collapse therapy’ to the current status where intricate, extensive lung and chest wall resections can be undertaken for various lung pathologies. It can be broadly categorised into diagnostic interventions and therapeutic interventions. In the developed world, the majority of lung resections are for bronchial carcinoma. However, in the developing world, TB remains the main indication for lung resection.

2. Evolution of Surgical Treatment of Pulmonary TB

The early period for the surgical treatment of TB is reflected in the three decades of the nineteenth century, when collapse therapy was performed by open surgical pneumothorax with a high rate of asphyxia–associated death. Induced pneumothorax was widely practiced in the pre-antibiotic era in more than 100,000 patients with pulmonary TB over a period of quarter century starting in 1882 until the early 20th century. Lobectomy, open drainage, and instillation of antiseptics into cavities was tried in the beginning of 20th century. Improved collapse therapy and increased quality of thoracic surgery took place from 1930 onwards along with the advent of better diagnostic procedures with bronchoscopy, improvement in X-ray technique and development of bronchospimetry. Initially surgical intervention in Pulmonary TB was not viewed positively due to the high risks associated with TB (disease). Nevertheless, pneumonectomies, lobectomies, thoracoectomy (removal of ribs to collapse the chest wall) and pleurolytic operations were performed in selected patients with some success. Throughout 1950s, thousands of Pulmonary TB patients received surgical resection as adjunctive therapy to Streptomycin therapy.

3. Lung Resection in TB

The classic indications for lung resection in TB are recurrent chest infections, recurrent minor hemoptysis, massive hemoptysis, DR-TB, any complication of TB (empyema thoracis, broncho-pleural fistula) persistent sputum positivity with irreversible pulmonary destruction: cavitation and/or bronchiectasis and suspicion of malignancy. Surgery usually entails either lobectomy, bilobectomy, pneumonectomy or staged lobectomies for localized bilateral disease. Wedge or segmental resections are usually avoided due to the increased risk of a bronchopleural fistula. Occasionally, it is performed in the case of upper lobar disease warranting upper lobectomy as well as apical lower segmental disease, given that the basal segments are adequate to fill the pleural space.

4. Surgery for DR-TB

Renewed interest in surgical intervention in TB was driven by increasing failures in TB chemotherapy, i.e., with the advent of MDR-TB, the emergence of XDR-TB and TDR-TB that are resistant to most drugs in use. Surgery for DR-TB has been shown to be safe and effective, with operative mortalities similar to surgery for lung cancer. We have also shown that surgery for XDR-TB and massive hemoptysis is safe. There are two specific indications for lung resection in DR-TB, i.e., failed medical treatment with persistent sputum positivity and patients who have had medical treatment and are sputum negative, but have localized cavitary disease or bronchiectasis. These are potential ‘safe-havens’ for mycobacteria that give rise to future relapses. Mycobacteria have developed mechanisms to overcome the host immune surveillance. Little is known about this in the human lung, a potential area for future investigation. The first report on lung resection from our center reviewed 23 patients of MDR-TB including 10 sputum culture positive over a 5-year period between 1996-2000. Pneumonectomy was performed in 17 patients and lobectomy in 6 individuals with no operative or postoperative mortality. Major complications developed in 4 patients (17.4%); 2 had post-pneumonectomy empyema and 2 underwent rethoracotomy for bleeding. The outcome was excellent with a cure rate of 95.6% (only 1 out of 10 remained sputum positive at the end of the follow-up period of the study). The Durban cardiothoracic surgical team suggested pulmonary resection as an important adjunct to medical therapy in carefully selected patients with localized disease with adequate pulmonary reserve, for patients who have multiple previous relapses, or for patients whose sputum remains positive after 4 to 6 months of appropriate medical treatment. In the authors’ view, surgery offers high cure rates with acceptable morbidity and mortality.

