Technical aspects of video-assisted thoracic surgery (VATS) pneumonectomy for tuberculosis: a review of attitudes to be taken

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Abstract: Closely related to the development of thoracic surgery, tuberculosis, once fully controlled through medical therapy, now emerges again as a threat, considering its multi drug-resistant and extensively drug-resistant forms. Pneumonectomy presents as a therapeutic option for treating complications of the disease, improving quality of life. Diseased lung harbors bacteria as a constant source of infection and antibiotic resistance development. The damaged lung also has no ventilatory function, working as a shunt, disturbing the patient's quality of life. Usually performed through conventional open thoracotomy, as video-assisted thoracic surgery (VATS) is now a well-established technique, its applicability in tuberculosis surgery must be addressed. Severe pleural adhesion, lymph node enlargement, hypertrophy of the bronchial circulation and difficult to compress lung parenchyma are the main technical difficulties found through this approach. Pneumonectomy is mostly described for the treatment of lung cancer in the literature. Here we review the indications and the main technical considerations to be taken during the thoracoscopic approach for this surgery, regarding the challenges presented by a benign inflammatory disease. Improving the health status of the patient, thorough previous nutritional and antibiotic therapy, taking care with adhesions, lymph nodes calcification, carefully identifying the structures and preventing bronchopleural fistula are the main points to be considered. Post-surgical chemotherapy is also of great importance. Pneumonectomy is a viable procedure through VATS. Conventional open thoracotomy, however, should not be neglected, associating both techniques as needed, always aiming for the best patient care.

Keywords: Tuberculosis (TB); multidrug-resistant (MDR); video-assisted; thoracic surgery; pneumonectomy

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Introduction

In the developed world, tuberculosis (TB), once a deadly and disseminated disease, is adequately controlled. Data available from the World Health Organization shows, in the United States, the mortality rate is of 0.16 per 100,000 population per year and the total incidence of 3.1 per 100,000 population per year (data from 2016). Yet, in 2016, about 10.4 million people were infected and 1.7 million died of TB in the world. About 95% of cases and 98% of deaths occur in developing countries (1). Brazil is one of the 22 countries with high burden of the disease worldwide. The country achieved, in 2011, the "STOP TB Partnership" (Partnership founded in 2001 with the goal to end tuberculosis epidemics by 2030 through the achievement of many targets) target to reduce mortality by 50% when compared to 1990 (2). The emergence of multidrug-resistant TB (MDR-TB), however, brings again TB as an increasing threat. In 2016, less than 12% of cases of MDR-TB were cured (3).

Thoracic surgery itself developed through the intent to treat patients suffering from complications of TB. Once based on healthy climate and sun exposure, TB treatment evolved from many surgical techniques (such as thoracoplasty, plombage and phrenic nerve crush) (4) to achievable cure with isoniazid and streptomycin protocols (5). Regardless of, MDR-TB and extensively-drug resistant TB (XDR-TB) proliferation brings again surgery as a necessary measure to manage affected patients (6,7). Approximately 5% of patients with pulmonary TB still require surgery (6). Pneumonectomy remains the ultimate curative treatment for TB complications (8).

Surgical lung resection for TB is able to remove active proliferation sites, which are also of difficult drug penetration. Areas of destroyed lung and wall thickening may harbor as many as 10^9 microorganisms, even when sputum is negative (9).

Lobectomy is the most common procedure described in the literature for XDR-TB and pneumonectomy was the second most common procedure (37.7%) (10). Pneumonectomy for a benign inflammatory lung disease has been considered a high-risk procedure, with high morbidity (11). Major complications are empyema, bronchopleural fistula, postoperative hemorrhage and respiratory insufficiency (4,8,10). Risk factors for complications are the presence of preoperative empyema, aspergilloma, violation of the parenchymal cavity during pneumonectomy, excessive blood loss, re-exploration of hemorrhage and intraoperative contamination of the pleural cavity (11). A minimum of three to six months of preoperative chemotherapy associated with nutritional supplementation and control of coexisting medical conditions are advocated by most authors as measures to prevent such complications (7,12).

