

## Original Article

# Clinical profile and surgical outcome for different types of chronic pulmonary aspergillosis

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**Abstract:** Background: Chronic pulmonary aspergillosis (CPA) has been reclassified as several different subtypes, and the clinical features of the different types should be further investigated. Surgery is a remedial option for patients who experience pharmacological treatment failure, though more information about the effectiveness and prognosis of surgical treatment and perioperative medication for different types of CPA is needed. Methods: This was a retrospective study of patients with proven CPA who underwent surgery between January 2001 and June 2018 at Nanjing Jinling Hospital. Results: Sixty patients underwent surgery. The median age was 52.5 years (22-80), and chronic cavitary pulmonary aspergillosis (CCPA) accounted for the largest proportion of cases (46.7%). The most common presenting symptom was hemoptysis (70%). Many patients had underlying lung disease, including bronchiectasis (30%) and obsolete tuberculosis (TB) (21.7%). The surgical procedures included lobectomy (76.7%), wedge resection (16.7%), segmentectomy (5%) and pneumonectomy (1.7%). In total, 33 patients (62.3%) received perioperative antifungal treatment, all of whom improved or were cured. Conversely, 22 patients did not receive perioperative anti-*Aspergillus* treatment; among them, 3 patients with subacute invasive aspergillosis (SAIA) and 1 with CCPA experienced disease progression or died. Conclusions: Surgery is needed in some patients with refractory CPA. We consider that SAIA and CCPA patients may benefit from perioperative antifungal therapy. However, due to the limited number of patients in this study, more evidence is needed to draw a conclusion about this issue.

**Keywords:** Chronic pulmonary aspergillosis, perioperative antifungal therapy, surgical treatment

## Introduction

*Aspergillus* is a ubiquitous fungus that causes a variety of clinical syndromes [1]. Pulmonary aspergillosis is the most common pulmonary fungal disease, and it has recently attracted clinical attention due to its high morbidity and mortality, with a heavy medical burden. According to guidelines, pulmonary aspergillosis is divided into acute invasive pulmonary aspergillosis (IPA), chronic pulmonary aspergillosis (CPA) and allergic bronchopulmonary aspergillosis (ABPA) [2]. At present, treatment of CPA mainly relies on antifungal drug therapy. However, antifungal drug therapy requires long-term treatment and can be ineffective; furthermore, relapse is inevitable. Thus, when conditions allow, surgical treatment is an important option for these patients. Most of the evidence to date for recommendations of surgical treatment of CPA is derived from patients with pulmonary aspergilloma [3-8], with only a few

studies involving other types of CPA [9]. In addition, the role of perioperative antifungal therapy remains controversial. Therefore, the management and long-term prognosis of surgical treatment for different types of CPA need further investigation. Using clinical data from our center, we herein describe the clinical features of different types of CPA and explore the use of surgical treatment to treat this infection.

## Patients and methods

From January 2001 to June 2018, 60 patients underwent surgery for CPA at Nanjing Jinling Hospital. The diagnosis of CPA was based on the updated criteria of the European Society for Clinical Microbiology and Infectious Diseases (ESCMID) and the European Respiratory Society (ERS) guidelines for the management of chronic pulmonary aspergillosis [10]. CPA diagnosis in these patients was histopathologically confirmed. The European clinical guidelines divide

## Surgical treatment for CPA

**Table 1.** Baseline characteristics, clinical presentation and underlying diseases of 60 patients undergoing surgical treatment of chronic pulmonary aspergillosis at Nanjing Jinling Hospital (2001-2018)

Variable	SAIA n = 9	Simple aspergilloma n = 14	CCPA n = 28	<i>Aspergillus</i> nodule n = 9	All n = 60	P value
Age (y)						0.182
Mean $\pm$ SD	57.6 $\pm$ 6.9	47.5 $\pm$ 16.1	53.3 $\pm$ 13.2	57.9 $\pm$ 9.6	53.3 $\pm$ 13.0	
Median (range)	60 (48-68)	47 (20-80)	51 (22-77)	55 (43-74)	52.5 (22-80)	
Sex, n (%)						0.896
Male	5 (55.6)	6 (42.9)	15 (53.6)	4 (44.4)	30 (50)	
Female	4 (44.4)	8 (57.1)	13 (46.4)	5 (55.6)	30 (50)	
Tobacco smoking ( $\geq$ 20 pack/year), n (%)	3 (33.3)	2 (14.3)	11 (39.3)	1 (11.1)	17 (28.3)	0.274
Excessive drinking <sup>a</sup> , n (%)	2 (22.2)	0 (0)	6 (21.4)	0 (0)	8 (13.3)	0.114

