Original Article

Surgical Treatment Outcomes of Pulmonary Aspergilloma in Central Chest Institute of Thailand

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Background: Pulmonary aspergilloma is a disease from colonization of *Aspergillus fumigatus* in the lung cavity with a difficult therapeutic problem. Surgery is an aggressive way to treat.

Objective: To analyze the early surgical treatment outcomes of pulmonary aspergilloma.

Materials and Methods: Fifty-nine patients that underwent surgery for pulmonary aspergilloma in Central Chest Institute of Thailand between January 2015 and August 2019 were reviewed. Patient characteristics and perioperative and operative outcomes were analyzed and reported.

Results: The most frequent symptoms were recurrent hemoptysis (54.2%). The main procedure was lobectomy. The most location of aspergilloma were the right upper lobe (38.98%) and left upper lobe (30.50%). The intraoperative blood loss ranged from 140 to 600 mL with a median of 350 mL. The mean hospital stay was 15 days. The mean duration of pleural drainage was 12 days. The mean follow up was 748 days. No intraoperative death. The mortality rate was 3.4%. The recurrence rate was 1.70%, and the overall complication rate was 52.54%. The most frequent early complications were prolonged air leaks (16.90%), treated by conservative treatment. Most late complications were recurrent hemoptysis (8.50%), and the mean occurrence time was 484 days. The reoperation treatment rate for complications was 25.8%.

Conclusion: Surgical treatment for aspergilloma can control symptoms, prevent recurrent hemoptysis, and save life. With the significant risk of postoperative complications, surgery should be offered primarily to patients with intense symptoms or medical failure.

Keywords: Pulmonary Aspergilloma; Surgical treatment; Pulmonary resection

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Aspergillus spp., specifically, *Aspergillus fumigatus*, are the most common etiologic agents of pulmonary aspergillosis[1]. Pulmonary aspergilloma is the most common and best-recognized form of pulmonary involvement due to *Aspergillus*, resulting from colonization in the lung cavity. Treatment of pulmonary aspergilloma is controversial[2,3]. Surgical resection is the main chance for preventing pulmonary aspergilloma recurrence, control symptoms, and safe life but has a higher complications rate. The surgical treatment of aspergilloma is associated with a high mortality rate that ranges between 5.6% and 22.6%[4]. The present study aimed to review the outcomes of surgical treatment in the patient that underwent surgery for pulmonary aspergilloma in the Central Chest Institute of Thailand (CCIT).

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Materials and Methods

Fifty-nine patients that underwent surgery for pulmonary aspergilloma and were confirmed by pathological report between January 2015 and August 2019 at CCIT were retrospectively reviewed. All the patients were diagnosed and decided for the surgical treatment by a multidisciplinary team of CCIT, which included pulmonologist, thoracic surgeon, and radiologist. The team used the computed tomographic (CT) scan characteristics, history of massive or recurrent hemoptysis, and the disease progression for the decision of the surgical treatment modality.

Patient characteristics and preoperative data included age, gender, American Society for Anesthesiologists (ASA) classification, body mass index (BMI), smoking history, underlying disease, indication for surgery, CT scan characteristic, pre- and post-surgery antifungal therapy, *Aspergillus*-related laboratory findings, and pulmonary function test results were recorded.

The perioperative outcome and postoperative outcome included surgical procedure, operative

time, blood loss, drain amount, intercostal drainage tube (ICD) duration, hospital stay, intermediated or intensive care unit (ICU) stay, duration of intubation, recurrence rate, mortality rate, respiratory failure rate, persistent air leak rate, re-operative rate from bleeding, pneumonia rate, infected wound rate, and bronchopleural fistula rate were reviewed.

Statistical analysis

Descriptive analysis was performed and expressed as the mean ± standard deviation for continuous variables and as frequencies and percentages for categorical variables. The software IBM SPSS Statistics, version 25.0 (IBM Corp., Armonk, NY, USA) was used to analyze the data.

Ethical approval

The present study was approved by the Ethics Committee of Central Chest Institute of Thailand (No.108/2563).

Results

Patient characteristics

Fifty-nine patients were operated for pulmonary aspergilloma with pathological confirmation. There were 37 male and 22 female patients with a mean age of 49 years, ranging from 22 to 73 years. Forty-five (76.3%) patients had underlying lung disease. Most were old pulmonary tuberculosis (Table 1). Pulmonary function test could not be performed in all cases because some patients had ongoing hemoptysis during admission. Thirty-six patients could perform the test, and had a mean FEV1 of 2.14 liters.