Conventional open lobectomy is well-established on the literature, related to favorable results, acceptable mortality and morbidity rates in relation to its satisfactory long-term survival (11). However, it involves large incisions, through multiple muscles, resulting in significant pain and morbidity and large scar tissue (6). Through development of video-assisted thoracic surgery (VATS), the rate of thoracoscopic lobectomies is steadily increasing in leading thoracic centers (exceeding already more than 50% of all resections) (13). Less post operatory pain, lesser complication rates, faster recovery and diminished hospitalization time are advantages brought by that technique.

Regarding pneumonectomy, it is mostly described for the treatment of lung cancer. This procedure brings significant trauma, often followed by postoperative complications, many of them life threatening. For patients with complex inflammatory lung disease, such as TB, undergoing this procedure was combined with even higher mortality and morbidity (14). When there is compromise of the quality of life of patients with TB complications, however, it is a suitable option. Minimally invasive surgery may be a resource for reducing the burden of those patients. Results are equivalent for long-term survival comparing elective standard thoracotomy and thoracoscopy (15). Pneumonectomy may be done through standard thoracotomy, 3-port VATS, 2-port VATS and uniportal VATS (5). It may even be done through robot assisted thoracic surgery, as there are lobectomies described through that technique (5).

Pulmonary resection combined with anti-tuberculous chemotherapy has shown success rates of 89–96% (9). Maintenance of medical treatment for 18 to 24 months after surgery and 12 months after culture conversion shows effective results (16). Considering the technical difficulty and poor healthy-status of most patients, pneumonectomy has favorable and satisfactory results if well indicated (8,11,17).

Surgery in TB

Though medical therapy is successful in most cases, approximately 5% of patients with pulmonary TB, require surgery (6). The aim of surgery is removal of bacilli present in necrotic and non-viable lung tissue (18). Many patients who are preoperatively sputum-culture negative have positive cultures from resected lung tissue (10). As the tuberculous cavity restricts drug penetration and protects the mycobacteria from host defenses, it is an optimal growth environment for TB (10). A systematic review and meta-analysis from Xu *et al.* estimates treatment success rate of pulmonary surgery for TB associated with chemotherapy with cure or completed treatment of 84% (9). Pneumonectomy could be performed with acceptable mortality and morbidity. It remains as the treatment of choice for MDR-TB (7,11,19,20).

Indications

Indications for resection includes failure of medical treatment (MDR-TB and XDR-TB), localized disease or persistent cavity with high probability of relapse, stenosis of bronchial TB, bronchial dilation, pulmonary atelectasis, aspergilloma and repeated or prolonged hemoptysis (6,14,16,18,21) (*Table 1*).

MDR-TB refers to *Mycobacterium tuberculosis* strains

Table 1 Indications for resection due to tuberculosis complications

Failure of medical treatment (MDR-TB and XDR-TB)
Localized disease or persistent cavity with high probability of relapse
Stenosis of bronchial tuberculosis
Bronchial dilation
Pulmonary atelectasis
Aspergilloma
Repeated or prolonged hemoptysis

MDR-TB, multidrug-resistant tuberculosis; XDR-TB, extensively drug-resistant tuberculosis.

with *in vitro* resistance to the two most effective anti-TB drugs: isoniazid and rifampin (5). When such an isolate is resistant to any second-line injectable agent (e.g., amikacin, capreomycin or kanamycin) and any fluoroquinolone, the strain is termed XDR-TB (9). Surgical resection of diseased lung areas is used to remove segments of the lungs containing high concentrations of those resistant bacilli. Through mycobacteria population reduction, the sterilizing properties of post-surgical chemotherapy is enhanced as is the likelihood of treatment success (5). Success rates of 89–96% are reported for the association of pulmonary resection with antituberculous chemotherapy (9).

Lung destroyed, and wall thickened areas may harbor from 10^7 to 10^9 microorganisms, even when sputum culture is negative. Host-specific immunity cannot control the infection in these locations (9,18). The tuberculous cavity is also an ideal growth environment as it can hinder the penetration of pharmacological agents. Those cavities might be sites of drug-resistance development (18). CD4 and CD8 T cells cannot access the lumen of those cavities. Bacillary growth is also highly active at the surface macrophages (10).

