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Efficacy and Safety of Bronchial Artery Embolization on Hemoptysis in Chronic Thromboembolic Pulmonary Hypertension: A Pilot Prospective Cohort Study

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Objectives: Managing hemoptysis in chronic thromboembolic pulmonary hypertension can be challenging due to the difficulties in maintaining coagulation homeostasis in affected patients. In this study, we evaluated the efficacy and safety of bronchial artery embolization in treating hemoptysis in chronic thromboembolic pulmonary hypertension patients.

Design: Pilot, prospective cohort study.

Setting: A large respiratory medical institute.

Patients: From January 1, 2012, to December 31, 2017, hospitalized chronic thromboembolic pulmonary hypertension patients were eligible for inclusion. Patients with pulmonary hypertension caused by other conditions, or who failed to participate in the follow-up were excluded.

Interventions: Hemoptysis in chronic thromboembolic pulmonary hypertension patients was treated with or without bronchial artery embolization based on whether the bleeding could be stopped with medication alone and patient willingness for bronchial artery embolization treatment.

Measurements and Main Results: A total of 328 patients diagnosed with chronic thromboembolic pulmonary hypertension were consecutively collected, 317 patients were completed the follow-up. There were 15 chronic thromboembolic pulmonary hypertension patients with hemoptysis in total, and the occurrence rate of hemoptysis in chronic thromboembolic pulmonary hypertension patients was 4.7%. Among the hemoptysis chronic thromboembolic pulmonary hypertension patients, 10 (67%) underwent bronchial artery embolization, and five (33%) were treated with medication only. The median follow-up period for hemoptysis patients was 7.6 months. In patients underwent bronchial artery embolization treatment, oxygenation index and right heart function showed no significant difference between pre bronchial artery embolization and post bronchial artery embolization. Hemoptysis relapse (20% vs 80%; $p = 0.025$) and hemoptysis-related mortality (0% vs 40%; $p = 0.032$) were significantly lower, whereas the overall survival (90% vs 40%; $p = 0.040$) was higher in patients treated with bronchial artery embolization than in patients treated without bronchial artery embolization.

Conclusions: Bronchial artery embolization procedure demonstrated effectiveness and safety to treat hemoptysis in chronic

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Dr. S. Yang had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs. S. Yang, Wang, Kuang, Gong, and Ma are responsible for acquisition of the data. Drs. S. Yang and Liang are responsible for analysis and interpretation of the data. Drs. S. Yang and Y. Yang are responsible for the study concept and design. Drs. S. Yang, Y. Yang, and Huang are the guarantors of the article. Drs. S. Yang, Shen, Y. Yang, and Huang are responsible for drafting of the article and critical revision of the article for intellectual content. All authors have provided final approval of the version to be published.

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thromboembolic pulmonary hypertension patients at our center, but further controlled studies are needed before it can be considered as an effective therapy for these patients. (*Crit Care Med* 2019; 47:e182–e189)

Key Words: chronic thromboembolic pulmonary hypertension; bronchial artery embolization; hemoptysis

Chronic thromboembolic pulmonary hypertension (CTEPH), caused by pulmonary vascular thromboembolism and subsequent wall remodeling and hypertrophy, is a serious life-threatening disease (1–3). Due to bronchial artery hyperplasia, distortion and high pressure, the distal bronchial arteries are prone to rupture into the airways, resulting in hemoptysis (8). Massive or life-threatening hemoptysis carries high mortality and requires rapid diagnosis and proper treatment (4, 5).

Compared with treating hemoptysis in patients with other lung diseases such as bronchiectasis, lung cancer, and tuberculosis, treating hemoptysis in patients with CTEPH is challenging because of the need for long-term anticoagulant therapy. Repeated cessation of anticoagulants due to hemoptysis increases the risk of CTEPH deterioration. Therefore, proper management of hemoptysis in CTEPH patients is of significant importance. However, limited studies regarding hemoptysis in CTEPH have been reported (6–8) and the precise occurrence rate and the optimal management of hemoptysis in CTEPH patients remain to be determined.