The predominance of left-sided resection in the first series and other published reports suggested that the more horizontal course of the narrower left main bronchus and the smaller peri bronchial space contribute to the left lung being more commonly involved. Preoperative sputum positivity is a recognized risk factor for post-pneumonectomy empyema, which developed in 2 of our patients, both of whom were sputum positive preoperatively. One of these patients was HIV positive with a preoperative empyema. Bronchial stump reinforcement has been advocated to prevent the postoperative development of bronchopleural fistula.

A subsequent report from our centre first reported surgical experience in XDR-TB in Africa reviewing 11 patients with confirmed XDR-TB referred for surgical resection between Jan 2007 to June 2010, due to failure of a treatment regimen appropriate for XDR-TB, complications of TB sequelae such as hemoptysis or recurrent chest infections. Among these, 6 were excluded from surgical intervention due to bilateral, extensive cavitory disease. Five patients were surgically treated, two with pneumonectomies and three with upper lobectomies with no perioperative mortality or major morbidity with cure in all these patients. One of these five was also HIV infected and two others were healthcare workers. The Durban cardiothoracic surgical team has stressed the necessity of appropriately selecting candidates with DR-TB for surgical intervention and in particular the ones with persistent sputum positivity with second line chemotherapy based on drug susceptibility.

A different study, performed in Georgia, showed results from MDR-TB and adjunctive surgical resection: resection was performed in 37 MDR/XDR-TB patients with 5 new cases and 32 of retreatment cases with favourable outcome in 29 out of 37 (78%). These favorable data suggested adjunct surgical treatment in the management of M/XDR-TB.

A systematic review and meta-analysis of adjunctive pulmonary resection for patients with MDR-TB with the inclusion of 15 studies (a total sample size of 949) showed the overall cure rate as high as 84%. Aggressive use of resectional lung surgery was practiced at the National Jewish Medical and Research Center (NJMRC) which is a specialized hospital for DR-TB care. The report covered the period 1984 to 1998 and described the clinical management and outcome of 205 MDR-TB cases, of which
130 patients underwent adjunctive surgical intervention with at least one resectional procedure. Of 122 patients who had resection performed in one lung, 63 had a pneumonectomy, and 59 had one or more lobectomies. Of eight patients who had resection performed in both lungs, five had one or more lobectomies, and three had a pneumonectomy in combination with contralateral lobectomy. One additional patient had a thoracoplasty, and another underwent pneumoperitonemus therapy. The progressive use of surgery reflected the evolution of their experience in which surgical intervention associated with low complication rates. The favorable data consolidated the notion that surgical intervention will lead to favorable outcomes in individuals undergoing surgery.

Our approach to lung resections for DR-TB has been to resect all diseased lungs similar to surgery for lung cancer. Lung resection includes all bronchiectatic and cavitary (TB) disease, as well as areas of nodularity: these may be macro abscesses containing mycobacteria. Ongoing studies are being undertaken to assess whether we have achieved the clinical objective of lung resection in DR-TB: Mtb culture conversion and prevention of future relapses. We work in close collaboration with the pulmonary physicians in managing these patients.

5. Surgery for Massive Hemoptysis

Lung resection has to be undertaken as an emergency only in the case of massive hemoptysis with cavitary lung disease or bronchiectasis. Patients with massive hemoptysis are referred directly to us or by the pulmonary physicians. While TB may present with pulmonary disease and symptoms, its effect and presence is beyond the lungs and should be regarded as a systemic/lymphatic disease. Surgery addresses only the ‘gross’, macroscopic disease, and not the systemic or disease beyond the resected lung. Therefore, most patients with pulmonary TB should undergo a full course of TB treatment. The Durban cardiothoracic surgical team advises surgery for patients who have completed at least 6 months of TB treatment prior to surgery. Various durations of treatment, from 0.6 months to up to 240 months, have been published in the literature and there is no consensus on this topic. Patients with massive hemoptysis along with cavitary lung disease have had little or no anti-TB treatment. Bronchial artery embolization has been shown to be less effective in cavitary lung disease and bronchiectasis; it has shown high recurrence rates of hemoptysis. The success rate of bronchial artery embolization for massive hemoptysis has been over 90%. But these data are collected from a heterogeneous population including infections other than TB, cystic fibrosis, malignancies and more importantly for bronchiectasis, not restricted to cavitary lung disease.

