Bronchial Artery Embolization for the Management of Frequent Hemoptysis Caused by Bronchiectasis

Guang-Dong Lu

the First Affiliated Hospital of Nanjing Medical University

Hai-Tao Yan

the First Affiliated Hospital of Nanjing Medical University

Jin-Xing Zhang

the First Affiliated Hospital of Nanjing Medical University

Sheng Liu

the First Affiliated Hospital of Nanjing Medical University

Hai-Bin Shi

the First Affiliated Hospital of Nanjing Medical University

Qing-Quan Zu (✉ zuqingquan@njmu.edu.cn)

the First Affiliated Hospital of Nanjing Medical University

Research Article

Keywords: bronchial arteries, bronchiectasis, embolization, therapeutic, hemoptysis

Posted Date: January 28th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-1282206/v1>

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Abstract

Background: To retrospectively evaluate effectiveness of bronchial artery embolization (BAE) for the treatment of frequent hemoptysis caused by bronchiectasis, comparing with patients treated with conservative therapy.

Methods: From January 2015 to December 2019, consecutive patients who admitted due to frequent (more than three times per year) bronchiectasis-related hemoptysis was retrospectively reviewed. They who treated with either BAE (n=69) or conservative therapy (n=47) were enrolled for analysis. Technical success, clinical success, and complications of BAE procedure were evaluated. Long-term hemoptysis-free survival rates were compared between the patients in BAE group with clinical success and the patients in conservative group. Cox proportional hazard regression model was used to identify the predictors of recurrent hemoptysis.

Results: Technical success rate was 100% for BAE procedure and clinical success was achieved in 92.8% (64 of 69) of cases. No procedure-related major complication occurred and minor complications were observed in 16 cases (23.2%). The 1-, 2-, and 3-year hemoptysis-free survival rates were 88.3%, 71.3%, and 66.2%, for BAE group and 31.9%, 17.6%, and 2.5%, for conservative treatment group, respectively ($P < 0.001$). Multivariate analysis showed that BAE was a protective factor of recurrent hemoptysis in these patients. In addition, the presence of cystic bronchiectasis was the only independent risk factor for re-bleeding in the whole population and in BAE group.

Conclusions: BAE could provide an effective option for these frequent bronchiectasis-related hemoptysis patients, especially for those patients without cystic bronchiectasis.

Background

Bronchiectasis is a chronic respiratory disease characterized by repeated airway infections, enlargement of bronchi, productive cough, and recurrent exacerbations [1-3]. There is a growing interest on this disease over the past decade raised by its increasing prevalence, associated mortality and significant financial burden [2,4,5]. Due to the structural damage caused by recurrent airway inflammation, 26.0%–51.2% of these patients were estimated to be accompanied by hemoptysis [6-8]. The occurrence of frequent episodes of hemoptysis accompanied a cascade of acute exacerbations which lead to increased mortality and declined quality of life eventually [9-11]. A recent study also confirmed that hemoptysis was positively correlated with the incidence of depression in these bronchiectasis patients [12].

Treatment for frequent bronchiectasis-related hemoptysis is still an open question in clinical practice. Prescription a hemostatic drug always brought a relative short-term hemoptysis-free period. Lobectomy or segmentectomy can provide definite curative effect, but, which was limited to the patients with sufficient respiratory reserve and localized lesions [13,14]. Now, bronchial artery embolization (BAE) procedure, possessing a stable hemostatic rate, has been accepted as the first-line treatment for life-threatening hemoptysis [15-17]. The immediate hemostatic effect of BAE for massive hemoptysis caused

by bronchiectasis have been well established by literatures[15,18,19]. However, there is a lack of effective concern and active treatment for this kind of frequent hemoptysis that can cause anxiety and decline the quality of life.

We therefore performed this retrospective study to evaluate efficacy of BAE for the treatment of frequent bronchiectasis-related hemoptysis, comparing with that of conservative therapy. We also tried to investigate factors associated with recurrence after successful hemostasis.

