

Surgical management outcomes of tuberculosis with hemoptysis and without hemoptysis

Hemoptizi olan ve olmayan tüberkülozlu hastaların cerrahi tedavi sonuçları

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Abstract

Purpose: Increased complication risk of surgical interventions performed in patients with hemoptysis is a common concern among surgeons. Therefore, here, we investigated the surgical outcomes of tuberculosis patients with hemoptysis.

Materials and methods: Patients, between 1985 and 2018, diagnosed with tuberculosis surgically, were analyzed retrospectively. The patients were divided into two groups; those without hemoptysis (Group 1) and those with hemoptysis (Group 2). The analysis included age, gender, symptoms, comorbidities, Positron Emission Tomography-Computed Tomography (PET-CT) findings, surgical interventions, perioperative complications, lengths of hospital stay, recurrence of hemoptysis, and comparison of Group 1 and 2.

Results: 541 patients with pulmonary tuberculosis diagnosed surgically were analyzed. 448 patients were in Group 1 and 93 patients were in Group 2. The patients in Group 2 were significantly younger than the patients in Group 1 (Group 1 mean age 57.8±6.2, Group 2 mean age 31.2±5.3, $p<0.01$). The most frequent comorbidity was malignancy in both groups. Cavitation was more common in Group 2 (Group 1 92 (20.5%), Group 2 79 (84.9%), $p<0.01$). Postoperative complications and hospital stay length were similar in both groups and there was no hemoptysis recurrence in Group 2. There was no perioperative death in Group 1 while 3 (3%) patients died in Group 2.

Conclusion: The surgical morbidity and mortality of patients diagnosed with tuberculosis after the surgical intervention performed for the diagnosis or treatment of the hemoptysis were not significantly different from those of the patients without hemoptysis

Key words: Complications, hemoptysis, mycobacterium tuberculosis, pulmonary tuberculosis, surgery.

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Öz

Amaç: Hemoptizi hastalarında uygulanan cerrahi girişimlerin artmış komplikasyon riski cerrahlar arasında yaygın bir endişedir. Bu nedenle burada hemoptizi olan tüberküloz hastalarının cerrahi sonuçlarını araştırdık.

Gereç ve yöntem: 1985-2018 yılları arasında cerrahi olarak tüberküloz tanısı alan hastalar retrospektif olarak incelendi. Hastalar iki gruba ayrıldı; hemoptizi olmayanlar (Grup 1) ve hemoptizi olanlar (Grup 2). Analiz yaş, cinsiyet, semptomlar, komorbiditeler, Pozitron Emisyon Tomografisi-Bilgisayarlı Tomografi (PET-CT) bulguları, cerrahi müdahaleler, perioperatif komplikasyonlar, hastanede kalış süreleri, hemoptizi nüksü ve Grup 1 ve 2'nin karşılaştırmasını içeriyordu.

Bulgular: Cerrahi olarak teşhis edilen akciğer tüberkülozu olan 541 hasta incelendi. Grup 1'de 448 hasta, Grup 2'de 93 hasta vardı. Grup 2'deki hastalar Grup 1'deki hastalara göre anlamlı olarak daha gençti (Grup 1 ortalama yaş 57,8±6,2, Grup 2 ortalama yaş 31,2±5,3, $p<0,01$). Her iki grupta da en sık komorbidite maligniteydi. Grup 2'de kavitasyon daha sıkı (Grup 1 92 (%20,5), Grup 2 79 (%84,9), $p<0,01$). Postoperatif komplikasyonlar ve hastanede kalış süresi her iki grupta benzerdi ve Grup 2'de hemoptizi rekürrensi yoktu. Grup 1'de perioperatif ölüm görülmezken Grup 2'de 3 (%3) hasta öldü.

Sonuç: Hemoptizi tanısı veya tedavisi için yapılan cerrahi girişim sonrası tüberküloz tanısı alan hastaların cerrahi morbidite ve mortalitesi, hemoptizi olmayan hastalardan anlamlı olarak farklı değildi.

Anahtar kelimeler: Komplikasyonlar, hemoptizi, mycobacterium tuberculosis, akciğer tüberkülozu, cerrahi.

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Introduction

Tuberculosis is an infectious disease that affects one third of the world's population and causes 1-3 million deaths each year [1]. It is one of the main global struggle issues of the World Health Organization (WHO) [2]. The gold standard method in diagnosis of tuberculosis is microbiological. However, sometimes, the diagnosis cannot be achieved microbiologically via noninvasive methods. In these patients, surgery can be applied for diagnostic purposes.