Most patients (n=53) were elective cases but two cases operated in a life-threatening condition, and four cases in urgent conditions. The most frequent symptoms were recurrent hemoptysis (54.2%). Chest CT showed that most patients were complex aspergilloma (91.52%) as shown with a thick wall cystic bronchiectasis with the fungal ball and chronic lung disease with bronchiectasis. Forty-two patients (71.19%) did not receive preoperative antifungal drugs, 31 patients (52.55%) received antifungal drugs postoperative (Table 2) with a mean duration of 180 days for the treatment.

Table 1. Patient characteristics

Characteristics (total n=59)	Result; n (%)
Age (years); mean±SD	48.7±11.72
Sex	
Male	37 (62.70)
Female	22 (37.30)
ASA	
1	48 (81.36)
2	11 (18.64)
Underlying	
No underlying	12 (20.30)
Old TB	44 (74.60)
DM	5 (8.46)
HT	6 (10.16)
DLP	1 (1.70)
COPD	1 (1.70)
Hypothyroid	1 (1.70)
Smoking	
Smoking	4 (6.80)
Stop smoking	20 (33.90)
Never	35 (59.30)
Pulmonary function (n=36); mean±SD	
FEV1 (liters)	2.14±0.61
% FEV1[a]	80.53±22.9

ASA=American Society for Anesthesiologists physical status; TB=tuberculosis; DM=diabetes mellitus; HT=hypertension; DLP=dyslipidemia; COPD=chronic obstructive pulmonary disease; FEV1=the first second forced expiratory volume; SD=standard deviation

[a] The ratio of the first second of forced expiration to the full forced vital capacity express in percent

Surgical outcomes

Perioperative outcomes: The operative procedures are shown in Table 3, included 49 lobectomies, one segmentectomy, one bilobectomy, one pneumonectomy, and seven combined procedures. The lobes' most location were the right upper lobe (38.98%) and the left upper lobe (30.50%). The incision was thoracotomy with muscle-sparing (52.54%) and mini-thoracotomy of less than 8 cm (35.60%). Video-assisted thoracoscopy was performed in three patients (5.08%) with two-port in two case and a uniport in one case. The median duration of the procedure was 200 minutes, ranging from 165 to 250, and intraoperative blood loss ranged from 140 to 600 mL with a median of 350 mL. There was no intraoperative death (Table 3).

Postoperative outcomes: The mean hospitalization time was 15 days, ranging from 6 to 63 days. Most patients could admit postoperatively at the intermediated ward, which is the normal condition position in the author's hospital, and the mean duration stay was 0.81 days, ranging from 0 to 2 days. Only 16 patients needed to stay in the intensive care unit. The mean duration of ICU stay was 1.38 days,

Table 2. Preoperative data

Parameter	Result; n (%)
Emergency/urgency/elective surgery	
Emergency	2 (3.40)
Urgency	4 (6.80)
Elective	53 (89.80)
Clinical presentation	
Massive hemoptysis	25 (42.40)
Recurrent hemoptysis	32 (54.20)
Pheumothorax	1 (1.70)
Mass	1 (1.70)
CT appearance	
Thick cystic bronchiectasis with fungal ball	45 (76.27)
Chronic destroy lung with bronchiectasis	9 (15.25)
Thin wall cavity with fungal ball	3 (5.08)
Patchy opacity	4 (1.70)
Mass	1 (1.70)
Type of preoperative antifungal	
Intraconazole	13 (22.03)
Fluconazole	1 (1.70)
Variconazole	3 (5.08)
Not received	42 (71.19)
Type of post-operative antifungal	
Intraconazole	28 (47.45)
Fluconazole	1 (1.70)
Variconazole	2 (3.40)
Not received	28 (47.45)

CT=computed tomographic

Table 3. Perioperative outcomes

Parameter	Result; n (%)
Procedure	
Lobectomy	49 (83.10)
Lobectomy with segmentectomy	4 (6.80)
Segmentectomy and wedge	2 (3.40)
Segmentectomy	1 (1.70)
Lobectomy with wedge	1 (1.70)
Bi-lobectomy	1 (1.70)
Pneumonectomy	1 (1.70)
Position of lobe	
RUL	23 (38.98)
LUL and S6 LLL	6 (10.16)
LUL	18 (30.50)
RML	1 (1.70)
LLL	5 (8.46)
RUL and S6 RLL	1 (1.70)
RML and RLL	2 (3.40)
RLL	2 (3.40)
Entire lung	1 (1.70)
Incision	
Thoracotomy with muscle-sparing	31 (52.54)
Mini-thoracotomy	21 (35.60)
Hybrid VATS	4 (6.78)
VATS	3 (5.08)
Duration of procedure; median (p25 to p75)	200 (165 to 250)
Blood loss; median (p25 to p75)	350 (140 to 600)