A publication from Turkey reported surgical management of TB-related hemoptysis in 59 patients with 21 performed in the context of emergency procedures for massive hemoptysis (>600 ml/d), in 24 over first 2 days with major hemoptysis (200-600 ml/d), and in 14 within first 4 days with persistent minor (<200 ml/d) hemoptysis. The bleeding area was localized in all patients prior to surgery by fiberoptic or rigid bronchoscopy. Pneumonectomy was undertaken in 4 patients due to destroyed lung, lobectomy was performed in 39 patients with cavitary lesions occupying the lobe, segmentectomy or wedge resection was performed in 16 patients due to cavitary lesion occupying one or more segments. Twenty of those patients were receiving anti-TB treatment and remaining 39 were asymptomatic with no current anti-TB medications even though they had irregular previous treatment history. Fifty one of 59 had AFB from cavitary lesion or sputum cultures. In their experience, thoracotomy with double-lumen endotracheal intubation and resection of cavity was curative and lifesaving in TB-related hemoptysis with only <7% perioperative mortality which included single-lumen endotracheal intubation.

Surgical therapy has been quite extensively pursued in the management of chronic pulmonary TB patients in Russia. Report with results from 109 patients (56 newly diagnosed TB and 53 retreatment cases) treated with artificial pneumothorax applied for average period of 4.5 months in the first group and for 9 months in the second group respectively, showed 100% clinical improvement in all new cases and 81% culture negativity in the retreatment cases. 80% of these cases had DR-TB.

A South Korean study addressing surgical intervention for M/XDR-TB in 72 patients during the period of 1996 to 2008 included 26 patients with XDR-TB and reported with 90% favourable outcome following surgical resection. The indications for surgery were failure of medical treatment (71%), localized disease or persistent cavity with high probability of relapse (24%) and combined complication of hemoptysis (5%). The majority of patients (81%) were culture positive. A lobectomy was performed in 53% of patients with or without segmentectomy or wedge resection, 32% had pneumonectomies, 14% had segmentectomies and only 1 out of 72 had multiple wedge resections. There were 11% post-operative complications. Adjunct surgical therapy with adequate chemotherapy was proposed to achieve high cure rated and to preserve lung parenchyma for selected patients of M/XDR-TB.

As massive hemoptysis is a life-threatening condition, lung resection is curative and bronchial artery embolization has high recurrence rates, we would recommend that lung resection is the primary modality of treatment of this group of patients. Patients with localized disease are assessed for suitability concerning lung resection using standard medical treatment options, including a 6 minute walk test, Karnovsky score, arterial blood gas on room air and pulmonary function tests.

Figure 1 shows a High Resolution CT Scan (HRCT) from a 40 year old patient treated at our Cardiothoracic Unit who presented with massive hemoptysis. The HRCT Scan of the chest showed bronchiectasis and cavitation in the right lung, the patient was treated with bronchial artery embolization and then underwent a right pneumonectomy. Our recommendation is that for patients with massive hemoptysis, with cavitary lung disease and/or bronchiectasis and who are suitable for a lung resection that this should be the definitive treatment modality.