Bronchial artery embolization (BAE), which controls the bleeding by angiography-guided injection of embolic substance into pathologic bronchial arteries, is considered safe first-line therapy for massive and life-threatening hemoptysis (9–13). However, its efficacy in treating hemoptysis in patients with pulmonary hypertension especially CTEPH is unclear.

Therefore, we performed this prospective cohort study aiming to examine the occurrence rate of hemoptysis in patients with CTEPH and to evaluate the efficacy and safety of BAE procedure in treating hemoptysis in CTEPH patients.

MATERIALS AND METHODS

Patients

This study was a single center prospective cohort study conducted at Beijing Chao-Yang Hospital (Beijing Institute of Respiratory Medicine, Capital Medical University, Beijing, China) from January 1, 2012, to December 31, 2017. The study protocol and consent procedure used in this trial were approved by the ethics committee of Beijing Chao-Yang Hospital (ethics number: 2009-1, 2014BJYYEC-051-02). Informed consent from all study patients was obtained.

The CTEPH was diagnosed based on the following indicators: at least 3 months after the effective anticoagulation treatment, mean pulmonary arterial pressure greater than or equal to 25 mm Hg, the pulmonary artery occlusion pressure less than or equal to 15 mm Hg, the mismatched perfusion defects on lung scan, and the specific diagnostic signs for CTEPH (such as ring-like stenoses, webs/slits and chronic total occlusions with pouch lesions, or tapered lesions) detected by the CT pulmonary angiogram (CTPA), MRI, or conventional pulmonary angiography (14).

Exclusion criteria: Patients with pulmonary hypertension caused by other conditions including severe chronic lung disease, left cardiac insufficiency, hematologic disorders, systemic disorders, metabolic disorders, fibrosing mediastinitis, chronic renal failure, or any other pulmonary arterial hypertension (PAH)-associated condition. Patients who failed to participate in the follow-up were excluded.

Treatment of CTEPH

All the CTEPH patients, treated with medication or pulmonary endarterectomy (PEA), received life-long anticoagulant therapy. Warfarin was the most commonly used anticoagulant to achieve an international normalized ratio (INR) of 2 to 3. The operabilities and decisions on treatment strategies were assessed by the multidisciplinary team of experts including at least one experienced PEA surgeon. Patients with inoperable CTEPH were treated using off-label use of drugs approved for PAH and interventional balloon pulmonary angioplasty (14).

Follow-Up

CTEPH patients were followed up at different time points of the 3rd, 6th, 12th, 18th, 24th months, and then yearly for up to 5 years. Detailed information was collected for CTEPH patients with hemoptysis. Patients appeared hemoptysis during the follow-up were admitted to the same hospital. All the patients with hemoptysis had chest CT scan and/or CTPA, biomarkers, and pathogenic microorganism examination to rule out other causes of hemoptysis, such as lung cancer, tuberculosis, fungal infection, bronchiectasis, and acute pulmonary embolism. All the patients with hemoptysis received medication for hemostasis. If medical therapy did not stop bleeding effectively, BAE procedure was performed after informed consent was signed. BAE were performed guided by the digital subtraction angiography (DSA) for the uncontrolled hemoptysis after medication. Information of demographics, clinical and laboratory data, echocardiography, right heart catheterization, medical therapy, DSA, and BAE procedures were collected for CTEPH patients with hemoptysis.

All the patients were followed up for at least 90 days after the treatment of hemoptysis. Information of arterial blood gas (ABG) and echocardiography was collected within 90 days after BAE. The relapse rate and overall survival were calculated.

The "life-threatening hemoptysis" was defined as any hemoptysis that 1) was more than 100 mL in 24 hours; 2) causes abnormal gas exchange/airway obstruction; or 3) causes hemodynamic instability. The cut-off volume of 100 mL per 24 hours was the smallest amount of hemoptysis had been reported to threaten the lives of patients (15).