CCPA = chronic cavitary pulmonary aspergillosis; SAIA = subacute invasive aspergillosis; SD: standard deviation. <sup>a</sup>Drinking alcohol every day; the total amount of alcohol was  $\geq$  3000 mL per month or at least 2 times a week, and the amount of alcohol is  $\geq$  100 mL each time.

CPA into the following five types: simple aspergilloma, chronic cavitary pulmonary aspergillosis (CCPA), chronic fibrosing pulmonary aspergillosis (CFPA), *Aspergillus* nodules and subacute invasive aspergillosis (SAIA) [10]. Clinical data were collected, including general information, preoperative diagnosis and treatment, surgical treatment, postoperative medication and prognosis, and the patients received follow-up interviews during the study. Statistical analyses were performed using SPSS 24.0. Normally distributed data are presented as the mean  $\pm$  standard deviation; discrete variables are expressed as percentages. Fisher's exact test or the chi-square test was used to compare categorical variables. Comparisons were considered to be statistically significant at a *P* value less than 0.05. This study was approved by the institutional review board (IRB) of the Nanjing Jinling Hospital. Written informed consent was obtained from all patients who participated in the study.

### Results

Sixty patients underwent surgery for CPA during the study period. The preoperative patient characteristics are shown in **Table 1**. Thirty-eight patients (63.3%) had a preoperative probable or proven diagnosis, whereas the diagnosis for 22 patients (37.7%) was confirmed postsurgery.

#### CPA types

Among the 60 CPA patients who underwent surgery, 28 (46.7%) had CCPA, 14 (23.3%) aspergilloma, 9 (15%) *Aspergillus* nodule and 9 (15%) SAIA. The typical radiologic findings for the different types of CPA are shown in **Figure 1**.

