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ORIGINAL ARTICLE

Outcomes of bronchial artery embolization for life-threatening hemoptysis due to tuberculosis and post-tuberculosis sequelae

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PURPOSE
To determine the long-term outcomes of bronchial artery embolization in patients with massive hemoptysis due to pulmonary tuberculosis and post-tuberculosis sequelae and to study the factors influencing success.

MATERIALS AND METHODS
In this study, 58 patients underwent 64 bronchial artery embolizations for massive hemoptysis due to tuberculosis or its sequelae between 1998 and 2008. Their images and procedure details were reviewed. Medical records and direct contact were used to obtain information on outcome. The cumulative hemoptysis control rate per follow-up interval was calculated.

RESULTS
The data showed that 25 patients presented with acute massive hemoptysis and 33 presented with chronic recurrent hemoptysis. The median quantity of blood was 400 mL (range, 70–2000 mL). The median follow-up period was 432 days (range, 11–1789 days). Twenty-seven patients had recurrence after a median period of 110 days after the procedure (range, 1–959 days). The hemoptysis control rate was 93% at 2 weeks, 86% at one month, 79.5% at 3 months, 63% at 6 months, 51% at one year and 39% at 2 years. Six patients underwent repeat procedures. Chest pain was the most common procedure-related complication (n=20, 34.5%); there was no spinal cord complication or mortality. There were seven deaths, five of which were related to hemoptysis. Nine patients were lost to follow-up. Lung cavities ($P = 0.08$), nonbronchial systemic artery collaterals ($P = 0.081$) and systemic-to-pulmonary venous shunts ($P = 0.053$) were more common in those who experienced recurrence.

CONCLUSION
Bronchial artery embolization is a relatively safe procedure that is lifesaving in patients who are not suitable for surgery. However, the associated long-term outcome is less satisfactory.

Key words: • *hemoptysis* • *tuberculosis* • *embolization* • *recurrence*

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Un its various manifestations, pulmonary tuberculosis is the most common cause of life-threatening hemoptysis in developing countries (1). Conservative or surgical management in these patients is associated with high morbidity and mortality (2, 3). Bronchial artery embolization (BAE) is an established procedure in the emergency management of massive hemoptysis; however, there are few reports on the long-term outcomes of BAE in these patients (4–6). Ongoing inflammation causes continuous recruitment of collaterals, rendering them vulnerable to the recurrence of hemoptysis. Seriously compromised lung function due to severe fibrosis makes them poor surgical candidates (5–9). This retrospective study was undertaken to determine the long-term outcomes in these patients as well as the factors influencing the outcome.

Materials and methods

Patients

A total of 124 patients were identified as having undergone bronchial artery embolization for various reasons from 1998 to 2008, using information from the database of the Department of Radiology, Christian Medical College, Vellore, a tertiary care teaching hospital in Southern India. Among these patients, 58 underwent BAE for massive hemoptysis due to tuberculosis or its sequelae and were chosen for the study. Patients with only chest radiographic features of post-tuberculosis sequelae without a documented diagnosis of previous tuberculosis were excluded.

"Massive hemoptysis" was defined as an amount of hemoptysis sufficient to cause a life-threatening condition in a patient; this was the criteria for referral for BAE. This decision was made by the physician in charge of the patient. A life-threatening condition was marked by severe loss of blood (>600 mL) causing hemodynamic instability, reduced hemoptysis with desaturation secondary to asphyxiation or underlying severe lung disease.

All of these patients were hospitalized according to protocol, and they underwent standard medical management, including correction of hypoxemia, correction of hemodynamic instability with fluids and blood products, antibiotics in case of documented or suspected secondary bacterial infection and cough suppressants, as required. Chest radiographs and sputum acid fast bacilli (AFB) assays were performed for all patients to identify active tuberculosis. Patients with active tuberculosis were promptly started on an antituberculosis treatment. Patients with post-tuberculosis sequelae had a documented past history of tuberculosis and a history of antituberculosis treatment. A fiber optic bronchoscopy (FOB) and contrast-enhanced computed tomography (CECT) or high-resolution computed tomography (HRCT) of the thorax were performed for all patients presenting with acute or chronic massive hemoptysis in

order to identify the cause of hemoptysis and to localize the site of bleeding. In some instances, CECTs of thorax and BAE were performed as an immediate life-saving measure to stop bleeding, and prior evaluation with a bronchoscopy was not possible. Two patients underwent BAE while on mechanical ventilation.