Methods

Study design

This study was a single tertiary referral center retrospective cohort analysis. Institutional review board approval was obtained and the requirement for informed consent was waived for its retrospective nature.

Patients

In total, 247 consecutive bronchiectasis-related hemoptysis patients between January 2015 and December 2019 were confirmed in our center. The diagnosis of bronchiectasis was confirmed by high-resolution computed tomography with a ratio of the cross-sectional diameter of the inner airway and its concomitant artery (inner airway-artery ratio) > 1.0 [20]. The flowchart of patients included is shown in **Figure 1**. Ultimately, 69 patients were assessed for the technique and clinical notes in the BAE group, while 47 patients who treated with conservative therapy were also enrolled. Non-contrast chest CT with or without CT angiography (CTA) was employed to evaluate the location, extent, and severity of bronchiectasis, the possible bleeding focus, and the suspicious culprit vessels.

Conservative therapy

After admission, standard medical management including vital signs monitoring, hypoxemia correction, stabilization of blood pressure, hemostasis and anti-infection were taken for the patients. The hemostatic drugs, e.g., pituitrin and phentolamine, were pumping continuously and lasting until three days after the hemoptysis stopped. The combination of third generation cephalosporins and quinolones were used as empirical antibiotics initially and were adjusted during hospitalization according to culture results. Blood products were transfused as necessary according to the results of laboratory tests. In the cases of massive hemoptysis, the patients were received in an intensive care setting with early endotracheal intubation. After discharge, patients were educated to abandon smoking, reduce exposure to polluted air, take respiratory rehabilitation, and orally low-dose macrolide to control pulmonary infections.

BAE Procedures

All BAE procedures were done by two interventional radiologists with over six years of experience. Access was achieved by a 5F vascular sheath via the femoral artery under local anesthesia, selective angiograms of the bronchial arteries and/or non-bronchial systemic collateral arteries (NBSAs) were performed with

angiographic catheters (Cobra, RLG or MIK catheter, Cook, USA). Positive angiographic findings included extravasation of the contrast agent, arterial hypertrophy and tortuosity, neovascularity, hypervascularity, systemic arterial-pulmonary circulation shunts, and aneurysms. These culprit arteries were embolized with polyvinyl alcohol (PVA) particles (300–500 µm; Cook, USA), microsphere particles (300–500 µm, 500–700 µm, Merit Maestro, USA), and gelatin sponge particles (350–560 µm; Hangzhou Aicon Pharmaceutical Co., Ltd., China). To avoid embolization of the important side branches or reflux of the embolic material, microcatheter (2.7 F; Terumo, Japan; or 2.4 F; Merit Maestro, USA) was employed for embolization in every case. Procedure-related complications that resulted in prolonged hospitalization, advanced care, permanent sequelae, or death were regarded as major complications.

Data collection and outcome evaluation

We collected data related to baseline clinical characteristics and non-contrast CT image features. Baseline clinical characteristics included age, gender, body mass index (BMI), history of hemoptysis, hemoptysis amount, smoking, comorbidities, admission systolic pressure, laboratory indexes and in-hospital days. Hemoptysis amount per day was divided into three levels: mild (≤ 100 ml), moderate (100–300 ml), and massive (≥ 300 ml) [17].

Non-contrast CT image features were evaluated by two thoracic radiologists independently and any differences would reach to a consensus by a third radiologist. The CT grading system was a modified version of that described by Reiff et al [21]. Each lung segment was scored for (1) presence of bronchiectasis (0 = none, 1 = presence); (2) severity of bronchial dilatation (0 = normal, 1 = less than twice diameter of adjacent pulmonary artery, 2 = 2–3x diameter of adjacent pulmonary artery, 3 = more than 3x diameter of adjacent pulmonary artery); (3) severity of bronchial wall thickening (0 = normal, 1 = 0.5x diameter of adjacent pulmonary artery, 2 = 0.5–1x diameter of adjacent pulmonary artery, 3 = more than 1x diameter of adjacent pulmonary artery). The extent of bronchiectasis was taken as the sum of the scores for each of the lung segments. The severity of bronchial dilatation score was calculated as the sum of the dilatation score for each segment divided by the total extent score and the severity of bronchial wall thickening score was estimated as the sum of the thickness score for each segment divided by the total extent score. The type of bronchiectasis was described as cylindrical, varicose, or cystic according to the Reid classification [22]. The diameter of the abnormal bronchial arteries was measured 1 cm from the aortic origin and perpendicular to the vessel axis on the angiographic images in the BAE group [23].