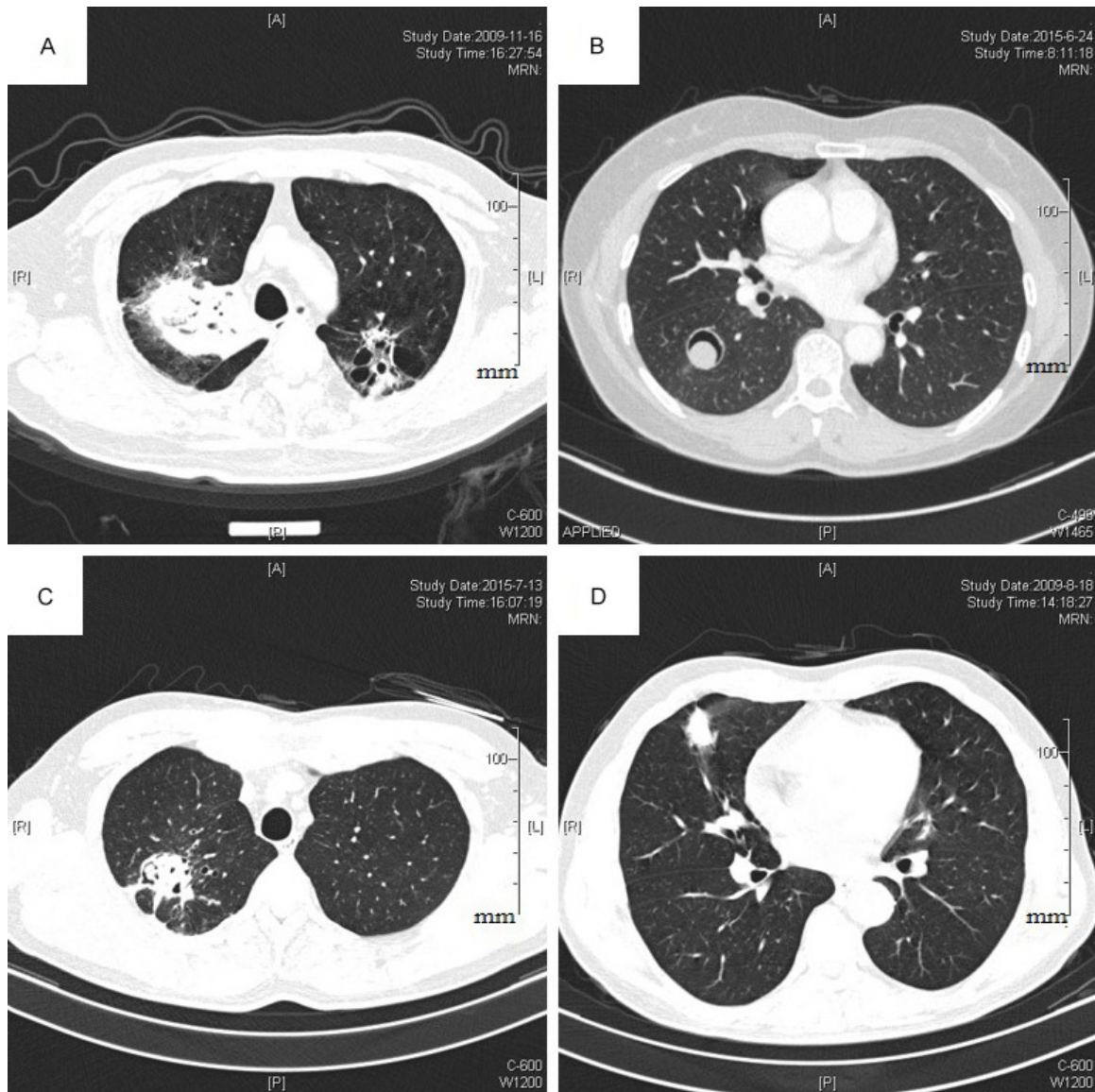
#### Clinical presentation before surgery

The clinical presentation of CPA before surgical treatment is shown in **Table 2**. Hemoptysis was the most common symptom, occurring in 42 patients (70.0%). Two of these patients, who both with CCPA, suffered from massive hemoptysis and accepted bronchial artery embolization, which provided temporary control of the hemorrhage before surgical intervention. Less common symptoms included expectoration (58.3%), chest pain (13.3%), fever (11.7%) and dry cough (8.3%). Asymptomatic patients accounted for 11.7% of the total. The fewest clinical symptoms were observed for *Aspergillus* nodule patients.

#### Underlying diseases and examinations

The underlying disorders of the patients are shown in **Table 2**. Eighteen (30.0%) patients had bronchiectasis, 13 (21.7%) had tuberculosis (TB), and 9 (15.0%) had chronic obstructive pulmonary disease (COPD)/emphysema/asthma. Other pulmonary diseases were less common, including abscess (1.7%), acute respiratory distress syndrome (ARDS) (1.7%) and lung cancer (1.7%). Among systemic diseases, hepatic disease was the most common (21.7%), followed by hypertension (16.7%), extrapulmonary malignancy (15.0%), diabetes (5.0%) and autoimmune disease (3.3%). Those with TB or bronchiectasis had received appropriate treatment for those conditions before the onset of aspergillosis. The presence of CPA without definite underlying disease was found in 30.0% of the patient population. Diagnostic procedures before surgery included sputum culture, lung biopsy and GM (galactomannan) assay in serum or BAL (bronchoalveolar lavage), with posi-

## Surgical treatment for CPA



**Figure 1.** Typical radiologic findings of patients in our research. A. The radiologic finding of one patient with subacute invasive aspergillosis: Occurrence over 1-3 months, variable radiological features including cavitation, nodules, progressive consolidation with 'abscess formation'. B. The radiologic finding of one patient with simple aspergilloma: a single pulmonary cavity containing a fungal ball. C. The radiologic finding of one patient with chronic cavitary pulmonary aspergillosis: one or more pulmonary cavities possibly containing an aspergilloma. D. The radiologic finding of one patient with *Aspergillus* nodule: one or more nodules which may or may not cavitate.

tivity rates of 40% (4/10), 90% (9/10) and 77.8% (7/9), respectively.