Figure 1. Massive Hemoptysis. A High Resolution CT Scan of a patient with massive hemoptysis, showing middle lobe bronchiectasis and lower lobe cavitation.
embolization should only be a temporary measure. We have shown that lung resection for massive hemoptysis is curative and can be safely undertaken. In addition, as a basic surgical principle, there must be irreversible pulmonary destruction, cavititation and/or bronchiectasis in order to offer surgical therapy. If there are reversible pulmonary changes, e.g. consolidation and tuberculoma, then medical treatment is the primary treatment. The failure of medical treatment, e.g. persistent sputum positivity along with a large inflammatory mass represents a clinical indication when lung resection can be considered in order to decrease the burden of disease and allow better access of the anti-TB drugs in order to be more effective. Thus, lung resection for pulmonary TB has been performed in the past for TB - prior to the availability of antibiotics for TB - and it has undergone a full circle: it is now indicated for the treatment of DR-TB and failed medical treatment in patients with localized disease.

6. Lung Resection in HIV Co-infected Patients

In medical patients with TB in Durban, 69.8% are HIV co-infected.24 Patients who are HIV positive, we assess the CD4 count and serum albumin levels. Patients who have a CD4 count <400/mm³ are treated with ARVs for at least 3 months prior to surgery. If their albumin levels are <30 g/dl, they are referred to the dietician for nutritional supplementation until their albumin levels are 30 g/dl or higher prior to surgery. In patients on anti-retroviral treatment, viral load level is also assessed. Only if the viral load is undetectable, surgery is performed in our Cardiothoracic Unit. Patients with detectable viral loads are referred back to the infectious diseases physicians for review and modification of their ARVs regimen until it is undetectable, prior to surgery. We have previously shown to achieve good results for cardiac surgical procedures in HIV positive patients25 and similar measures can be used to manage patients with Mtb-HIV co-infections.

In HIV positive patients that would require emergency lung resection (usually massive hemoptysis), our approach is to assess the patient on general grounds for suitability for lung resection, effort tolerance before hemoptysis, nutritional status, stigmata of AIDS and specific investigations include arterial blood gas and albumin levels. Another group of patients that requires special attention concerning lung resection are children with bronchiectasis secondary to pulmonary TB. These patients usually present with a history of recurrent chest infections, hemoptysis, persistent sputum positive state or empyema. We have previously shown that pneumonectomy can be safely undertaken in children.26 In the intra-operative management of these patients, lung isolation and prevention of contamination of the opposite lung with Mtb positive tissue can be challenging. We use double-lumen tubes to isolate the lung in older children and a bronchus blocker and/or positioning when it is not possible to place a double lumen tube.

The extent of lung resection is usually the equivalent of one lung. Bilateral lung operations in our practice have been staged upper lobectomies for hemoptysis or DR-TB. We have occasionally undertaken a left pneumonectomy and subsequently a tightly shrunk, bronchiectatic right upper lobe resected for the management of symptom recurrence. The dilemmas arise in patients with scattered bronchiectasis, bronchiectasis in un-shrunken lung and patients warranting upper lobectomy, with middle lobectomy on the right in the presence of apical lower segmental bronchiectasis. The surgical options are pneumonectomy, apical lower segmental resection with/without thoracomyoplasty.

7. Preparation of Patients for Lung Resection

As in any patient undergoing a major thoracic surgical procedure, the pre-operative preparations of these patients are critical for ensuring a good outcome. We ensure at least 3-6 months of TB treatment before surgery. Patients with hemoptysis or recurrent chest infections are also treated with appropriate antibiotics if an organism is isolated or if sputum cultures are negative or in emergency surgery with empiric triple antibiotics. The crucial role of the physiotherapist cannot be emphasized enough in the pre-operative preparation and post-operative care of these patients to ensure a successful outcome.