BAE

All the BAE were performed by one of the three different interventional radiologists who had more than 12 years of experience

in interventional radiology. DSA was carried out with a pigtail catheter and positioned in the ascending aorta. Various catheters with different shapes and angles were used based on the anatomies of the involved vessels to achieve the selective catheterization of bronchial arteries. The coaxial microcatheter was used for super selective catheterization. According to the origin and tortuosity of the arteries, polyvinyl alcohol (PVA) particles and/or metal microcoils were used for embolization. A final angiographic scan was performed to confirm that the bleeding had been stopped and the possible collateral supply of bronchial and nonbronchial circulation after the target arterial embolization.

Statistical Analysis

All statistical analyses were performed with SPSS software Version 19.0 (SPSS, Inc., Armonk, NY). Therefore, sample size was not calculated due to the pilot study. The Kolmogorov-Smirnov test was used to assess the normality of continuous variables. Normally distributed data were expressed as mean ± SD. Data without normal distribution were expressed using median or interquartile range (IQR). All variables were analyzed with descriptive methods. *t* test was used to compare between two groups under the premise of normal distribution. Cross-tabulations were checked with chi-square test. Kaplan-Meier survival plots were analyzed using the log-rank test. A *p* value of less than 0.05 was considered statistically significant.

RESULTS

The Occurrence Rate of Hemoptysis in CTEPH Patients

The study was performed at Beijing Chao-Yang Hospital from January 1, 2012, to December 31, 2017. A total of 328 CTEPH patients were consecutively enrolled during hospitalization, and 317 CTEPH patients completed the follow-up. A total of 15 CTEPH patients had hemoptysis, and the period between the onset of CTEPH symptoms and hemoptysis was 4.5 ± 4.3 years. Among the 15 patients, six patients had hemoptysis as a main complication when CTEPH was diagnosed, nine patients developed hemoptysis during the follow-up period and were admitted to the same hospital for treatment. The occurrence rate of hemoptysis in CTEPH patients was 4.7% (15/317) (**Fig. 1**).

Baseline Characteristics of CTEPH Patients in BAE and Non-BAE Groups

Among all the 15 CTEPH patients with hemoptysis, 10 underwent BAE treatment, and five were treated without BAE (Fig. 1). In the five patients without BAE treatment, four patients (80%) were treated successfully with medication, one patient refused BAE due to the advanced age. No significant difference was observed in the baseline characteristics between the BAE group and the non-BAE group at the initial diagnosis of CTEPH (**Table 1**).

Among all the 15 CTEPH patients with hemoptysis, recurrent hemoptysis accounted for 60%, life-threatening hemoptysis accounted for 53.3%, and recurrent and/or life-threatening hemoptysis accounted for 66.7%. INR of two patients was over five due to excessive anticoagulant therapy. However, initial medication could not alleviate the hemoptysis of one patient. A 47-year-old female patient underwent PEA and developed hemoptysis 14 days after PEA. Clinical characteristics of patients at the onset of hemoptysis showed no significant difference between the BAE and non-BAE group (**Table 2**).

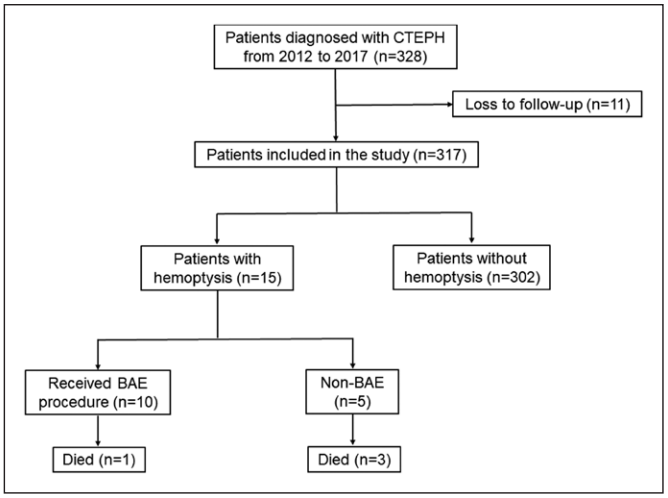

Figure 1. Flow chart of study. BAE = bronchial artery embolization, CTEPH = chronic thromboembolic pulmonary hypertension.