### Lesion features and distribution

Computed tomography (CT) scan findings and CPA locations for this cohort are listed in **Table 3**. CPA lesions were often found in the right upper lobe (22 patients, 36.7%). Thirty-eight patients (63.3%) had a preoperative probable or proven diagnosis. Diagnosis before surgery

was most common among simple aspergilloma patients (n = 14), possibly because these patients had typical chest CT signs.

### Surgical treatment

Over one-third of the patients (n = 22, 36.7%) were not diagnosed with CPA prior to surgery. Indeed, it was particularly common for patients with *Aspergillus* nodules or SAIA to be diagnosed postsurgery, as they often received diag-

## Surgical treatment for CPA

**Table 2.** Clinical presentation and underlying diseases of chronic pulmonary aspergillosis before surgery at Nanjing Jinling Hospital (2001-2018)

Variable n (%)	SAIA n = 9	Simple aspergilloma n = 14	CCPA n = 28	<i>Aspergillus</i> nodule n = 9	All n = 60	P value
Hemoptysis	6 (66.7)	10 (71.4)	21 (75)	5 (55.6)	42 (70)	0.754
Cough/Sputum	6 (66.7)	10 (71.4)	20 (71.4)	4 (44.4)	40 (66.7)	0.542
Chest pain	2 (22.2)	0 (0)	6 (21.4)	1 (11.1)	8 (13.3)	0.236
Fever	1 (11.1)	1 (7.1)	5 (17.9)	0 (0)	7 (11.7)	0.714
Asymptomatic	0 (0)	3 (21.4)	0 (0)	4 (44.4)	7 (11.7)	0.001
No definite underlying diseases	4 (44.4)	5 (35.7)	6 (21.4)	3 (33.3)	18 (30)	0.534
Pulmonary disease						
Bronchiectasis	1 (11.1)	5 (35.7)	10 (35.7)	2 (22.2)	18 (30)	0.561
TB	3 (33.3)	0 (0)	9 (32.1)	1 (11.1)	13 (21.7)	0.047
COPD/emphysema/asthma	2 (22.2)	1 (7.1)	4 (14.3)	2 (22.2)	9 (15)	0.661
Lung cancer	0 (0)	0 (0)	0 (0)	1 (11.1)	1 (1.7)	0.300
Other	1 (11.1)	0 (0)	1 (3.6)	0 (0)	2 (3.3)	0.565
Systemic disease	7 (77.8)	7 (50.0)	15 (53.6)	8 (88.9)	37 (61.7)	0.149
Hepatic disease	4 (44.4)	2 (14.2)	4 (14.3)	3 (33.3)	13 (21.7)	0.164
Extrapulmonary malignancy	0 (0)	1 (7.1)	5 (17.9)	3 (33.3)	9 (15)	0.203
Hypertension	1 (11.1)	4 (28.6)	4 (14.3)	1 (11.1)	10 (16.7)	0.683
Diabetes	2 (22.2)	0 (0)	1 (3.6)	0 (0)	3 (5)	0.171
Autoimmune disease	0 (0)	0 (0)	1 (3.6)	1 (11.1)	2 (3.3)	0.571
Diagnostic procedures						
Positive/sputum culture	1/3 (33.3)	1/3 (33.3)	2/4 (50)	-	4/10 (40)	1.000
Positive/lung biopsy	1/1 (100)	1/1 (100)	6/7 (85.8)	1/1 (100)	9/10 (90)	1.000
Positive/GM in BAL or serum	-	1/2 (50)	6/7 (85.8)	-	7/9 (77.8)	0.417

ARDS = acute respiratory distress syndrome; BAL = bronchoalveolar lavage; CCPA = chronic cavity pulmonary aspergillosis; GM = galactomannan; SAIA = subacute invasive aspergillosis; TB = tuberculosis. A positive GM assay:  $\geq 0.5$  optical densities in serum and  $\geq 0.7$  optical densities in BAL specimens.

noses of lung tumors or undetermined masses before surgery. CCPA patients were occasionally diagnosed with other hemoptysis-related diseases, such as pulmonary TB and bronchiectasis. In contrast, all simple aspergilloma patients had received a correct diagnosis before surgery.