Patients with tuberculosis can apply with various symptoms. One of the most important symptoms is hemoptysis, that is also one of the most fatal complications. It is also the symptom that forces the patient to seek medical attention in a short time. Early diagnosis and treatment is important for the global control of tuberculosis [3-6]. In this regard, even if it is a major concern for the patient and even if it is a fatal complication, hemoptysis may actually be a chance for early diagnosis and the global control of the disease. On the other hand, hemoptysis can also be confusing, since cancer is almost always found in differential diagnosis of hemoptysis. Moreover, sometimes hemoptysis can not be controlled by medical treatment and even the diagnosis is certain microbiologically, resection of the cavity becomes inevitable. So surgery takes place sometimes for the diagnosis and sometimes for the therapy in tuberculosis.

Here in this study, we evaluated all the patients diagnosed with tuberculosis who had undergone surgery for diagnosis or treatment. We compared surgical morbidity and mortality in patients with hemoptysis.

Participants and methods

A retrospective database search was performed for patients with pulmonary tuberculosis diagnosed surgically at University Faculty of Medicine Thoracic Surgery Department between 1985 and 2018. The patients were divided into two groups; those without hemoptysis (Group 1, 448 patients), and those with hemoptysis (Group 2, 93 patients). Analysis included age, gender, symptoms, comorbidities, Positron Emission Tomography-Computed Tomography (PET-CT) imaging, surgical interventions, complications, lengths of hospital stay, postoperative anti-tuberculosis treatment implementations of both Group 1 and 2.

We performed pleural biopsy in patients with pleural effusion, bronchoscopy in patients with mass in the hilum, mediastinoscopy in patients with mediastinal lymph nodes in PET/CT or CT. If samples obtained through mediastinoscopy or bronchoscopy were not diagnostic, then we performed surgical mass resection. Primarily we preferred wedge resection or segmentectomy. We performed lobectomy and pneumonectomy in patients with suspicious-frozen or in whom complete mass resection was impossible by segmentectomy or wedge resection.

Medical treatment was prioritized in patients with minor hemoptysis. In cases responsive to medical treatment, we performed bronchoscopy electively. In cases of unresponsiveness to this therapy, or in cases with major and massive hemoptysis, we performed bronchoscopy to stop bleeding. If the bleeding did not stop, then according to the bronchoscopic and radiological findings, we performed the surgery.

The study was conducted in accordance with the Helsinki Declaration Rules after approval from the Clinical Researches Ethics Committee of Akdeniz University Faculty of Medicine. The study was approved by the local ethics committee.

Statistical analysis

SPSS 21.0 statistical package program was used for the statistical analysis. P value < 0.05 was accepted statistically significant. Descriptive statistics were presented with frequency, percentage, mean, standard deviation (SD), median (median), minimum (min.) and maximum (max.) values. Fisher's Exact Test or Pearson chi-square test was used to analyze the relationships between categorical variables and Kolmogorov Smirnov, T test, Mann Whitney U test, ANOVA and Sidak test were used for the distribution of numerical measurements. Statistical analysis of the study was performed by Akdeniz University Statistical Consultancy Application and Research Center.

Results

A total of 541 patients with pulmonary tuberculosis diagnosed surgically were included in this study. 448 of them were in Group 1 (patients without hemoptysis) and 93 patients were in Group 2 (patients with hemoptysis). 254 (56%) of the patients in Group 1 and 69 (74%) of the patients in Group 2 were male (Table 1).

The mean age of the patients was 57.8 ± 6.2 in Group 1 and 31.2 ± 5.3 in Group 2. The male gender was significantly more frequent in Group 2 than in Group 1 and the patients in Group 2 were younger than those in Group 1 ($p < 0.01$, $p < 0.01$, respectively).

The most common symptom in Group 1 was dyspnea (173, 38%). Cough (141, 31%) and loss of weight (134, 29%) were the other common symptoms in Group 1. 62 (67%) patients had massive or major hemoptysis in Group 2 while, minor hemoptysis was present in 31 (33%) patients.

The most common comorbidity was malignancy (n:68) in group 1. The other most common diseases were rheumatoid arthritis (n:30), ulcerative colitis (n:23), and diabetes mellitus (n:23). The most common disease in group 2 was malignancy also (n:16). The comorbidity incidence was higher in group 2 than in group 1, but the difference was not statistically significant.