Bronchial dilation causes persistent cough, building up sputum. Associated with pulmonary atelectasis, the patient develops important dyspnea, tachypnea and respiratory distress, worsening the quality of life.

Preexisting cavities in the lungs are favorable for the proliferation of aspergillomas. Actually, they usually always arise in such conditions. Prior pulmonary disease is often found in patients with aspergillosis, TB presenting a high chance for that development (22). *Aspergillus spp* infections brings dense fibrous adhesions and vascularized pleura. VATS may significantly lower the risk of complications and amount of blood loss through its sharp vision (23). Pleural-based aspergillomas may present a high risk of complicating with empyema, as the residual space may be infected (24). Pneumonectomy for aspergilloma, however is not suitable for VATS (23). As have been found in our department cases and in some authors opinion, the shifted mediastinum, narrowed intercostal space (ICS), severe adhesion and calcified lymph nodes distort the vascular and bronchial anatomy, making the thoracoscopic access difficult (22,23).

Massive recurrent hemoptysis may cause a patient to require repetitive hospitalization. Blood loss may be greater than 500 mL in 24 h. Even bronchial artery embolization may bring temporary relief. Some patients present with more than four episodes a year. Pneumonectomy in those cases improves the quality of life (16).

Why pneumonectomy?

The diseased lung harboring mycobacteria is a constant source of infection. When a single lung is seriously damaged, it presents as a risk of dissemination to the healthy, functioning lung. As its structure is destroyed and fibrous tissue prevails, that lung works as a shunt, presenting no ventilating function at all. Anatomical resection in the early stage enhances the efficacy of medical treatment and prevents further disease spread, also reducing the likelihood of drug resistance (18). In developing countries where access to healthy is not readily available, however, patients may present with complicated and irreversible damage. Pneumonectomy, then, presents as a possibility of improving life quality by solving those complications.

Difficulties of pneumonectomy

Pneumonectomy for TB is a high-risk procedure and technically hazardous. Multiple adhesions and scarring fills the thorax, creating an area of chronic sepsis (25).

Culture-conversion after over 18 months of drug treatment is recommended for treating MDR-TB patients, before surgery is attempted, minimizing the risk of complications (5,25). Another advantage is to allow time for nutritional supplementation and control of coexisting medical conditions, as those patients almost always present with a very poor health status (5).

Some authors list as limitations for VATS in patients with TB, severe pleural adhesion, non-reactive lymph node enlargement in the peri-bronchial area, limited and localized lesion, hypertrophy of the bronchial circulation and difficult to compress lung parenchyma. Those are listed

Table 2 Main complications of tuberculosis surgery

Complications of tuberculosis surgery
Bronchopleural fistula
Hemorrhage (postoperative)
Respiratory insufficiency

as the main technical difficulties (6,26). Often, surgery-related hemorrhage is induced as a result of injury of pulmonary hilar vessels. Due to the dense scar tissue and inflammatory adhesions around the vessels, the surgeon cannot readily identify the anatomic structures near the hilum (27).

Regarding anatomical resection through VATS, the high prevalence of pulmonary TB in Asia was an initial concern when 3-port VATS was introduced (as it was well established for lung cancer treatment). Yet, extensive pleural adhesions and difficult to dissect calcified lymph nodes did not prevent development of 3-port VATS in Asia (28). Those concerns, as many authors experience demonstrates, are not contraindications even for uniportal VATS. In Sao Paulo, Brazil, we have been promoting the development of uniportal surgery with satisfactory results in our Thoracic Surgery Department (Beneficencia Portuguesa Hospital, Sao Paulo, Brazil) (29). Concerning pneumonectomy, specifically designed long instruments and long energy sources, as ultrasonic devices, as well as curved dissecting instruments have made the difficulties of pleural adhesiolysis manageable (28).

Currently, many centers prioritize the use of VATS for pulmonary resections (6,27). Thoracoscopic pneumonectomy is a safe alternative to open pneumonectomy, showing equivalent results. It requires several small incisions (even only one in uniportal VATS), does not involve latissimus dorsi, serratus magnus, pectoralis major or pectoralis minor muscles, remaining the scapulae and ribs intact (6).