The surgical treatments performed are shown in **Table 4**. Lobectomy (46 patients, 76.7%) was the most frequent procedure for CPA, followed by wedge resection (10 patients, 16.7%). Pneumonectomy was the rarest procedure, and this was only performed on one SAIA patient. Typical postoperative pathological images are presented in **Figure 2**.

### Perioperative anti-*Aspergillus* treatment and prognosis

The median follow-up time after surgery was 66 months (3 days-341 months). Five cases were

not included because these patients were lost to follow-up. Thirty-three patients (62.3%) received perioperative antifungal treatment, including 5 (5/9) with SAIA, 8 (61.5%) with simple aspergilloma, 18 (69.2%) with CCPA and 2 (2/7) with *Aspergillus* nodules; all these patients improved or were cured during follow-up. In contrast, 22 patients did not receive standard perioperative anti-*Aspergillus* treatment; among them, 3 with SAIA and 1 with CCPA experienced disease progression or died. Thus, perioperative anti-*Aspergillus* treatment may be beneficial for the prognosis of SAIA patients (**Table 5**), and this should be further explored in the future.

### Postoperative complications of CPA

Postoperative complications (**Table 6**) occurred in 11 patients (20.0%), including wound pain in 6 (10.9%), pulmonary infection in 2 (3.6%), atelectasis in 1 (1.8%), and death within 30 days in



## Surgical treatment for CPA

**Table 3.** CT scan findings and location of chronic pulmonary aspergillosis in 60 patients at Nanjing Jinling Hospital (2001-2018)

Variable n (%)	SAIA n = 9	Simple aspergilloma n = 14	CCPA n = 28	<i>Aspergillus</i> nodule n = 9	All n = 60	P value
CT scan finding						
Cavity	3 (33.3)	9 (64.3)	14 (50.0)	0 (0)	26 (43.3)	0.661
Mass	4 (44.4)	1 (7.1)	9 (32.1)	0 (0)	14 (23.3)	0.033
Opacity	2 (22.2)	0 (0)	2 (7.1)	0 (0)	4 (6.7)	0.197
Cyst	1 (11.1)	2 (14.3)	1 (3.6)	0 (0)	4 (6.8)	0.391
Nodule	0 (0)	0 (0)	3 (10.7)	9 (100)	12 (20.0)	0.000
Location						
Right upper lobe	1 (11.1)	4 (28.6)	16 (57.1)	1 (11.1)	22 (36.7)	0.014
Right middle lobe	1 (11.1)	2 (14.3)	2 (7.1)	1 (11.1)	6 (10.0)	0.926
Right lower lobe	1 (11.1)	3 (21.4)	5 (17.9)	2 (22.2)	11 (18.3)	1.000
Left upper lobe	5 (55.6)	3 (21.4)	5 (17.9)	2 (22.2)	15 (25.0)	0.185
Left lower lobe	2 (22.2)	2 (14.3)	2 (7.1)	2 (22.2)	8 (13.3)	0.445
Multiple lobes	1 (11.1)	0 (0)	2 (7.1)	0 (0)	3 (5.0)	0.639

CCPA = chronic cavitary pulmonary aspergillosis; SAIA = subacute invasive aspergillosis. nodule: less than 3 cm in diameter; mass: more than 3 cm in diameter; cavity: formed by the discharge of necrotic tissue through the drainage bronchus; cyst: thickness of the wall is thinner than the cavity wall, in general, approximately 1 mm.

**Table 4.** Type of surgical procedure used to treat chronic pulmonary aspergillosis at Nanjing Jinling Hospital (2001-2018)

Procedure n (%)	SAIA n = 9	Simple aspergilloma n = 14	CCPA n = 28	<i>Aspergillus</i> nodule n = 9	All n = 60
Lobectomy	8 (88.9)	10 (71.4)	23 (82.1)	5 (55.6)	46 (76.7)
Wedge resection	0 (0)	3 (21.4)	3 (10.7)	4 (44.4)	10 (16.7)
Segmentectomy	0 (0)	1 (7.1)	2 (7.1)	0 (0)	3 (5.0)
Pneumonectomy	1 (11.1)	0 (0)	0 (0)	0 (0)	1 (1.7)

CCPA = chronic cavitary pulmonary aspergillosis; SAIA = subacute invasive aspergillosis.