All 15 patients received anticoagulant therapy before the onset of hemoptysis. At the time of hemoptysis, three patients (20%) received calcium channel blockers because of their positive response to acute vasoreactivity testing, two patients (13.3%) received anticoagulant and diuretic therapy only. Ten patients (66.7%) received off-label drugs: four patients (26.7%) received phosphodiesterase type 5 inhibitor (PDE-5i), one patient (6.7%) received endothelin receptor antagonist (ERA), one patient (6.7%) received soluble guanylate cyclase stimulators, one patient (6.7%) received prostacyclin analogs, one patient (6.7%) received PDE-5i combined with ERA, one patient (6.7%) received prostacyclin analogs combined with ERA, and one patient (6.7%) received PDE-5i combined with prostacyclin analogs.

Details of the BAE Treatment

Patients with BAE treatment received PVA particles (with diameters ranging between 500 and 700 μm) and/or metal microcoils. One patient received PVA particles only, four patients received metal microcoils only, and five patients received both PVA particles and metal microcoils. All patients were administered medication at the same time. Anticoagulation therapy was restarted after 4.9 ± 3.5 days after the BAE treatment. Bleeding was successfully stopped in all the 10 patients received the BAE treatment. Two patients reported chest pain after BAE treatment, which was relieved within 5 days, and no more serious complications occurred.

A total of 16 arteries in all the 10 patients required BAE treatment, and 11 arteries (68.8%) were right bronchial artery (RBA), two (12.5%) were left bronchial artery (LBA), and three (18.7%) were nonbronchial systemic arteries (NBSA). Thirteen arteries were successfully embolized (average per procedure 1.3 ± 0.7), 10 (76.9%) were RBA, one (7.7%) was LBA, and two (15.4%)

TABLE 1. Characteristics of Hemoptysis Patients at the First Diagnosis of Chronic Thromboembolic Pulmonary Hypertension

Characteristics	All Patients ($n = 15$)	BAE Patients ($n = 10$)	Non-BAE Patients ($n = 5$)	p
Age, yr, mean ± SD	52.0 ± 13.7	53.5 ± 10.3	49.0 ± 19.9	0.567
Male, *n* (%)	9 (60)	5 (50)	4 (80)	0.264
Comorbidities, *n* (%)				
Coronary heart disease	3 (20)	2 (20)	1 (20)	NA
Hypertension	3 (20)	2 (20)	1 (20)	NA
Chronic lung disease	2 (13.3)	2 (20)	0	0.283
Diabetes	3 (20)	1 (10)	2 (40)	0.171
Lower-limb varicose veins	2 (13.3)	2 (20)	0	0.283
Splenectomy	1 (6.7)	0	1 (20)	0.143
Echocardiography, mean ± SD				
Right atrial short axis diameter, mm	49.1 ± 6.6	47.4 ± 5.9	52.6 ± 7.2	0.153
Right atrial long axis diameter, mm	56.4 ± 6.3	54.5 ± 6.1	60.2 ± 5.1	0.095
Systolic pulmonary arterial pressure, mm Hg	87.6 ± 15.3	85.8 ± 13.9	91.1 ± 18.9	0.541
Tricuspid annular plane systolic excursion, mm	14.0 ± 2.4	14.6 ± 2.4	12.9 ± 2.2	0.234
Right ventricular fractional area change, %	27.6 ± 5.7	27.1 ± 5.2	28.5 ± 7.3	0.709
Myocardial performance index	0.8 ± 0.3	0.9 ± 0.4	0.8 ± 0.1	0.749
Right heart catheterization				
Systolic pulmonary arterial pressure, mm Hg, mean ± SD	85.2 ± 12.1	84.2 ± 11.3	87.3 ± 15.2	0.695
Mean pulmonary arterial pressure, mm Hg, mean ± SD	46.9 ± 3.9	47.1 ± 3.1	46.5 ± 5.9	0.808
Right atrial pressure, mm Hg, mean ± SD	4.5 ± 3.1	3.9 ± 1.9	5.8 ± 4.9	0.345
Pulmonary vascular resistance, dyn.sec/cm^5, mean ± SD	854.7 ± 400.7	821.8 ± 426.4	928.8 ± 383.2	0.676
Cardiac index, L/min/m^2, mean ± SD	2.3 ± 0.8	2.4 ± 0.9	1.9 ± 0.2	0.274
Acute vasoreactivity testing positive, *n* (%)	3 (20)	3 (30)	0	0.157
6-min walking distance, m, mean ± SD	330.1 ± 119.2	347.1 ± 107.3	279.0 ± 186.7	0.526
World Health Organization functional class II/III/IV, *n*	8/6/1	7/2/1	1/4/0	NA
Treatment before BAE, *n* (%)				
Anticoagulation	15 (100)	10 (100)	5 (100)	NA
Calcium channel blockers	3 (20)	3 (30)	0	0.171
Other specific drug therapy	10 (66.7)	7 (70)	3 (60)	0.699
Pulmonary endarterectomy	1 (6.7)	1 (10)	0	0.464