The mean diameter of nodules was 2.1 cm (range:0.8 to 3.7 cm) in Group 1 and 2.8 cm (range:0.7 to 4.5 cm) in Group 2. The mean maximum standardized uptake value (SUV_{max}) were 7.8 (range:2.1 to 26) in Group 1 and 9.3 (range:3.2 to 30) in Group 2.

Although right lung involvement was excessive in both groups, this was not statistically significant. Cavitation was present in 92 (20.5%) of the patients in Group 1 and

79 (84.9%) of the patients in Group 2 and this radiological finding was significantly higher in Group 2 ($p < 0.01$) (Table 1).

The most common procedure performed was wedge resection (214; 47.7%) in group 1 and lobectomy (45;48.3%) in group 2. There was no pleural biopsy or mediastinoscopy in Group 2. The most frequent postoperative complication was prolonged air leakage in both groups. There was no significant difference between the groups in terms of the frequency of the complications (Table 2).

The mean hospital stay length was 6.8 days in Group 1 (range: 1 to 22) and 11 days in Group 2 (range: 7 to 28). When patients who underwent mediastinoscopy were excluded from the study, the average length of hospital stay in Group 1 increased to 9.9 days. There was no perioperative death in Group 1 while 3 (3,2%) patients died in Group 2. Twenty-three (5.1%) patients in Group 1 and 5 (5.5%) patients in Group 2 died due to tuberculosis during the follow up. No hemoptysis recurrence was reported during follow up.

Discussion

In this study, we investigated the surgical morbidity and mortality of patients diagnosed with tuberculosis after the surgical intervention performed for the diagnosis or treatment and compared the patients with hemoptysis and those without hemoptysis. We found that the patients with hemoptysis were younger than

Table 1. Demographic and clinical characteristics of patients

| | Grup 1 (n=448) | Grup 2 (n=93) | <i>p</i> |
|------------------------|-------------------|------------------|-----------------|
| Gender | | | |
| Male | 254 (56.7%) | 69 (74.2%) | <0.01 |
| Female | 194 (43.3%) | 24 (25.8%) | |
| Age (Mean±SD) | 57.8±6.2 | 31.2±5.3 | <0.01 |
| Comorbidity | | | |
| Malignancy | 68 (15.1%) | 16 (17.2%) | 0.62 |
| Others | 120 (26.7%) | 20 (21.5%) | 0.29 |
| PET-CT/CT (Mean±SD) | | | |
| Diameter of nodules cm | 2.1±0.5 cm | 2.8±0.4 cm | 0.17 |
| SUV_{max} | 7.8±2.4 | 9.3±2.9 | 0.24 |
| Cavitation | 92 (20.5%) | 79 (84.9%) | <0.01 |

PET-CT: Positron Emission Tomography-Computed Tomography
 SUV_{max} : The maximum standardized uptake value