Complications

As risk factors for major complications, tuberculous lesion and pulmonary abscess, blood loss of 1,000 mL or greater, operative duration of 4 h or longer are the main factors (11). Pulmonary abscess, percent predicted forced expiratory volume in 1 second less than 60% and the use of suture for closing the bronchial stump are risk factors for bronchopleural fistula (11,27). Sequential examinations with chest radiography after pneumonectomy are an invaluable method of screening for complications, especially in the early postoperative period. In the late postoperative period, CT is often superior to chest radiography (30) (*Table 2*).

VATS technique

VATS is based on some basic steps. Patients should undergo standard cardiopulmonary work up, with at least transthoracic echocardiogram and pulmonary function testing, split lung function testing, cardiopulmonary exercise testing and frailty testing (21).

It has the advantages of being more aesthetic, having less post-operative pain, giving lower complication rates and having a faster recovery (14).

General anesthesia is induced via a double-lumen tube for single lung ventilation (31) Thoracic epidural analgesia may be associated for post operatory pain reduction. The use of patient-controlled anesthesia also may be employed for that purpose (14).

The patient is positioned in lateral decubitus with flexion of the operating table at the level of the tip of the scapula to widen de ICSs (6,13,21,31).

The incision is made as usual at the 7th or 8th ICS midaxillary line for introduction of the thoracoscope (generally 10-mm trocar), generally 3 to 4 cm in length. The second port is inserted anteriorly at the 4th or 5th ICS in anterior axillary line (12-mm diameter) and the third one at the 5th or 6th ICS in posterior axillary line. Both are made under thoracoscopic guidance (6,13,14,21,31).

First, it is important to ensure the safety of the procedure. Benign lesions, associated with chronic pleurisy and repeated and persistent infection, cause severe pleural adhesion and hilar and mediastinal lymph nodes calcification (14). Hilar lymphadenopathy is a very common finding in those patients (5). The first step after the instruments placement is the lysis of adhesions and through exploration of the pleura (21). Separating the pleural adhesion during the operation is of prime importance (27). Complete mobilization of the lung is essential to enable the assessment of the feasibility of a thoracoscopic resection (21). Pleural adhesions and bleeding are the most frequent reason of conversion (31), even thoracoscopy providing a wide visual field. Moderate adhesions can generally be divided with an ultrasonic device (6), The surgeon may need to convert the surgery to open pneumonectomy if thick and adherent adhesions of difficult lysis are found, if lung collapse is contra-indicated or if there is difficult to isolate hilar structures.

The lung needs to be completely mobilized and the feasibility of the surgery assessed. After deflation of the lung, the hilum should be visualized, the pulmonary ligament freed and the posterior mediastinal pleura of the hilum dissected (13). The meticulous and careful dissection and isolation of the hilar structures should then be done (32). The major bronchi, pulmonary veins and pulmonary artery and peri-hilar lymph nodes should be identified. Hilar lymphadenopathy is a very common finding in these patients. Careful dissection of the hilar lymph nodes will increase exposure of the hilar vessels and make vascular control safer (5). Also, lymphadenectomy is not always necessary.

Arteries, veins and bronchi are isolated and sectioned separately with a mechanical endostapler. When thin, they may be sectioned by applying clips and cutting with ultrasonic devices. From most authors and our experience, the pulmonary vein dissection should be done first, allowing division in a rapid succession (6,32). That allows the isolation of the pulmonary artery with full attention and without delay and also minimizes vascular congestion that may occur from systemic bronchial artery collateral circulation in the lung (32).

Exposure of the pulmonary artery and bronchi can then be achieved. Widely opening the mediastinal pleura and lymphadenectomy of stations 5 and 6 allow proper visualization of the main pulmonary artery. The main pulmonary artery is then dissected from the mainstem bronchus, through blunt dissection towards the bronchi—avoiding potential injury to the artery (32). Adhesions between pulmonary artery and adjacent lymph nodes are removed. If necessary, the main port may be extended to facilitate this step. If disease course has been long, dense adhesion between calcified lymph nodes and the pulmonary artery may be present, contributing to the risk of bleeding (6). A red rubber catheter can be placed in between the two structures and used as a guide to safely bring the stapler across the artery (32). Dissection of any additional peri bronchial or adventitial tissue facilitates the passage of the stapler. We always have to check if there is hemodynamic compromise prior to firing the stapler, as it suggests lesion of the main pulmonary artery (32).