2 (3.8%). The highest incidence of postoperative complications was observed for SAIA patients, and the two patients who died within 30 days both had SAIA. Simple aspergilloma and *Aspergillus* nodule patients experienced few postoperative complications.

The patient with atelectasis required additional exploration via thoracotomy, and the patient with a pulmonary infection recovered after antibiotic therapy. Six patients reported long-term wound pain.

### Discussion

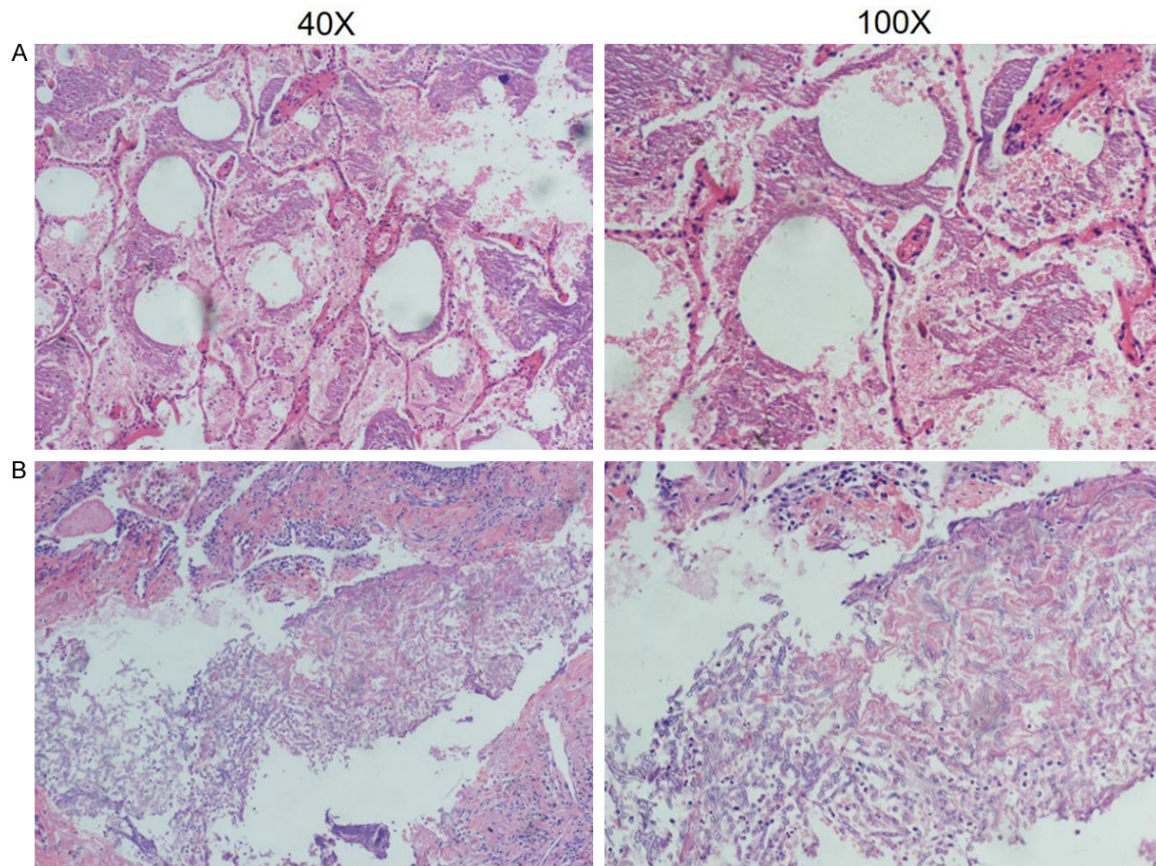
The incidence of CPA has grown in recent years, which has led to an increase in surgical treatment of CPA. Most published studies have focused on the surgical treatment of pulmonary

aspergilloma [3-8]. In addition, detailed recommendations regarding the management of aspergilloma were published by the Infectious Diseases Society of America in 2000 [11] and updated in 2008 [2]. In this study, we analyzed the surgical treatment of four types of CPA according to the 2015 ESCMID/

ERS guidelines (CFPA was not assessed because no CFPA patients underwent surgery during our study period), with CCPA (46.7%) being the most common type.