BAE = bronchial artery embolization, NA = not available.

were NBSA (**Table 3**). Representative angiograms before and after embolization in a patient were shown in **Figure 2**.

Echocardiography Variables and ABG in Pre- and Post-BAE Periods

During the follow-up period, eight patients finished their ABG analysis within 90 days (time between BAE and ABG was 44.5 ± 36.4 d), and nine patients underwent echocardiography (time between BAE and echocardiography was 43.8 ± 44.3 d). Data such as oxygenation index ($p = 0.652$), right atrial short axis diameter ($p = 0.203$), right atrial long axis diameter ($p = 0.072$), systolic pulmonary arterial pressure ($p = 0.232$), tricuspid annular plane systolic excursion ($p = 0.759$), right ventricular fractional area change

TABLE 2. Characteristics of Patients at the Onset of Hemoptysis

Characteristics	All Patients (*n* = 15)	BAE Patients (*n* = 10)	Non-BAE Patients (*n* = 5)	*p*
Periods between the onset of chronic thromboembolic pulmonary hypertension symptoms and hemoptysis[a], yr, mean ± SD	4.5 ± 4.3	3.9 ± 3.7	5.5 ± 5.7	0.538
Hemoptysis				
Hemoptysis volume, mL, mean ± SD	221.0 ± 298.6	156.5 ± 245.1	350.0 ± 381.7	0.251
Recurrent hemoptysis, *n* (%)	9 (60)	6 (60)	3 (60)	NA
Life-threatening hemoptysis, *n* (%)	8 (53.3)	4 (40)	4 (80)	0.143
Recurrent and/or life-threatening hemoptysis, *n* (%)	10 (66.7)	6 (60)	4 (80)	0.439
Systolic blood pressure, mm Hg, mean ± SD	124.6 ± 20.6	127.8 ± 22.9	118.2 ± 14.9	0.415
Diastolic blood pressure, mm Hg, mean ± SD	75.7 ± 12.9	75.9 ± 14.5	75.2 ± 10.5	0.925
Heart rate, beats/min, mean ± SD	85.1 ± 15.6	82.6 ± 14.3	90.0 ± 18.6	0.406
Hemoglobin, g/L, mean ± SD	135.7 ± 22.9	140.4 ± 22.7	126.2 ± 22.5	0.273
Hematocrit, %, mean ± SD	39.8 ± 6.7	41.1 ± 6.9	37.1 ± 6.2	0.289
Platelet, 10^9/L, mean ± SD	219.4 ± 97.6	237.2 ± 92.7	183.8 ± 107.8	0.336
Uric acid, μmol/L, mean ± SD	391.2 ± 146.8	413.5 ± 151.9	346.5 ± 140.5	0.420
Total bilirubin, μmol/L, mean ± SD	22.0 ± 19.3	15.3 ± 5.7	35.3 ± 30.0	0.055
Creatinine, μmol/L, mean ± SD	77.2 ± 26.2	75.3 ± 14.0	80.9 ± 44.0	0.714
International normalized ratio, mean ± SD	2.0 ± 1.8	1.7 ± 1.3	2.6 ± 2.5	0.408
Activated partial thromboplastin time, s, mean ± SD	38.0 ± 18.9	31.3 ± 6.3	50.2 ± 28.2	0.070
N-terminal prohormone of brain natriuretic peptide, pg/mL, mean ± SD	4216.5 ± 8671.4	1900.6 ± 1600.4	8848.4 ± 14737.3	0.150
Arterial blood gas analysis, mm Hg, mean ± SD				
Pa_{O_2}	68.9 ± 31.9	69.8 ± 36.9	67.1 ± 21.8	0.886
Pa_{CO_2}	34.7 ± 4.3	35.2 ± 5.1	33.9 ± 2.2	0.592
Oxygenation index	253.0 ± 70.7	276.5 ± 68.0	206.0 ± 54.6	0.055
Echocardiography, mean ± SD				
Right atrial short axis diameter, mm	47.9 ± 8.8	47.1 ± 9.4	49.6 ± 8.2	0.621
