

Mortality Rate of Patients with Tuberculosis-Destroyed Lung Who Underwent Pulmonary Resection: Evidence Based Case Report

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ABSTRACT

Introduction: Tuberculosis (TB) is a leading cause of death worldwide alongside with HIV. Globally, there were an estimated 9.6 million new TB cases and 1.5 million deaths from TB in 2014. Tuberculosis-destroyed lung is a complication of severe pulmonary tuberculosis that can causes various respiratory symptoms and pulmonary dysfunction. Destroyed lung can seriously compromises long-term survival, so it is imperative to do the surgery.

Objective: to determine the chance of survival in patients with tuberculosis-destroyed lung who underwent pulmonary resection.

Method: Literature searching on PubMed, Cochrane Library, ProQuest, EBSCOHost, Science Direct and ClinicalKey was conducted on March 15th, 2016. Three articles were included to be appraised for its validity and relevance using several aspect based on Center of Evidence-Based Medicine, University of Oxford for prognostic study.

Result: Study by Byun CS. et al showed operative mortality of 6.8%, SE 2.9%, 95% CI (3.9% to 9.7%). The post-operative mortality rate in 5 years is 11.1%, SE 3.7%, 95% CI (7.4% to 14.8%) and 23.8%, SE 5%, 95% CI (18.8% to 28.8%) in 10 years. Rifaat A. et al revealed post-operative mortality rate of 7.1%, SE 6.8%, 95% CI (0% to 20.3%). Bai L. et al presented post-operative mortality rate of 5.8%, SE 1.8%, 95% CI (4% to 7.6%).

Conclusion: Pulmonary resection for tuberculosis-destroyed lung patients can be achieved with low overall mortality rate (operative and post-operative).

Keywords: destroyed lung, mortality, resection, surgery, tuberculosis

ABSTRAK

Latar Belakang: Tuberkulosis (TB) merupakan salah satu penyebab utama kematian di dunia. Pada tahun 2014, diperkirakan terdapat 9.6 juta kasus TB baru dan terdapat 1.5 juta kematian yang disebabkan oleh TB dari seluruh dunia. *Tuberculosis destroyed lung* merupakan komplikasi dari TB paru berat dan dapat menyebabkan berbagai gangguan dan disfungsi pernapasan. *Destroyed lung* dapat mempengaruhi angka harapan hidup sehingga perlu dilakukan pembedahan. Pembedahan dapat membantu mencapai terapi yang efektif dengan membuang jaringan TB aktif.

Tujuan: Untuk menentukan peluang kelangsungan hidup pada pasien dengan *tuberculosis-destroyed lung* yang menjalani operasi.

Metode: Pencarian literatur dilakukan pada tanggal 15 Maret 2016 pada PubMed, Cochrane Library, ProQuest, EBSCOHost, Science Direct and ClinicalKey. Tiga artikel diikuti sertakan untuk ditelaah klinis untuk menilai validitas dan relevansinya menggunakan *Center of Evidence-Based Medicine, University of Oxford for prognostic study*.

Hasil: Studi oleh Byun CS dkk menunjukkan angka mortalitas operatif sebesar 6.8%, SE 2.9%, 95% CI (3.9% to 9.7%). Mortalitas dalam 5 tahun sebesar 11.1%, SE 3.7%, 95% CI (7.4% to 14.8%) dan 23.8%, SE 5%, 95% CI (18.8% to 28.8%) dalam 10 tahun. Rifaat A. dkk menunjukkan mortalitas *post-operasi* sebesar 7.1%, SE 6.8%, 95% CI (0% to 20.3%). Bai L. dkk memperlihatkan mortalitas *post-operasi* sebesar 5.8%, SE 1.8%, 95% CI (4% to 7.6%).

Simpulan: Tindakan pembedahan pada pasien dengan *Tuberculosis destroyed lung* dapat dilakukan dengan angka mortalitas yang rendah (operatif dan *post-operatif*).

Kata Kunci: bedah, *destroyed lung*, mortalitas, reseksi, tuberkulosis.