After discharge, the patients' status was followed-up through outpatient or telephone visit at the first month after BAE and at every 6 months later. Clinical success was defined as no more coughing up fresh blood during hospitalization. Recurrence was defined as a hemoptysis volume ≥ 30 ml/d, requiring repeat BAE, requiring lobectomy, or death due to recurrence. Recurrence-free time was defined as the duration between the date of hemostasis during this hospitalization to the date of recurrence or the date of last follow-up (October 2020 for available patients).

Statistical Analysis

Continuous variables were described as mean $\pm$ standard deviations or median with interquartile range. Categorical variables between groups were compared with χ^2 test or Fisher's exact test, while continuous variables were compared with t test or Wilcoxon test. The recurrence-free survival rates were estimated by Kaplan-Meier method and log-rank test was used to identify the differences between recurrence-free rate curves. Patients who died for reasons not related to hemoptysis were censored at the time of death. We examined predictive factors of recurrent hemoptysis by using univariate and multivariate Cox proportional hazards regression models and factors with a P value < 0.1 in the univariate analysis were included in the multivariate analysis with an Enter method. Data analyses were performed with SPSS (version 24.0, Armonk, NY, USA) and P < 0.05 was considered statistically significant.

Results

Characteristics of BAE and short-term outcomes

For the 69 patients treated with BAE, technical success was achieved in all cases. Clinical success was achieved in 64 patients (92.8%), while 4 of them were lost follow-up. For the five patients without clinical success after BAE, two of them received conservative treatment, two underwent lobectomy and one died because of uncontrolled hemoptysis.

A total of 181 arteries were embolized during procedure: 162 bronchial arteries (90 right, 72 left) and 19 NBSAs (five intercostal arteries, three internal thoracic arteries, seven phrenic arteries, three esophageal arteries, and one thyrocervical trunk). The average number of culprit vessels was 2.6 ± 1.2 arteries per patient. The average diameter of the bronchial arteries measured on the angiographic images was 3.1mm (range, 1.9-6.3mm). After admission, 55 patients (79.7%) in BAE group and 13 patients (27.7%) in conservative group underwent CTA. All of the abnormal bronchial arteries embolized during BAE in the 55 patients could be identified on CTA before procedure.

Minor complications were observed in 23.2% (16 of 69) of the patients, including chest or back pain in 10 (14.5%), fever in 8 (11.6%), and puncture site hematoma in 2 (2.9%). All these symptoms were resolved with medical care. No major procedure-related complications occurred.

Baseline characteristics in two groups

The baseline characteristics of 107 patients with long-term outcomes are shown in **Table 1**. The BAE group had more male patients (P = 0.009), more severe hemoptysis (P < 0.001), and higher admission white blood cell (WBC) count (P = 0.002). The bronchiectasis types between groups were also different (P = 0.019). The other variables were not significantly different between groups.

Recurrence of hemoptysis

During follow-up, recurrence of hemoptysis occurred in a total of 66 (66/107, 61.7%) patients (21 in BAE group, 45 in conservative group), including five patients died directly related to recurrent hemoptysis

locating in conservative group. For these patients, BAE was performed in twelve, lobectomy was performed in five and conservative treatment was taken for the others. The 1-, 2-, and 3-year hemoptysis-free survival rates were 88.3%, 71.3%, and 66.2%, for BAE group and 31.9%, 17.6%, and 2.5%, for conservative treatment group, respectively ($P < 0.001$) (**Figure 2**).