Preoperative physiotherapy, pulmonary function testing, arterial blood gas on room air and a six minute walk testing are undertaken. Use of bronchodilators in patients with a history of smoking or evidence of bronchospasm on pulmonary function testing is also essential. We undertake a bronchoscopy in the preoperative workup of the patient. This is for ‘air-way toilet’ and serves at the same time to sample specimens for microbiological testing. This is repeated at weekly intervals, until the airways are clear. This may not be always possible, for instance, if the surgeon undertakes lung resection in the presence of scattered upper lobar bronchiectasis and lower lobe bronchiectasis. The aim would be here to remove the bronchiectatic lower lobe that would bring about amelioration of the symptoms associated with recurrent chest infections. When operating thorough an empyema space, a pus swab is taken about 72 hours preoperatively and these patients receive the appropriate antibiotics peri-operatively. If there is minimal drainage from the empyema space, lung resection is only planned weeks/months later, then the intercostal drainage (ICD) is removed and the wound is allowed to close. This allows the possibility of operating through a “clean” field, since drains are potentially two-way streets for infective organisms. Intra-operative management would include lung isolation with a double lumen tube or a bronchus blocker, meticulous hemostasis and a thoracic epidural for intraoperative and post-operative analgesia. Post-operatively patients are usually extubated and managed in an intensive care ward.

8. Novel method of managing a chronic TB associated empyema thoracis

A chronic TB empyema space requires excellent drainage. Methods of drainage include ICD, rib-resection if not amenable to ICD, and ambulatory drainage (Figure 2 and 3). An ambulatory drain is used in our patients with a chronic empyema with a non-pliable cortex covering the lung until completion of TB treatment and in patients with a chronic empyema not amenable to definitive surgery.

This is determined by comparing the chest radiography with the ICD connected to an underwater drain, with a chest radiograph with the ICD open to air. If the lung does not collapse upon opening the ICD to air, this indicates that the cortex covering the lung is non-pliable and the ICD is converted to an ambulatory drain. The self-retaining intercostal drain is cut about 5 cm from the skin, a sterile safety-pin is passed through the cut drain to prevent it falling into the empyema space and the drain is allowed to drain into a colostomy bag (Figures 2). This allows patients greater mobility, without being tethered to an underwater drain; patients can also be treated this way in an outpatient setting. This is also an important modality of treatment in patients with an empyema, not amenable to definitive surgical intervention, e.g. lung resection. It is also suitable to use in patients with thick pus, since there are no valves in the system that can be occluded (by pus). Post-pneumonectomy empyema is a dreaded complication after lung resection. It is especially common after trans-empyema pneumonectomies. In our practice, it occurs in 44% of trans-empyema pneumonectomies. The key to drainage of an empyema is dependent drainage. If a plain antero-posterior (AP) and lateral chest radiograph is not helpful, we use a two view sinogram, and AP and lateral chest radiograph with contrast instilled through the
intercostal drain to determine the most suitable part of the empyema space.

9. Less common indications for thoracic surgical interventions in TB:

1. In 1997, Hewitson, et al.\textsuperscript{28} described lymph node (LN) evacuation for airways compression in 36 patients from a total of 161 children that underwent 168 therapeutic surgical interventions. These patients had airway compression and impairment that did not respond to high dose corticosteroids. Of note, Hewitson stated that the LN should not be excised, just evacuated as the nodes are densely adherent to the airways. Figure 2 shows the typical CT scan of a 4 year old child with TB lymphadenitis. The lymph nodes typically show ring enhancement with central breakdown. In our Cardiothoracic unit, about 40 lung resections/year are being undertaken for children for pulmonary TB; yet there was until now no clinical need for the selective LN evacuation procedure. This patient was managed successfully with TB treatment and steroids.

2. Cavernostomy is an uncommon procedure indicated for patients with massive hemothysis who are not candidates for lung resection.\textsuperscript{29,30} Bronchial artery embolization is now also an option, although it is less successful long term in patients with cavitary lung disease and bronchiectasis, the pathologies most common in patients with hemothysis secondary to TB.\textsuperscript{10,19} We would therefore strongly recommend that patients with massive hemothysis should be seen by a joint thoracic surgical, pulmonologist and interventional radiology team to decide on the best treatment strategy.