Lymphatic and fibrous tissues nearest to the bronchus can then be removed. The bronchus dissection is done up to the level of the carina, avoiding a long bronchial stump (6,32). Regional tuberculous lymph nodes are removed as they may break up or perforate into the bronchus. This procedure decreases the chances of empyema or bronchopleural fistula (33). Normal lymph nodes do not necessarily need to be dissected, as this preserves the vasculature around the bronchial stump, preventing bronchopleural fistula (33). After closing the bronchial stump with the endostapler, we recommend its coverage with pericardial fat pad, pericardium or intercostal muscle flaps. Some authors submerge the bronchial stump underwater to check for air leak (13). Minimal dissection and avoidance of electrical diathermy could prevent bronchopleural fistula (25).

The deflated specimen is extracted enclosed inside a plastic bag. Hemostasis and wound closure is done (12). A 28F chest tube is inserted through the anterior port, connected to an underwater seal (13). Some authors routinely use metoprolol, digoxin and furosemide post-operatively, preventing acute pulmonary edema after surgery (14). Treatment with anti-tuberculous drugs should be maintained after surgery. The treatment regimen of MDR-TB and XDR-TB should include one fluoroquinolone (moxifloxacin, gatifloxacin, levofloxacin, ofloxacin or ciprofloxacin) in combination with pulmonary resection (26) (*Table 3*).

Discussion

Closely related to the development of thoracic surgery, TB, once fully-controlled through medical therapy, now emerges again as a threat, considering its MDR-TB and XDR-TB forms. Pneumonectomy is the ultimate therapeutic option for complications of the disease that compromise quality of life.

Patients with failure to medical treatment, persistent cavity with high relapse probability, stenosis, bronchial dilation or atelectasis, associated aspergilloma or repeated hemoptysis are candidates for pneumonectomy.

Tough most of the literature data describes anatomic resections for TB, we find it is a viable procedure through VATS technique, as long some aspects are taken into consideration. The surgeon must properly prepare his patient prior to the procedure. Improving the usual poor health status, taking care the severe adhesions associated with chronic benign inflammatory disease and lymph nodes calcification, carefully identifying all structures and preventing bronchopleural fistula are the main points to be considered. The post-surgical chemotherapy is also of great importance.

In situations where it is difficult to circumvent adhesions and calcification of structures, the intrapericardial vascular ligation may be needed, which may limit thoracoscopy. Completing the surgery with VATS should not be an obligation. The surgeon must use his judgment to consider

Table 3 Main aspects to be taken into consideration during pneumonectomy for complications of tuberculosis

Main aspects during tuberculosis surgery	Solutions
Patients poor health status	Chemotherapy prior to surgery
	Nutritional improvement
	Comorbidities addressing
Severe pleural adhesion; hilar and mediastinal lymph nodes calcification	Meticulous dissection of the pulmonary hilum and complete mobilization of the lung, properly identifying the vessels
Pulmonary vein dissection	Allows isolation of pulmonary artery
	Minimizes congestion from systemic bronchial artery collateral circulation
Bronchus dissection up to the level of the carina	Avoiding long bronchial stump
Bronchopleural fistula prevention	Coverage of bronchial stump with pericardial fat pad, pericardial tissue or with intercostal muscle and its neurovascular bundle flaps
Remaining bacilli in the microcirculation	Post-surgery chemotherapy

converting to conventional open thoracotomy, avoiding exceedingly lengthy surgeries because of hard to isolate hilar structures, severe adhesions or local inflammation.

Conclusions

TB incidence in Brazil has declined, as long as its complications. For such cases, pneumonectomy is an option to improve the patient's quality of life. The use of VATS is now well established, being the main option in many centers. It can be used for TB pneumonectomy, being a powerful tool for its treatment. Conventional open thoracotomy should not be neglected, however. Both techniques must be used in association if needed, always aiming the best option for the patient.

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