Univariate and multivariate analyses of the variables associated with recurrence are shown in **Table 2**. Multivariate analyses demonstrated that BAE procedure [hazard ratio (HR), 0.155; 95% confidence interval (CI), 0.082-0.293; $P < 0.001$] and bronchiectasis type of cystic (HR, 1.940; 95% CI, 1.134-3.320; $P = 0.016$) were independently associated with recurrence. The factors related to recurrent hemoptysis in BAE group are shown in **Table 3**. Ultimately, only the bronchiectasis type of cystic (HR, 1.973; 95% CI, 1.029-3.782; $P = 0.041$) was an independent predictor for recurrent hemoptysis. The Kaplan-Meier estimated curves of recurrence-free survival for patients with or without cystic bronchiectasis in all patients and BAE subgroup are shown in **Figure 3**.

Discussion

In the present study, we evaluated BAE as a treatment for frequent hemoptysis caused by bronchiectasis. Technical success was achieved in all patients and instant hemostasis was achieved in the majority of the patients (92.8%). No procedure-related major complications occurred. These results indicated that BAE was an alternative effective and safe treatment for these patients.

Our results demonstrated that BAE, yielding a better long-term control of hemoptysis, which was better than conservative treatment for these frequent onset bronchiectasis patients. This benefit of BAE was also evident with a multivariate analysis. The results suggested that BAE treatment was an independent protective factor for recurrent hemoptysis. BAE, as a reliable treatment option, occluded the systemic arterial inflow into the fragile vessels within inflammatory tissue, reduced the perfusion pressure and the likelihood of further bleeding [16]. Though the high control rates of BAE in massive hemoptysis due to bronchiectasis have been well described by previous reports [15,24,25], this study initially demonstrated that BAE also could be trusted for the management of bronchiectasis-caused frequent hemoptysis. However, the hemoptysis-free rates in the present study was a little lower than those in previous studies [15,18]. That might be because of that the severity of disease in bronchiectasis patients with frequent hemoptysis was more serious. On the other hand, it also suggests that after successful hemostasis, these bronchiectasis patients still require long-term comprehensive management, which is also worthy of further investigation.

Furthermore, our results indicated that the bronchiectasis type of cystic was a risk factor for recurrence, even in patients receiving BAE. This may be attributed to the nature of this pathomorphological change. The presence of cystic bronchiectasis facilitates local accumulation of fluid and bacterial colonization, which causes repeated bacterial infections and continuous inflammation within the bronchial wall and surrounding tissue. These processes stimulate the formation of new blood vessels which are usually fragile and easy to rupture and bleeding. Even BAE could control hemoptysis with a longer duration, the

benefit seems to be inferiority to the effect accompanying by the deterioration of specific bronchiectasis subtype. Given that, lobectomy or segmentectomy may be another choice for localized cystic lesions in these bronchiectasis-related frequent hemoptysis patients [13,14].

During follow-up period, five cases, locating in the conservative treatment group, died due to recurrent hemoptysis. These results suggested that BAE might be conducive to reduce mortality in bronchiectasis patients with frequent hemoptysis. Previous studies indicated that hemoptysis is a main symptom and also a trigger of acute exacerbation in bronchiectasis patients, which lead to increased mortality [9,10]. The longer hemoptysis-free time acquired by receiving BAE may, on the other hand, reduce the likelihood of an acute exacerbation. Further research is needed to confirm whether BAE treatment could reduce frequency of exacerbations in these bronchiectasis patients with frequent hemoptysis.

As shown in our results, the culprit vessels in the frequent bronchiectasis-related hemoptysis patients are usually dilated, which could be easily identified by CTA. Premature CTA will help to determine the location and severity of lung lesions, identify the culprit vessels, evaluate the possibility of embolization treatment, and differentiate pulmonary source hemoptysis [26,27]. Therefore, CTA is a useful tool for clinical decision making. We also recommend that evaluation of CTA should be performed in each patient with recurrent hemoptysis.