RUL=right upper lobe; LUL=left upper lobe; LLL=left lower lobe; RML=right middle lobe; RLL=right lower lobe; VATS=video-assisted thoracic surgery

ranging from 1 to 3 days. The duration of pleural drainage ranged from 3 to 51 days, with a mean of 11.58 days. The duration of postoperative follow-up ranged from 38 to 1,997 days with a mean of 747.54 days (Table 4).

Table 4. Postoperative outcomes

Parameter (n=59)	Result; mean±SD (range)
Length of intensive care unit stay (days) (n=16)	1.38±0.62 (1 to 3)
Duration of ventilator support (hours) (n=10); median (p25 to p75)	7 (2 to 26)
Intermediate ward stay duration (days)	0.81±0.43 (0 to 2)
Length of hospital stay (days)	15.02±12.11 (6 to 63)
Length of intercostal drainage (day)	11.58±10.07 (3 to 51)
Follow up time (days)	747.54±461.09 (38 to 1,997)

SD=standard deviation

Complications

There was no intraoperative death. Two patients died. The first patient underwent repeated surgery due to bleeding on the first postoperative day, and then he had the complication of prolonged air leak and the duration of pleural drainage was 40 days. On the postoperative day 60, he developed sepsis and died on postoperative day 63. The second patient died from pneumonia 2-year postoperative. The mortality rate was 3.4%.

Overall complications rate was 52.54% with 31 of 59 patients. The frequent intraoperative complications were rupture of aspergilloma mass (3.40%). Eighteen patients (30.5%) developed early complications within 90 days postoperative. The most frequent complications were prolonged air leaks (16.90%), treated by conservative treatment. The late complications developed in 11 patients (18.64%). The

Table 5. Complications

Complication (n=59)	Result; n (%)
Intraoperative complications	
Rupture mass	2 (3.40)
Postoperative complications within 90 days	
Bleeding	3 (5.10)
Infected wound	1 (1.70)
Prolong air leak (over seven days postoperative)	10 (16.90)
Post-resection empyema	2 (3.40)
Infected clotted hemothorax	1 (1.70)
Chylothorax	1 (1.70)
None	41 (69.50)
Late complications (>90 day postoperative)	
Space	1 (1.70)
Massive hemoptysis	1 (1.7)
Recurrent hemoptysis	5 (8.50)
Pneumonia	3 (5.10)
Sepsis	1 (1.70)
None	48 (81.40)
Conservative treatment for complications rate (n=31)	23 (74.2)
Reoperation for complications rate (n=31)	8 (25.8)
Recurrence aspergilloma	1 (1.70)
Death	2 (3.40)
Duration of late complications occur after operation (day); mean±SD (range)	483.7±263.23 (50 to 866)

SD=standard deviation

complications occurred 50 to 866 days postoperation, with a mean of 483.7 days. The most recurrence were hemoptysis (8.50%). The reoperation treatment rate for complications was 25.8% as eight patients had reoperation. The recurrent rate of aspergilloma was 1.70% as it was seen in only one patient (Table 5).

Discussion

Aspergillus spp., and specifically, *A. fumigatus*, is the most common etiologic agent that causes the formation of the fungal ball. Aspergilloma (fungal ball) consists of a mass of fungal mycelia, fibrin, mucus, and inflammatory cell, usually developing in the lung cavity[1]. In one study of the patients with pulmonary cavities secondary to tuberculosis, 11% had radiologic evidence of aspergilloma[5]. An aspergilloma may develop secondary to invasive aspergillosis and chronic necrotizing pulmonary aspergillosis. The most common predisposing factor is the presence of lung cavity formed secondary to tuberculosis[6,7]. The author confirmed that 74.60% of the patients had history of tuberculosis infection. The clinical presentation of pulmonary aspergilloma range from an incidental radiologic finding to life-threatening hemoptysis. The present series showed the most frequent symptoms were recurrent hemoptysis (54.2%).

The diagnosis is based on the various sign of CT scan. The presence of radiological opacity with an air crescent sign is of specific importance. This air crescent sign reflects the presence of a fungal ball in the parenchyma cavity. The present series found the fungal ball in CT scan in 81.35%. Another appearance on CT scan was chronic damage to the lung with bronchiectasis in 15.25%, Patchy opacity in 1.7%, and mass in 1.7%. The main sites were the upper lobes. The size or number of aspergilloma was not related to the severity of hemoptysis[8].