Right atrial long axis diameter, mm	59.2 ± 7.0	58.5 ± 6.8	60.6 ± 7.9	0.601
Systolic pulmonary arterial pressure, mm Hg	91.3 ± 26.1	87.5 ± 28.2	98.7 ± 22.1	0.454
Tricuspid annular plane systolic excursion, mm	14.7 ± 4.0	15.6 ± 4.1	13.2 ± 3.7	0.300
Right ventricular fractional area change, %	27.1 ± 6.3	24.7 ± 6.2	32.6 ± 0.9	0.068
Myocardial performance index	0.6 ± 0.1	0.6 ± 0.1	0.7 ± 0.2	0.599

BAE = bronchial artery embolization, NA = not available.

[a]The common symptoms of chronic thromboembolic pulmonary hypertension include shortness of breath, fatigue, weakness, angina, syncope, and dry cough, which are typically induced by exertion.

($p = 0.056$), and myocardial performance index ($p = 0.275$) showed no significant difference between pre- and post-BAE periods. Variables of echocardiography and ABG were compared between pre- and post-BAE (**Supplemental Table 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/E223).

Comparisons of the Recurrent Hemoptysis and Mortality Rates in BAE and Non-BAE Groups

The median follow-up period after hemoptysis in all the 15 patients was 7.6 months (IQR, 3.8–14.8 mo). Detailed information for each patient is presented in **Supplemental Table 2** (Supplemental Digital Content 2, http://links.lww.com/CCM/E224).

TABLE 3. Details of Digital Subtraction Angiography and Bronchial Artery Embolization

Characteristics	*n*
Digital subtraction angiography	
Arteries required intervention (average per procedure) (mean ± SD)	16 (1.6 ± 0.7)
Right bronchial artery (%)	11/16 (68.8)
Left bronchial artery (%)	2/16 (12.5)
Nonbronchial systemic arteries (%)	3/16 (18.7)
Embolization	
Successful arteries intervention (average per procedure)	13 (1.3 ± 0.7)
Right bronchial artery (%)	10/13 (76.9)
Left bronchial artery (%)	1/13 (7.7)
Nonbronchial systemic arteries (%)	2/13 (15.4)
Post embolization chest pain (%)	2/10 (20)

In the BAE treatment group, two of the patients (20%) had recurrent hemoptysis at the 20th and the 121st days after embolization, respectively, and both were improved by medication. One patient (10%) died of retroperitoneal hemorrhage after a radical resection for the left renal mass (pathologically confirmed as clear cell carcinoma) 15 days after the embolization. There was no hemoptysis-related death. Three months after the BAE treatment, one patient underwent PEA successfully. In the non-BAE group, four patients (80%) appeared recurrent hemoptysis during follow-up, and three patients (60%) died. Two of them died of fatal bleeding, and one patient died of catastrophic antiphospholipid syndrome combined with severe lung infection.