Limitations should be mention in the present study. First, it was a retrospective study, with data extracting from a single center. There were differences in baseline characteristics between the BAE and conservative treatment groups. Though multivariate analysis was employed to confirm our conclusion, prospective studies are still warranted to confirm the benefit of BAE for the bronchiectasis-related frequent hemoptysis patients. Second, we evaluated the bronchiectasis severity by modified Reiff score, while did not investigate all clinical index, such as bronchiectasis severity index or FACED scores, which might also be also related to recurrent hemoptysis.

Conclusions

In conclusion, our study provided preliminary evidences that BAE was an alternative effective and safe treatment for frequent hemoptysis caused by bronchiectasis. The presence of cystic bronchiectasis was independently associated with recurrent hemoptysis, which may raise a concern of the priority treatment exploration.

List Of Abbreviations

BAE, bronchial arterial embolization; CTA, CT angiography; NBSAs, non-bronchial systemic collateral arteries; PVA, polyvinyl alcohol; BMI, body mass index; SD, standard deviations; WBC, white blood cell; RBC, red blood cell; PLT, blood platelet; SBP, systolic blood pressure; HR, hazard ratio; CI, confidence interval; IQR, interquartile range.

Declarations

Ethics approval and consent to participate:

Institutional review board approval was obtained and the requirement for informed consent was waived for this retrospective study.

Consent for publication:

Not applicable

Availability of data and materials:

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

Funding:

This study was funded by Jiangsu Province's KeyTalents Program (QNRC2016559 to Qing-Quan Zu) and Construction Program of Jiangsu Province Clinical Research Center Support System (BL2014084 to Qing-Quan Zu).

Authors' contributions:

Concepts/study design: G-D L, H-T Y, Q-Q Z; data analysis/ interpretation: G-D L, H-T Y, J-X Z, Q-Q Z; data collection: G-D L, H-T Y; manuscript drafting: G-D L, H-T Y, J-X Z, S L, Q-Q Z; critical revision of the article: S L, H-B S, Q-Q Z; overall responsibility: H-BS, Q-Q Z. All authors read and approved the final manuscript.

Acknowledgements:

Not applicable.

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Tables

Table 1. The baseline characteristics of 107 patients with long-term outcomes.

Variables	BAE (n=60)	Conservative (n=47)	P value
Female, No. (%)	27 (45.0)	33 (70.2)	0.009
Age, median, years	59.88±10.35	58.06±10.63	0.347
BMI, median, kg/m ²	22.27±3.28	22.86±3.03	0.463
History of hemoptysis more than 10 years, No. (%)	31 (51.7)	20 (42.6)	0.349
Extent of hemoptysis, No. (%)			< 0.001
< 100mL	19 (31.7)	34 (72.3)	
100-300mL	26 (43.3)	11 (23.4)	
≥ 300mL	15 (25.0)	2 (4.3)	
Smoke, No. (%)	12 (20.0)	7 (14.9)	0.493
Hypertension, No. (%)	13 (21.7)	10 (21.3)	0.961
Diabetes, No. (%)	4 (6.7)	2 (4.3)	0.693
Admission SBP, median (IQR), mmHg	124 (115-130)	128 (117-138)	0.464
Admission hemoglobin, median, (g/L)	123.03±18.78	125.60±16.58	0.278
RBC, median, *10 ⁹ /L	4.12±0.63	4.23±0.46	0.411
PLT, median, *10 ⁹ /L	185.75±59.64	189.53±51.81	0.770
WBC, median, *10 ⁹ /L	7.97±2.73	6.46±1.91	0.002
Number of lung segments involved, median (IQR)	4 (2-7)	5 (2-8)	0.578
Bronchial dilatation severity score, median (IQR)	1.8 (1.0-2.7)	2.1 (1.7-2.6)	0.072
Bronchial wall thickening severity score, median (IQR)	2.4 (1.8-3.0)	2.4 (2.0-3.0)	0.765
Bronchiectasis type, No. (%)			0.019
Column	17 (28.3)	5 (10.6)	
Varicose	21 (35.0)	13 (27.7)	
Cystic	22 (36.7)	29 (61.7)	
In-hospital days, median (IQR)	5 (4.0-7.8)	7 (6.0-9.0)	0.003
Hemoptysis recurrence, No. (%)	21 (35.0)	45 (95.7)	< 0.001
Follow-up period, median (IQR), months	31.2(21.4-55.5)	27.7(8.1-48.5)	-

Note: BAE = bronchial artery embolization; IQR = interquartile range; BMI = body mass index; SBP = systolic blood pressure; RBC = red blood cell; PLT = blood platelet; WBC = white blood cell.