Of the CPA patients evaluated, 70.0% had hemoptysis, which was consistent with a previous report [8]. In the present study, 2 CCPA patients had life-threatening hemoptysis; as hemoptysis was still present after bronchial artery embolization, these patients required surgical treatment. When an intervention is necessary, many clinicians prefer surgical treatment for CPA patients with moderate/severe hemoptysis [3, 8, 12, 13].

With regard to etiology, structural pulmonary damage such as cavities or bronchiectasis caused by underlying lung disease facilitates



**Figure 2.** Typical postoperative pathological images in our research. A. The pathological image of one patient with subacute invasive aspergillosis: localized hyphal invasion in destroyed lung tissue (Hematoxylin-Eosin, left: 40×, right: 100×). B. The pathological image of one patient with chronic cavitary pulmonary aspergillosis: fungal us hyphae can be seen in the cavity. (Hematoxylin-Eosin, left: 40×, right: 100×).

**Table 5.** Perioperative anti-*Aspergillus* treatment and prognosis

	No perioperative anti- <i>Aspergillus</i> treatment n = 22 (37.7%)		Perioperative anti- <i>Aspergillus</i> treatment n = 33 (62.3%)		P value
	Improve or cure	Progress or death	Improve or cure	Progress or death	
SAIA (n = 9)	1/4	3/4	5/5	0	0.048
Simple aspergilloma (n = 13)	5/5	0	8/8	0	1.000
CCPA (n = 26)	7/8	1/8	18/18	0	0.308
<i>Aspergillus</i> nodule (n = 7)	5/5	0	2/2	0	1.000
ALL (n = 55)	18/22	4 /22	33/33	0	0.021

CCPA = chronic cavitary pulmonary aspergillosis; SAIA = subacute invasive aspergillosis.

*Aspergillus* colonization of the lungs. In our study, pulmonary TB (22.8%) and bronchiectasis (31.6%) were the most common underlying pulmonary comorbidities. Consistent with other reports, CPA lesion sites were most commonly

observed in the right upper lobes [3, 7, 8, 12-14], perhaps because TB often occurs in the right upper lobe. The operative method chosen mainly depends on the extent of the lesions, and the surgical principle is to remove the lesion and retain as much healthy lung as possible. Wedge resection is recommended, especially if the lesion is located peripherally. None-

theless, lobectomy is recommended for those with basic pulmonary disease, large lesions or lesions located in the pulmonary hilar area near the great vessel or major bronchi. If the lesion invades the pleura, a pleurectomy should

## Surgical treatment for CPA

**Table 6.** Postoperative complications of chronic pulmonary aspergillosis

Complications n (%)	SAIA n = 9	Simple aspergilloma n = 13	CCPA n = 26	<i>Aspergillus</i> nodule n = 7	All n = 55
Wound pain	1 (11.1)	0 (0)	5 (19.2)	0 (0)	6 (10.9)
Lung infection	1 (11.1)	1 (7.7)	0 (0)	0 (0)	2 (3.6)
Atelectasis	0 (0)	0 (0)	1 (3.8)	0 (0)	1 (1.8)
Death within 30 days	2 (22.2)	0 (0)	0 (0)	0 (0)	2 (3.6)
ALL	4 (44.4)	1 (7.7)	6 (23.1)	0 (0)	11 (20)

CCPA = chronic cavitary pulmonary aspergillosis; SAIA = subacute invasive aspergillosis.

be performed. In our study, lobectomy was the most common operative approach (**Table 4**).