The hemoptysis relapse rate (20% vs 80%; $p = 0.025$) and the hemoptysis-related mortality (0% vs 40%, $p = 0.032$) were significantly lower, whereas the overall survival rate (90% vs 40%; $p = 0.040$) was significantly higher in patients treated with BAE than in patients treated without BAE (**Supplemental Fig. 1**, Supplemental Digital Content 3, http://links.lww.com/CCM/E225; **legend**, Supplemental Digital Content 4, http://links.lww.com/CCM/E226).

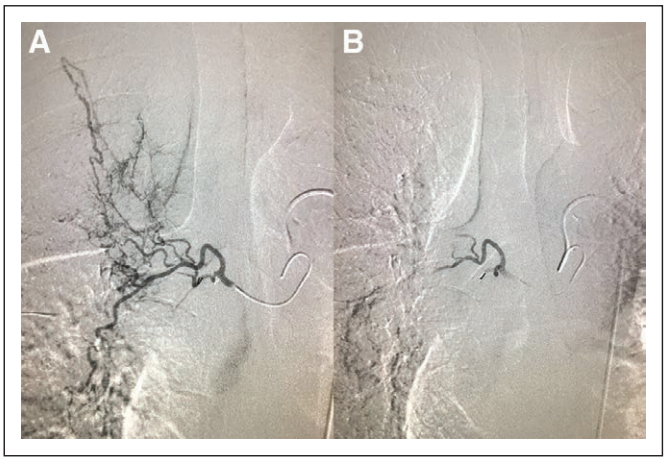

Figure 2. A patient with chronic thromboembolic pulmonary hypertension underwent bronchial artery embolization procedures. **A**, Hyperplasia and distortion of right bronchial artery. **B**, The tortuous artery disappeared after embolization.

DISCUSSION

In our current study of the largest sample size to date, we observed that the occurrence rate of hemoptysis in CTEPH patients was 4.7%. Patients treated with BAE had lower recurrent hemoptysis and higher survival than in patients treated without BAE.

Little is known about the occurrence rate and the optimal management of hemoptysis in CTEPH. To date, only one study reported that the occurrence rate of moderate to severe hemoptysis in CTEPH patients was 6% (five out of 79) (6). Meanwhile, only 0.1% (two out of 1,844) of moderate to severe hemoptysis was associated with CTEPH from 21 studies (6). Thus, hemoptysis, especially severe hemoptysis, was considered rare in CTEPH patients. Consistent with the previous report, our study showed that the occurrence rate of hemoptysis in CTEPH patients was 4.7%.

The pathogenesis of hemoptysis in CTEPH patients is complicated. One possible mechanism is compensational increase in large bronchopulmonary collaterals and collateral flow caused by occluded pulmonary arteries and subsequent lung ischemia in CTEPH, in which pulmonary arteries are replaced by the hyperplastic systemic arteries such as bronchial arteries and intercostal arteries (3). Presumably, the hemoptysis caused by the torrential blood flow through the tortuous vessels fed the greatly expanded bronchial circulation (16). One patient in our study experienced hemoptysis after PEA. Hyperplasia and distortion of the bronchial arteries before PEA surgery and anticoagulant therapy after surgery may contribute to hemoptysis in the patient.