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INTRODUCTION

Tuberculosis (TB) is a leading cause of death worldwide alongside with HIV. Globally, there were an estimated 9.6 million new TB cases and 1.5 million deaths from TB in 2014. A timely diagnosis and correct treatments is the key to successfully reduce TB burden.¹ Most patients with pulmonary tuberculosis can be treated with combined anti-tuberculous drugs, however some small cases still need surgical intervention.^{1,2} Although surgical intervention is considered a high risk procedure, it is still indicated when anti-tuberculous drugs fail to control TB and its complications.^{2,3} Tuberculosis-destroyed lung, chronic TB empyema, persistent cavity, destroyed lung, pneumothorax, bronchiectasis, tracheal or bronchial stenosis, and massive hemoptysis remain as valid indications for surgery in both drug-sensitive and drug-resistant TB.²⁻⁵

Tuberculosis-destroyed lung is a complication of severe pulmonary tuberculosis that can cause various respiratory symptoms and pulmonary dysfunction.^{6,7,8} Most cases of destroyed lung have a history of undergoing retreatment for TB, with delayed healing or resistance to anti-tuberculous drugs.⁶ Areas of destroyed lung and thick walled cavitary lesions have less exposure to host defenses and are poorly penetrated by anti-tuberculous drugs. These cavities act not only as huge reservoir for TB infection, but also as the site for drug resistance development.⁵

Surgical resection is usually done because the bacterial count within the cavity is high and antibiotic treatments fail to reach the site of infection.⁴ Excision of these lesion will reduce the overall organism load in the lung while concurrently eliminating sites of high concentrations of drug-resistant bacilli.⁵ Therefore, the major point in surgery is to resect the active TB lesions as effectively as possible to achieve a relatively effective treatment.^{4-5,8}

As destroyed lung itself can seriously compromises long-term survival, it is imperative to do the surgery. In destroyed lung patients without surgical treatment, the overall mortality rate was only 28% and the median survival was estimated at only 39 months.⁹ The objective of this report is to determine the chance of survival in patients with tuberculosis destroyed lung who underwent pulmonary resection.

CASE ILLUSTRATION

Patient, male 69 years old with worsening symptoms of dyspnea 4 days prior to hospital admission. There were productive cough with greenish tint. Dyspnea was felt continuously, not precipitated by exercise, weather, or certain position. No nausea and vomiting. Patient has a history of asthma since childhood and has been treated with salbutamol. Three months before admitted to hospital, patient was admitted to RSCM due to dyspnea. Patient was diagnosed with lung infection.

Patient had history of pulmonary tuberculosis (TB) 14 years ago and completed his 6 months therapy in local community health center (*Puskesmas*). Eleven years ago, he developed TB again but only received treatment for 2 months from *Puskesmas* because of poor compliance. Two years before hospital admission, the patient was diagnosed with TB and had been on tuberculosis treatment but hasn't been declared cured by the doctor.

On the physical examination of the lungs, there were dyspnea, reduced vesicular sound on the left lung, and wet rhonchi from both lungs. The blood examination showed anemia, leukocytosis, thrombocytosis, and high erythrocyte sedimentation rate; the leukocyte differential count showed low lymphocyte and high monocyte. The patient also suffered from decreased serum protein, albumin, and albumin-globulin ratio. According to thorax x-ray, there was impression of pleural effusion and atelectasis in the left lung. From thorax CT Scan examination, the patient was confirmed with destroyed lung in the left lung.

Patient was diagnosed with Health Care-Associated Pneumonia (HCAP) with differential diagnosis of tuberculosis with secondary infection; destroyed lung on the left lung; and malnutrition. The management given to the patient were oxygen 3 lpm, IVFD NaCl 0.9% 500 mL/day, 1900 ccal diet (protein 1,2 g/kgBB), cefepime 2 x 1 g, acetylcysteine 3 x CI, acetaminophen 3 x 500 mg, salbutamol inhalation every 6 hours, budesonide inhalation every 8 hours, and omeprazole 1 x 40 mg. The patient was planned to undergo front lobectomy for the destroyed lung.

The prognosis of this patient for *ad vitam*, *ad functionam*, and *ad sanationam* were *dubia ad malam*.

CLINICAL QUESTION

Based on the illustration above, the clinical question is formulated as follow: “What is the mortality rate of patients with tuberculosis-destroyed lung who underwent pulmonary resection?”