The patients who underwent surgery were primarily simple aspergilloma and CCPA patients for whom antifungal therapy failed as well as SAIA and *Aspergillus* nodule patients who were not properly diagnosed before surgery. Hemoptysis was the most common indication (70.0%), and 38 patients (63.3%) had a preoperative probable or proven diagnosis; in contrast, 22 (37.7%) were confirmed postoperatively. Exhibiting typical imaging features (**Table 3**), the patients with simple aspergilloma were often correctly diagnosed preoperatively, whereas those with *Aspergillus* nodules and SAIA were often diagnosed as having lung tumors. Furthermore, the CCPA patients were sometimes misdiagnosed with other hemoptysis-related diseases, such as pulmonary TB and bronchiectasis. Overall, surgical treatment is preferred for patients with simple aspergilloma with hemoptysis; patients with CCPA require surgical treatment when the disease is refractory to antifungal treatment and/or they experience life-threatening hemoptysis [10, 15]. In our study, the indications for surgery largely included lung lesions with hemoptysis, indeterminate lung masses and no response to antibiotic and/or antifungal treatment.

Although antifungal therapy after surgery is helpful for preventing *Aspergillus* empyema and disease recurrence [10, 12], there is no evidence that conventional antifungal therapy is required after complete surgical resection of simple aspergilloma or a single *Aspergillus* nodule [6, 10, 16]. In fact, it is thought that antifungal therapy is not necessary if there is no contamination of healthy tissue by fungal elements during complete resection of simple aspergilloma. Regardless, perioperative antifungal treat-

ment is often required for patients with CCPA or SAIA, especially when the lesions cannot be fully resected or spread of the fungal infection is suspected during surgery [10]. By analyzing the effect of perioperative antifungal therapy on prognosis, we found that 3 of the 4 SAIA pa-

tients who did not receive any perioperative anti-*Aspergillus* treatment experienced disease progression or died but that the 5 SAIA patients who accepted perioperative anti-*Aspergillus* treatment all improved or were cured ( $P < 0.05$ ) (**Table 5**). ESCMID/ERS guidelines recommend treatment of SAIA as acute invasive aspergillosis [10]. A multinational cohort study showed that 6 of 109 patients who received perioperative antifungal treatment all had survived at 6 weeks after IPA diagnosis [17], which is consistent with our findings. One of the 9 CCPA patients in our study who did not receive perioperative anti-*Aspergillus* treatment progressed or died, but the 18 who accepted perioperative anti-*Aspergillus* treatment all improved or were cured ( $P > 0.05$ ) (**Table 5**). Based on the postoperative outcomes of various types of CPA (**Table 5**), we recommend that simple aspergilloma and *Aspergillus* nodule patients who have persistent symptoms should receive surgery after diagnosis, without perioperative drug therapy. Nonetheless, due to the relatively small cohort of SAIA patients, it remains unclear whether perioperative antifungal treatment can improve the perioperative outcomes of SAIA patients; however, according to our experience, we still recommend perioperative antifungal treatment for those patients, and evidence to date needs to be strengthened in the future.

Some articles have reported that compared with simple aspergilloma, patients with CCPA have more postoperative complications, higher recurrence rates and greater risk of mortality [3, 7, 8, 12-14]. Reported 5-year survival rates for simple aspergilloma and CCPA patients are 91.6-100% and 60-85%, respectively [3, 7, 8, 12, 14], with 10-year survival rates of 62.5-92% and 68.5-79.6%, respectively [3, 8, 12], and postoperative relapse rates of 0-16.67% and 5.56-33.33%, respectively [7, 12]. The



postoperative mortality of SAIA patients is approximately 40% [18-21]; therefore, surgical indications should be carefully considered.

Except for the 3 deaths, no other deaths occurred during the follow-up period in our study.

The limitations of this study are its retrospective, observational, non-randomized design and the fact that some clinical data could not be retrieved for all cases. Moreover, the results should be interpreted with particular caution due to the limited sample size. Large randomized trials are needed to confirm our results.

In summary, we report the clinical features and outcomes of patients with different types of CPA who underwent surgery. The postoperative morbidity rate was higher in SAIA patients compared with other three types. In light of our experience, we consider that SAIA and CCPA patients may benefit from perioperative antifungal therapy, but due to the limitation of our study, large randomized trials are needed to confirm our results.

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## Disclosure of conflict of interest

None.

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