Consistent with previous reports (7), recurrent hemoptysis and life-threatening hemoptysis accounted for the majority of the hemoptysis in our study, which underscores the urgency of prompt and proper treatment of hemoptysis in CTEPH patients. It should be noted that although bronchial circulation is the main source of hemoptysis, bleeding may come from NBSA (11). RBA and intercostal arteries are the main arteries that require intervention in hemoptysis caused by other diseases (17). In our study, RBA and NBSA accounted for 87.5% of the arteries that required intervention. Most of these arteries were in the right lung, which may be accounted for by right pulmonary arteries being more prone to pulmonary embolism.

In our study, each episode of hemoptysis was acutely terminated with BAE, a successful rate that was similar to those in PAH and other diseases (4, 7, 10, 18). In addition, complete embolization was achieved in 13 of 16 arteries (81.3%) of the arteries requiring intervention. Embolization failed in the other three arteries (in three different patients) that showed obvious hyperplasia and distortion, a restriction for BAE in PAH (19). The average number of embolized arteries per procedure was

1.3 ± 0.7, which was similar with that of patients with other causes of hemoptysis treated by BAE (7). It showed that the use of BAE in the treatment of CTEPH patients with hemoptysis was not very complicated, and it was feasible in operation.

As mentioned in the literatures, chest pain as one of the most common post embolization complications (7, 11). It has been reported that no complications require prolonged hospital stay in patients with recurrent hemoptysis without pulmonary hypertension treated by BAE (20). However, other reports showed that the complications occurred in 15% of the patients with BAE for hemoptysis (17).

Varying outcomes after BAE have been noted, depending on the underlying pathogenesis. Outcomes are favorable in patients with active tuberculosis, but poor in patients with aspergilloma and pulmonary malignancy (4). It has been reported that the mortality rate after BAE was 11.3% in nonpulmonary hypertension patients (21) and 13.6% in pulmonary hypertension patients at the 90th day after BAE (7). Our results showed that the hemoptysis-related mortality was lower and the overall survival rate was higher in CTEPH patients with BAE during the follow-up period than patients without BAE. Embolizing the bronchial system for hemoptysis may be a life-saving procedure in patients with pulmonary hypertension.

Repeated BAE treatment is often needed in recurring instances of hemoptysis (6, 17, 22). The long-term effect of BAE in preventing recurrent hemoptysis needs to be established. It has been reported that recurrent hemoptysis after BAE occurs in 10–55.3% in predominant bronchiectasis, tuberculosis, and cystic fibrosis (4, 20, 21), and 31.5% in pulmonary hypertension (7). In our study, the hemoptysis recurrence after BAE was 20% in CTEPH, even though long-term anticoagulation was used in these patients. It is important to note that hemoptysis recurrence was significantly lower in patients treated with BAE than in patients treated without BAE. Furthermore, one patient underwent successful PEA 3 months after the BAE procedure without relapse of hemoptysis. Thus, we believe that BAE provided opportunities for some of CTEPH patients with hemoptysis to perform PEA in the future.

It was unclear whether the pulmonary hypertension was deteriorated and gas exchange of patients was affected after BAE because pulmonary artery pressure in CTEPH patients was increased. Our present study showed that oxygenation index and right heart insufficiency were not deteriorated after BAE procedure by ABG analysis and echocardiography before and after BAE, which further proved the effectiveness and safety of BAE procedure in the treatment of hemoptysis in patients with CTEPH.

Limitations also existed. First, this is a single center pilot study, as the sample size is small, a possibility of bias is existed especially in the difference in mortality between the two groups. Additionally, five patients did not perform DSA during the event of hemoptysis. Thus, we are not sure about their specific vascular morphologies. Prospective multi-center large sample studies might be needed in the future to further confirm the findings in our current study.

CONCLUSIONS

Our current study showed a 4.7% occurrence rate of hemoptysis in CTEPH patients and preliminarily demonstrated that BAE procedure was effectiveness and safety to treat these patients at our center. However, further controlled trials are needed before BAE can be considered as an effective and safe therapeutic option for the management of CTEPH patients with hemoptysis.

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