METHOD

Literature searching on PubMed, Cochrane Library, ProQuest, EBSCOHost, Science Direct and ClinicalKey was conducted on March 15th, 2016 using key words ‘lobectomy’, ‘pneumonectomy’, ‘resection’, ‘surgery’, ‘tuberculosis’, and ‘destroyed lung’. The specific search terms and Boolean operators are recapitulated in **Table 1**. Hand searching was also done on The International Journal of Tuberculosis and Lung Disease.

Studies obtained from literature searching were screened based on titles and abstracts. Articles were scanned for double and full text availability. If an article appeared relevant, it was examined in full text. Search strategy, results, and the inclusion and exclusion criteria are shown in the flowchart (**Figure 1**). From the search criteria, six articles met the inclusion and exclusion criteria. Through further selection process, only three studies have relevant statistical analysis. Those three studies, which included three cohort studies, were eligible for this report:

1. Byun CS, Chung KY, Narm KS, Lee JG, Hong D, Lee CY. Early and long-term outcomes of pneumonectomy for treating sequelae of pulmonary tuberculosis. *Korean J Thorac Cardiovasc Surg.* 2012;45:110-15.¹⁰
2. Rifaat A, Ghally MA, Sobhy E, Badr A, Metwally A. Pulmonary resection can improve treatment outcome in re-treatment pulmonary tuberculosis and its complications. *Egypt J Chest Dis Tuberc.*2014;63:385-388.¹¹
3. Bai L, Hong Z, Gong C, Yan D, Liang Z. Surgical treatment efficacy in 172 cases of tuberculosis-destroyed lungs. *Eur J Cardiothorac Surg.* 2012;41:335-40.¹²

RESULT

After literature selection, all included trials were appraised for its validity and relevance using several aspect based on Center of Evidence-Based Medicine, University of Oxford for prognostic study (**Table 2** and **Table 3**). The summaries of the appraised articles and included studies are depicted in **Table 4** and **Table 5**.

Validity

All studies included patients with tuberculosis-destroyed lung who underwent any types of pulmonary resection, including: pleuropneumonectomy, pneumonectomy or lobectomy. Blinding for outcome assessors is not needed because the outcome is objective (mortality).

Table 1. Search Strategy

| Database | Search Strategy | Finding | Selected |
|---------------|--|---------|----------|
| Pubmed | ((surgery[Title/Abstract] OR resection[Title/Abstract] OR pneumonectomy[Title/Abstract] OR lobectomy[Title/Abstract])) AND tuberculosis[Title/Abstract] AND destroyed lung[Title/Abstract] | 49 | 4 |
| Cochrane | (surgery OR resection OR pneumonectomy OR lobectomy) AND tuberculosis AND destroyed lung | 0 | 0 |
| ScienceDirect | (resection OR pneumonectomy OR lobectomy) AND tuberculosis AND destroyed lung | 282 | 3 |
| EBSCOhost | AB (surgery OR resection OR lobectomy OR pneumonectomy) AND AB tuberculosis AND AB destroyed lung | 30 | 4 |
| ProQuest | ab(surgery OR resection OR pneumonectomy OR lobectomy) AND ab(tuberculosis) AND ab (destroyed lung) | 8 | 1 |
| ClinicalKey | surgery AND tuberculosis AND destroyed lung | 68 | 3 |

Table 2. Validity Assessment of the Included Studies

| Parameter | Byun CS. <i>et al</i> | Rifaat A. <i>et al</i> | Bai L. <i>et al</i> |
|--|--|--|---|
| Sample | 73 patients with tuberculosis-destroyed lung who underwent surgery | 14 patients with tuberculosis-destroyed lung who underwent surgery | 172 patients with tuberculosis-destroyed lung who underwent surgery |
| Complete patient follow up | Yes, median of 96.7 months (range from 6 to 353 months) | Yes, 21.4 ± 6 months | Yes, 6 months |
| Blinded assessment of outcome | Objective outcome (mortality) | Objective outcome (mortality) | Objective outcome (mortality) |
| Adjustment for subgroups with different prognoses (if present) | Yes, outcome of study are subdivided by age | No | No |
| Validation in an independent group of people | No | No | No |