Table 2. Analysis of complications between two groups

| | Grup 1 n | Complication | n | % | Grup2 n | Complication | n | % | p |
|------------------------|----------|-----------------------|----|------|---------|-----------------------|----|------|------|
| BRONCHOSCOPY | 14 | | | | 24 | | | | |
| | | Pneumonia | 0 | 0 | | Pneumonia | 1 | 4.1 | 1 |
| | | Arrhythmia | 2 | 14.2 | | Arrhythmia | 0 | | 0.12 |
| PLEURAL BIOPSY | 76 | | | | 0 | | | | |
| | | Pneumonia | 3 | 3.9 | | Pneumonia | 0 | 0 | + |
| | | Wound infection | 4 | 5.2 | | Wound infection | 0 | 0 | + |
| MEDIASTINOSCOPY | 112 | | | | 0 | | | | |
| | | Wound infection | 2 | 1.7 | | Wound infection | 0 | 0 | + |
| WEDGE RESECTION | 214 | | | | 9 | | | | |
| | | Prolonged air leakage | 75 | 35.0 | | Prolonged air leakage | 6 | 66.6 | 0.07 |
| | | Atelectasis | 39 | 18.2 | | Atelectasis | 2 | 22.2 | 0.06 |
| | | Pneumonia | 18 | 8.4 | | Pneumonia | 1 | 11.1 | 0.55 |
| | | Wound infection | 8 | 3.7 | | Wound infection | 1 | 11.1 | 0.31 |
| | | Empyema | 7 | 3.2 | | Empyema | 0 | 0 | 1 |
| | | Arrhythmia | 3 | 1.4 | | Arrhythmia | 0 | 0 | 1 |
| SEGMENTECTOMY | 6 | | | | 8 | | | | |
| | | Prolonged air leakage | 3 | 50 | | Prolonged air leakage | 5 | 62.5 | 1 |
| | | Atelectasis | 1 | 16.6 | | Atelectasis | 1 | 12.5 | 1 |
| | | Pneumonia | 2 | 33.3 | | Pneumonia | 1 | 12.5 | 0.53 |
| | | Wound infection | 2 | 33.3 | | Wound infection | 1 | 12.5 | 0.53 |
| | | Empyema | 3 | 50 | | Empyema | 1 | 12.5 | 0.24 |
| LOBECTOMY | 25 | | | | 45 | | | | |
| | | Prolonged air leakage | 11 | 44 | | Prolonged air leakage | 30 | 66.6 | 0.08 |
| | | Atelectasis | 6 | 24 | | Atelectasis | 4 | 8.8 | 0.15 |
| | | Pneumonia | 2 | 8 | | Pneumonia | 2 | 4.4 | 0.61 |
| | | Wound infection | 1 | 4 | | Wound infection | 2 | 4.4 | 1 |
| | | Empyema | 5 | 20 | | Empyema | 2 | 4.4 | 0.08 |
| PNEUMONECTOMY | 1 | | | | 7 | | | | |
| | | Pneumonia | 0 | | | Pneumonia | 1 | 14.2 | 1 |
| | | Wound infection | 0 | | | Wound infection | 1 | 14.2 | 1 |
| | | Arrhythmia | 1 | 100 | | Arrhythmia | 1 | 14.2 | 0.25 |

+ Statistical analysis could not be performed between the two groups

those without hemoptysis. The ratio of males in the group of patients with hemoptysis was significantly higher than those without hemoptysis. There was no significant difference between the groups in terms of nodule metabolic activity and diameter. There was no significant difference between the groups in terms of perioperative complications and mortality either. Based on these findings, first of all, we suggest

keeping in mind tuberculosis in the cases of young and male patients with hemoptysis and a cavitory lesion in the lung. In cases of tuberculosis not diagnosed by noninvasive methods or hemoptysis not treated medically, we recommend surgical intervention because surgical interventions for both diagnosis and treatment have negligible complication and mortality rates.

Turkey is one of the countries where tuberculosis is endemic [7]. The gold standard method in the diagnosis of tuberculosis is the detection of the bacilli [2]. However, sometimes noninvasive methods may not be enough for the microbiological diagnosis. In this situation, surgical interventions become inevitable [4]. In our study, all the patients had already been investigated for tuberculosis via noninvasive methods and not diagnosed with tuberculosis.

Hemoptysis, one of the common symptoms of that disease, is also the major symptom forcing patients more urgently apply healthcare professionals [3]. The early diagnosis of tuberculosis is extremely crucial in terms of the worldwide control of this disease. Hemoptysis may be a chance for disease control in this regard [6]. But, sometimes medical treatments are not enough for the control of hemoptysis. So, surgical interventions are required in cases with medically uncontrolled hemoptysis also [4]. Here in this study, we investigated the patients who could not be diagnosed via noninvasive methods or required surgical intervention for either tuberculosis diagnosis or treatment of hemoptysis.

The risk of tuberculosis is higher in patients aged below 50 and above 70 [8]. Previously, the incidence of tuberculosis has been reported to be higher in patients aged 20-24 years [9]. In our study, the patients' ages were very variable in both groups but the patients with hemoptysis were younger than those without hemoptysis. In this study, we observed that tuberculosis may occur at every age and young patients with hemoptysis should be vigorously investigated for tuberculosis.