Studies, such as Jewkes et al, comparing the long-term outcome of conservative and surgical treatment for aspergilloma, found the 5-year survival rate was 41% of the patients treated conservatively and 84% among patients that underwent surgery. However, in the asymptomatic patient, there was not difference[8]. For recommendations[9,10] in the indication for surgery, the patient should undergo surgery in symptomatic or fail medical treatment. The indications for surgery in the present study are the appearance of aspergilloma on CT scan with recurrent, massive hemoptysis, progressive infiltration surrounding the aspergilloma[9], or fail medical therapy.

The surgery has three potential benefits, control of symptoms, prevent recurrent hemoptysis, and lifesaving. However, the technique involved ranks among the most complex in thoracic surgery. All patients indicated for pulmonary surgery should perform pulmonary function tests and performance status test. In the present study, the physicians could not perform the tests in all patients because ongoing hemoptysis could cause more hemoptysis. Even though postoperative pulmonary function could not be expected exactly, the authors used the performance status before hemoptysis and CT chest appearance to estimate the patient's postoperative performance and lung function. Therefore, the mean FEV1 in the present study was 2.14 liter (n=36).

The Practice Guidelines for the Diagnosis and Management of Aspergillosis 2016[10] suggests that peri- or post-operative antifungal therapy is not routinely required. However, if the risk of surgical spillage of the aspergilloma was moderate, related to the cavity's location and morphology, antifungal therapy is suggested to prevent *Aspergillus* empyema. Peri- or post-operative antifungal therapy in the

present study was not given in all patients with only 29% who received it pre-operatively and 52% who received it post-operatively because of the pulmonologist or surgeon preference. One patient had a disease recurrence. He had ruptured mass intraoperative and received postoperative antifungal only 90 days. In another case who had rupture mass intraoperative, she received postoperative antifungal 180 days and had no recurrence of the disease. Based on the few and the various schemes for antifungal medications in the present study, the author cannot propose any antifungal treatment recommendations.

Recurrence of aspergilloma after surgical resection has been reported in 7% of patients[8]. The mortality rate was ranging from 7% to 10%[11-13]. The present study's recurrence rate was 1.70%, and the mortality rate was 3.40% in a mean follow-up time of 747 days. Because the quality of lung parenchyma after resection is listed as one of the most important factors determining survival, in many cases, the cause of death is either pneumonitis or respiratory failure[14]. The author recommends the involvement and widespread damage of the parenchyma as the conditions to consider the type of procedure. The main procedure is lobectomy. The present study showed that the main incision was thoracotomy with muscle-sparing in 52.54%, and mini-thoracotomy of less than 8 cm in 35.60%. In some cases, especially in central lesions, the surgeon could perform the video-assisted thoracoscopic method for surgery.

In a previous study, the morbidity including excessive hemorrhage, residual space, prolonged air leakage, and empyema thoracis was up to 60%[15]. The present series overall morbidity rate was 52.54%. A study by Kuptarnond et al from Thailand reported 20.8% of early surgical complications[16]. Jean-Francois Regnard et al reported early postoperative complications at 33.7%[4]. The present study showed that the early complication rate was 30.5%, and the late complication rate was 8.64%. Prolonged air leak was the most common postoperative complication in the present series at 16.90%. These complications were managed with conservative treatment, with prolonged chest tube and physiotherapy. Recurrent hemoptysis was the most common late complications and could be managed by conservative treatment. Eight patients needed reoperation for complications such as post-resectional empyema in two cases, bleeding in three cases, infected clot hemothorax in one case, residual space in one case, and massive hemoptysis in one case. The reoperation rate was 25.8%.

Conclusion

In the present study experience and the recent literature, the surgical treatment for aspergilloma can control symptoms, prevent recurrent hemoptysis, and save lives. With the significant risk of postoperative complications, surgery should be offered primarily to patients with intense symptoms or medical failure.

What is already known on this topic?

Surgical treatment is the only realistic chance of a permanent cure for aspergilloma, but it has a high postoperative complication incidence. Indication for surgery is still controversial.

What is the study adds?

Due to the high rate of postoperative complications, the surgery should be offered primarily to patients with intense symptoms or medical treatment failure. The surgical procedure is one of the risk factors of the post-operation complications, especially in complex aspergilloma.

Conflict of interest

The authors declared no conflict of interest

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