Importance

Table 3. Importance Assessment of the Included Studies

| Author | Outcomes of the study | Precision of the prognostic estimates |
|-------------------------------------|--|---|
| Byun CS. <i>et al</i> ⁰ | The operative mortality is 6.8% After patients follow-up and using the Kaplan-Meier survival curve, the 5 year and 10 year survival rate were 88.9% and 76.2% respectively Post-operative complication is 40.3%. | Operative mortality is 6.8%, SE 2.9%, 95% CI (3.9% to 9.7%) Post-operative mortality rate in 5 years is 11.1%, SE 3.7%, 95% CI (7.4% to 14.8%) and 23.8%, SE 5%, 95% CI (18.8% to 28.8%) in 10 years Post-operative complication is 40.3%, SE 5.7%, 95% CI (34.6% to 46%) |
| Rifaat A. <i>et al</i> ¹ | After 21.4 ± 6 months follow-up, one patient died post-operative due to respiratory failure (mortality rate is 7.1%) | Post-operative mortality rate is 7.1%, SE 6.8%, 95% CI (0% to 20.3%) |
| Bai L. <i>et al</i> ² | After 6 months follow-up, the overall post-operative mortality rate is 5.8% (10/172). Five patients died 30 days post-surgery due to pleural hemorrhage and hemorrhagic shock. Another five died within six months due to acute respiratory failure, BPF, and massive hemoptysis. Operative complication rate is 18.6%. The most common complication being empyema. | Post-operative mortality rate is 5.8%, SE 1.8%, 95% CI (4% to 7.6%) Operative complication rate is 18.6%, SE 1.23%, 95% CI (15.59% to 21.01%) |

Table 4. Summaries of the Appraised Articles

| Articles | Validity | | | | | | | Relevance | | | |
|-------------------------------------|--------------|--------------------|-------------------|------------------------------------|-----------|------------------|--------------------------|------------------------------------|--------|-------------|------------------------|
| | Study design | Number of patients | Level of evidence | Sample assembled at a common point | Follow-up | Blinding outcome | Adjustment to sub groups | Validation in an independent group | Domain | Determinant | Measurement of outcome |
| Byun CS, <i>et al</i> ⁰ | Kohort | 73 | 1B | + | + | + | + | - | + | + | + |
| Rifaat A, <i>et al</i> ¹ | Kohort | 14 | 1B | + | + | + | - | - | + | + | + |
| Bai L, <i>et al</i> ² | Kohort | 172 | 2B | + | + | + | - | - | + | + | + |

Table 5. Summaries of the selected articles

| Author | Primary Endpoint | Result | Summary |
|-------------------------------------|--|---|--|
| Byun CS. <i>et al</i> ⁰ | Operative mortality and post-operative mortality | Operative mortality is 6.8%, SE 2.9%, 95% CI (3.9% to 9.7%) Post-operative mortality rate in 5 years is 11.1%, SE 3.7%, 95% CI (7.4% to 14.8%) and 23.8%, SE 5%, 95% CI (18.8% to 28.8%) in 10 years Post-operative complication is 40.3%, SE 5.7%, 95% CI (34.6% to 46%) | Although the post-operative complication rate was still high, the overall survival rate was found to be satisfactory. |
| Rifaat A. <i>et al</i> ¹ | Post-operative mortality | Post-operative mortality rate is 7.1%, SE 6.8%, 95% CI (0% to 20.3%) | Surgery is effective when pharmacological therapy fails and can be achieved with low mortality rate |
| Bai L. <i>et al</i> ² | Post-operative mortality | Post-operative mortality rate is 5.8%, SE 1.8%, 95% CI (4% to 7.6%) Operative complication rate is 18.6%, SE 1.23%, 95% CI (15.59% to 21.01%) | Surgical treatment for destroyed lung is difficult, but can be achieved with low mortality rate with careful management of surgery |

Applicability

The participants of all the studies are similar to the illustrated patient, hence the evidences from the included studies are important in making conclusion of regarding the management of the patient.