Cough, dyspnea, weight loss, anorexia, hemoptysis, and night sweats are the common symptoms of tuberculosis. In our study, the most common symptoms were dyspnea (173, 38%) cough (141, 31%), and loss of weight (134, 29%) in patients without hemoptysis. The patients with hemoptysis had various amounts of daily hemorrhage and about 2/3 of them had major or massive hemoptysis. Rasmussen aneurysms, which is a reason for massive hemoptysis, were detected in 45 (4%) of 114 autopsies with chronic tuberculosis with cavitation in a study before [10]. In our study, the patients with hemoptysis had cavitation more frequently than those without hemoptysis

also. Probably hemoptysis is associated with the presence of the cavity. With tuberculosis reaching the adventitia and media of the vascular wall, a vein hernia occurs in the cavity lumen, and massive bleeding occurs from time to time from that site [11]. Moreover, hemoptysis in any amount may be present in tuberculosis. In our study, among the patients with hemoptysis, most of them had major or massive hemoptysis. So in patients with tuberculosis if hemoptysis is present, most of the time, it is major or massive and intervenes the management and therefore surgical interventions may be required not just for the diagnosis, but also for the management.

Tuberculosis is more common in patients with cancer [12, 13]. Malignancy was the most common comorbidity in both groups in our study also. In patients with malignancy, the lung lesions cause the suspicion of metastasis most of the time. However, the togetherness of these diseases is common, thus in such cases, tuberculosis should be kept in mind in the differential diagnosis and investigated. Diabetes mellitus, rheumatoid arthritis, and ulcerative colitis are the other most common diseases accompanying tuberculosis. Acquired immune deficiency syndrome, cancer, immunosuppression, diabetes, malnutrition, cirrhosis, and kidney diseases were reported as the most common comorbidities in patients with tuberculosis [13]. In our study, the number of patients without any comorbidity was very high also. So, tuberculosis is also possible in patients without any apparent health problems.

PET/CT may not be sensitive enough for distinguishing between lung malignancies and benign diseases [14, 15]. Due to the low diagnostic accuracy of using a SUV_{max} cutoff of 2.5 in TB-endemic regions, Du Toit et al. [16] derived using an SUV cutoff of 5.0 in a TB-endemic area. Subotic et al. [13] have stated that $SUV_{max} < 2$ has a high specificity for the differentiation of lung cancer from tuberculosis, while $SUV_{max} \geq 2.5$ has a high sensitivity for the differentiation of lung cancer from tuberculosis. In our study, many of the patients had SUV_{max} above 2.5, which was offered cut-off value for the differentiation of tuberculosis from lung cancer. According to this finding, we suggest that this cut off value is not useful for the differentiation between tuberculosis and malignancy in tuberculosis endemic areas.

Moreover, in our study we observed that right lung involvement was more prominent in both groups. With respect to the lateralization of the involvement, there was no difference between the groups. But cavitation was a significant radiological finding which was more common in patients with hemoptysis. Previously, the most frequent symptom in patients with tuberculosis-cavitation was hemoptysis [5]. Surgical interventions improved patient outcomes and enabled a cure in a high portion, even in cases of bilateral cavitation due to advanced tuberculosis also [17]. We also achieved a good symptom (hemoptysis) control and no hemoptysis recurrence was reported during follow-up in our study.

Although some authors suggested that the complication risk of surgical interventions performed in patients with hemoptysis is very high, there was no significant difference between the groups in our study [3, 7, 12]. The perioperative mortality rate in patients with surgical management of tuberculosis-related hemoptysis was reported as 6.8% [4]. In our study, the perioperative mortality rate was 3.2% (n:3). Besides medical treatment and pulmonary artery embolization, surgical intervention may be inevitable, especially in the case of massive hemoptysis. Surgical resection may be a crucial part of the MDR-TB treatment [3, 6, 12, 18, 19]. The most common postoperative complication was a prolonged air leak in both groups in our study. So, we suggest that the presence of hemoptysis seem not to increase the risk of prolonged air leakage.

This study has also some limitations. First of all, it was a single-centered, retrospective database search. Secondly, the patient number in group 2 was significantly lower compared to group 1. Lastly, in this study, long-term data were evaluated, thus there may be differences in the preferred surgical approaches.

In conclusion, in our study, the surgical morbidity and mortality of patients diagnosed with tuberculosis after the surgical intervention performed for the diagnosis or treatment of the hemoptysis were not significantly different from those of the patients without hemoptysis. We suggest if the noninvasive methods are not enough for the diagnosis, surgical intervention can be performed for both the diagnosis and

even treatment of hemoptysis with an affordable complication risk and complete resection hinders the recurrence.

Conflict of interest: No conflict of interest was declared by the authors.

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Authors' contributions

H.K. and H.D. designed the study. H.K. and M.E. collected the data. M.E. and H.D. performed the analysis and wrote the manuscript. All authors read and approved the final manuscript.