3. Thoracoplasty is a cosmetically unappealing procedure undertaken to collapse the chest wall onto the lung during partial lung resection and the remaining lung is deemed unlikely to fill the pleural space,\textsuperscript{29} as well as for the treatment of a post-pneumonectomy empyema. It may also be undertaken as a secondary procedure (for the same indication) or for patients with chronic pleuro-pulmonary suppuration not amenable to decortication, nor for lung resection.\textsuperscript{31,32} More commonly, this procedure is undertaken for the treatment of a post-pneumonectomy empyema; it is important to close the broncho-pleural fistula, if present. Myoplasty without thoracoplasty is preferred. However, a large number of patients in need a thoraco-myoplasty are malnourished and lack the muscle mass for a myoplasty. Therefore, a thoracoplasty in our Cardiothoracic Unit is the procedure most frequently performed. Surgery through progressively smaller incisions and Video Assisted Thoracic Surgery (VATS) has become increasingly frequent. Generally, lung resection for TB complications does not represent a good case for video-assisted surgery. In the majority of these patients, the lung is firmly attached to the chest wall and has to be carved using cautery and careful hemostasis. Predictors of unsuitability for VATS lung resection are multiple cavities, multi-lobar tuberculosis, extensive pleural thickening and peribronchial lymph node calcification.\textsuperscript{33} We had to occasionally perform a posterior rib osteotomy to get adequate exposure in order to safely mobilize the lung.
10. The pre-clinical and clinical collaboration offers new insights

Lung resection in the setting of active TB, DR-TB and HIV co-infection provides exciting prospects for collaboration between thoracic surgeons and laboratory scientists undertaking TB research to decipher the pathophysiology of TB granuloma. This collaboration may also aid in design more effective intervention(s) targeting lung tissue. While the animal models have been a major endeavor in the development of drugs and vaccines, it is well known that there is lack of central caseous necrosis in the murine lung granuloma, the TB–associated pathology is different than those seen in human patients. Differences in TB pathophysiology between mice and humans may be one of the many reasons for failures in translation of novel TB vaccines and TB drugs. Access to surgical pulmonary tissues may aid to elucidate the mechanisms of lung destruction and cavitation in TB, it may also represent a unique opportunity to work in a symbiotic collaborative interdisciplin ary approach between clinicians and clinical researchers. The clinically impressive data after surgical pulmonary resections may also encourage are more detailed immunological evaluation of the role of high antigenic (bacterial) burden and its role on expanding anti-M. tuberculosis directed immune responses, particularly in the case of DR-TB. It is also reasonable to speculate that surgical resection options should be discussed as an option in combination with drug-therapy as well as with any emerging novel therapies which would curtail the period of treatment and to achieve cure or non-infectivity in a shorter time frame.

11. Discussion

There is renewed interest in the surgical treatment of complicated pulmonary TB, including DR-TB. Surgery has been shown to be safe and in the presence of localized cavitary or bronchietatic disease, lung resection is potentially curative. Massive hemoptysis may be a life-threatening complication of TB. While bronchial artery embolization is able to stop hemoptysis in up to 90% of cases, recurrence of hemoptysis is frequent in the presence of bronchiectasis and cavitary lung disease. This experience has guided our thoracic surgical unit’s practice to prioritize lung resection as the primary treatment option in such patients. The indications for surgery in patients with TB are recurrent chest infections, recurrent minor hemoptysis, massive hemoptysis, DR-TB and the complications of TB such as empyema thoracis. Lung resection can also safely be undertaken in reasonably immunocompetent HIV co-infected patients. A novel technique (ambulatory drain) for the management of a chronic empyema thoracis is also described. Observational studies with surgical interventions have shown a high treatment success rate when used as adjunctive therapy in M/XDR-TB patients, however there has been lack of randomized controlled trials of surgical resections. In many cases of complicated M/XDR-TB with localized lesions and tissue destruction along with failure to become culture negative, adjunctive surgical therapy may play a major role in improving clinical outcome. Collaboration and synergy between clinicians (from various disciplines) and basic scientists is critical for making tangible progress toward achieving control of the TB epidemic.

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References