DISCUSSION

Tuberculosis-destroyed lung (TDL) is a complication of severe pulmonary tuberculosis that can causes various respiratory symptoms and pulmonary dysfunction.^{6,8} TDL results from years of chronic progressive TB and

inadequate treatment. Patients with TDL showed extensive parenchymal destruction and obstructive ventilator defect that may be due to bronchiectasis and emphysema. The extend of lung destruction is related to decreased lung function and can seriously compromises long-term survival.^{6,9,13-14} Pulmonary destruction is usually present in situations of poor medical treatment or multidrug resistance. It is often accompanies by mixed infection and usually associated with complications, which includes pulmonary superinfections, aspergilloma, recurring or massive hemoptysis, and bronchopleural fistula (BPF).^{8,15}

Areas of destroyed lung and thick walled cavitary lesions can contain up to 10^7 to 10^9 actively replicating *Mycobacterium tuberculosis*, even in patients with culture-negative sputum. These tuberculous lesions have less exposure to host defenses and are poorly penetrated by anti-tuberculous drugs. These cavities act not only as huge reservoir for TB infection, but also as the site for drug resistance development.⁵ The overall prognosis of TDL is poor. According to a study of non-operated patients, overall mortality was 27.8% and median survival was estimated at only 39 months.⁹

Surgical resection is usually done because the bacterial count within the cavity is high and antibiotic treatment fails to reach the site of infection.⁴ The major point in surgery is to resect the active TB lesions as effectively as possible to achieve a relatively effective treatment.⁸ Excision of these lesion will reduce the overall organism burden in the lung while simultaneously removing sites of high concentrations of drug resistant bacilli.⁵ Therefore, the surgical removal of these lesion will enhance the likelihood of curing the disease completely.^{4,5} There were no therapeutic trials that have been performed in TDL patients, and there are no standard therapies for TDL. Patients have to be assessed and treated on an individual basis.⁹

From three studies that we analyzed in this EBCR, we found three cohort studies that were appropriate for this report. One study by Byun CS. *et al* reported operative mortality rate, which was 6.8%.¹⁰ All three studies followed the patients for a period of time. Bai L. *et al* followed the patients for 6 months and the post operative mortality was the lowest at 5.8%.¹² Rifaat A. *et al* followed the patients for the median of 21.4 ± 6 months. The post-operative mortality was 7.1%.¹¹ Study by Byun *et al* followed the patients for the longest, with the median of 96.7 months (range from 6 to 353 months). It is the only study that analyzed the long-term survival rates in post-operative patients. The 5 year and 10 year survival rates were 88.9% and 76.2% respectively. We can determine the overall mortality in 10 years was 23.8%.¹⁰ Compared to median survival rate of non-operated patients, the post-operative mortality rate of both study is satisfactory.⁹⁻¹¹

Although all studies display low mortality rates, post-operative complications were still high. In studies by Bai *et al* and Byun *et al*, post-operative complication rates were 18.6% and 40.3% consecutively. The most

common post-operative complication was empyema, 16.7% (Byun *et al*) and 34.4% (Bai *et al*).^{10,12} Surgery for destroyed lung is indeed complex, and complications may arise, such as: respiratory failure, bronchopleural fistula, empyema, infection and bleeding.^{10,12,15-17} Complication rate varies between areas of low and high prevalence of tuberculosis. In countries with a high prevalence of tuberculosis, the incidence of complications such as empyema and bronchopleural fistula is reported to be fewer than 10%.¹⁸⁻¹⁹ By contrast, in low prevalence country, the incidence of such complications can occur up to 25%.¹⁹

However, surgery remains an important part of management for sequelae of tuberculosis. There are ways to reduce the risk of complications.^{15-16,20} When resection is indicated, careful surgical technique is mandatory in limiting the risk of complications; identifying the optimal point of time for surgery also has a strong impact on the further course of the healing process and thus on the prognosis.^{16,20} Managing the modifiable preoperative risk factors (BMI, smoking, AS score) can reduce the risk of developing post-operative complications.²¹ Covering the bronchial stump with intercostal muscle, pleura, biologic glue, and omentum can be of assistance in preventing postoperative BPF.^{3,16}

There are some limitations to this review. There is no study that compares the mortality rate between TDL patients who underwent surgery and those who didn't, as it was unethical to not operate someone who was indicated for surgery.

CONCLUSION

Pulmonary resection for TDL patients can be achieved with low overall mortality rate (operative and post-operative). Surgery needs to be done if indicated and can increase the survival rate of TDL patients. Although surgery for TDL is difficult and complications may occur, preventive measures can be done to prevent undesirable outcome.

RECOMMENDATION

Future studies are recommended for a therapeutic trial in TDL patients to measure the efficacy of surgery compared to non-surgical therapy.

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