Table 2. Univariate and multivariate analyses of the variables associated with recurrence of hemoptysis in the whole patients (n = 107).

Variables	Univariate		Multivariate	
	HR (95% CI)	P value	HR (95% CI)	P value
Age, years	0.99 (0.96-1.01)	0.332		
Gender (male)				
Female	1		1	
Male	0.65 (0.40-1.08)	0.098	1.28 (0.74-2.24)	0.381
BMI, median, kg/m ²	0.96 (0.89-1.04)	0.280		
History of hemoptysis ≥ 10 y	1.22 (0.75-1.98)	0.433		
Extent of hemoptysis, mL		0.069		0.138
<100	1		1	
100-300	0.85 (0.50-1.44)	0.550	1.63 (0.92-2.89)	0.094
≥ 300	0.38 (0.17-0.87)	0.021	0.81 (0.34-1.95)	0.642
Smoking	0.67 (0.34-1.31)	0.240		
Hypertension	1.00 (0.55-1.81)	0.996		
Diabetes	1.01 (0.32-3.24)	0.986		
Admission SBP, mmHg	1.01 (0.99-1.03)	0.118		
Admission hemoglobin (g/L)	1.00 (0.99-1.01)	0.808		
PLT, $\times 10^9$ /L	1.00 (0.99-1.00)	0.405		
WBC, $\times 10^9$ /L	0.87 (0.78-0.96)	0.009	0.94 (0.84-1.06)	0.332
Number of lobes involved	1.05 (0.99-1.12)	0.114		
Bronchial dilatation severity score	1.28 (0.94-1.75)	0.123		
Bronchial wall thickening severity score	1.10 (0.79-1.54)	0.582		
Bronchiectasis type				
Column or Varicose	1		1	
Cystic	2.63 (1.59-4.37)	< 0.001	1.94 (1.13-3.32)	0.016
Treatment				
BAE	0.14 (0.08-0.25)	< 0.001	0.16 (0.08-0.29)	< 0.001
Conservative	1		1	
In-hospital days	1.02 (0.95-1.08)	0.624		

Note: BMI = body mass index; SBP = systolic blood pressure; RBC = red blood cell; PLT = blood platelet; WBC = white blood cell; BAE = bronchial artery embolization.

Table 3. Multivariate analysis of predictive factors for recurrent hemoptysis after BAE.

Variables	HR (95%CI)	PValue
BMI, kg/m ²	0.882 (0.754-1.032)	0.117
History of hemoptysis		
< 10 years	1	
≥10 years	2.084(0.808-5.372)	0.129
Bronchiectasis type		
Column or Varicose	1	
Cystic	1.973 (1.029-3.782)	0.041

Note: BMI = body mass index; HR = hazard ratio.

Figures

Figure 1

Flowchart of the included patients.

Figure 2

Cumulative recurrence-free rate curves stratified according to the treatment method used. The 1-, 2-, and 3-year hemoptysis-free survival rates were 88.3%, 71.3%, and 66.2%, respectively, for BAE group and 31.9%, 17.6%, and 2.5%, respectively, for conservative treatment group ($P < 0.001$).

Figure 3

The estimated curves of cumulative recurrence-free rate curves for patients with or without cystic bronchiectasis. A) Recurrence-free rate curves in all 107 included patients [hazard ratio (HR), 2.63; 95% confidence interval (CI): 1.59-4.37; $P < 0.001$ by using Cox proportional regression analysis). B) Recurrence-free rate curves in 60 patients received BAE treatment. (HR, 2.305; 95% CI: 1.259-4.218; $P=0.007$).