The institutional review board (IRB) approved this study, and informed consent was waived. The IRB approval number is RC 6417.

Bronchial artery embolization

BAE was performed using Siemens Multistar TOP DSA. In most cases, the right common femoral artery was accessed with a retrograde puncture using the Seldinger technique. Using a pigtail catheter, an arch aortogram was performed on all of the patients. A selective angiogram of abnormal bronchial, intercostal, and subclavian artery branches visualized on the aortogram was performed to note the abnormality. Visualization of the spinal artery was not considered a contraindication for BAE; however, the vessel from which the spinal artery originated was carefully excluded. This was followed by particle embolization (poly vinyl alcohol, [PVA] 150–500 microns) of the abnormal vessels using a coaxial microcatheter system (Progreat 2.5 F, Somerset, New Jersey, USA) in select cases. In ill patients, embolization of the bronchial arteries most likely responsible for causing the bleeding was carried out. A limited search for bronchial or nonbronchial systemic artery collaterals was performed if abnormal vessels were not found during the aortogram. Pulmonary angiography was performed only when no abnormality was found on bronchial angiography.

Images were recorded as angiographic runs on a compact disc and stored on the Picture Archiving and Communication System (PACS). Plain radiographs and CT thorax images were also stored in the PACS. Procedure details and complications were also documented on the procedure notes attached to the angiogram images and inpatient records. All of the patients who underwent BAE were admitted as inpatients for at least three days postprocedure. Patients were followed up for observation of the immediate response to the procedure and procedure-related complications. Active tuberculosis patients were put on an appropriate antituberculosis regimen.

Source of data and outcome analysis

The data for outcome analysis were obtained from inpatient and outpatient medical records and from direct contact with the patient through letters or telephone calls. Outcome analysis was performed for the following periods: the immediate control of bleeding and recurrence of hemoptysis within the first 2 weeks, within the first month, between 1 to 3 months, between 3 to 6 months, between 6 months to 1 year, between 1 to 2 years and beyond 2 years of the procedure. Morbidity and mortality due to the procedure were also assessed.

Successful control of hemoptysis was defined as no hemoptysis or minimal hemoptysis after BAE. Immediate control of hemoptysis was defined as successful control of hemoptysis up to 2 weeks after BAE. Recurrent hemoptysis was defined as single or multiple episodes of hemoptysis causing a total of >30 mL of bleeding per day. Some patients coughed up previously expectorated blood for a couple of days after the procedure; this was not deemed a lack of control. The decision to repeat BAE was based on the same indications as the first BAE. Minor hemoptysis was managed conservatively. Follow-up continued until September 2008 in patients for whom follow-up was available. The date of death or the date after which the patient was unavailable for follow-up was noted.

The cumulative hemoptysis control rate for patients who underwent BAE at each follow-up interval was calculated by the Kaplan-Meier method. Statistical differences in the factors influencing patient outcomes among patients with recurrence versus those without recurrence were determined using the chi-square test and Yates correction. The *P* value for significance was set at <0.05.

Results

Descriptive statistics

A total of 58 patients (46 males, 12 females), with an age range of 18–68 years (median, 43 years), underwent 64 BAE procedures for massive hemoptysis due to tuberculosis or its sequelae. Among those studied, 25 (43%) patients presented with acute massive hemoptysis and 33 (57%) patients with chronic hemoptysis; 13 (22.4%) experienced single episodes and 45 (77.6%) experienced multiple episodes of hemoptysis, with the quantity of bleeding ranging 70–2000 mL (median of 400 mL). Fourteen (24%) patients had active tuberculosis at presentation, while 44 (76%) patients had post-tuberculosis sequelae. Among patients with active tuberculosis, four were on the category 1 and five were on the category 2 revised national tuberculosis control program (RNTCP) directly observed treatment short course (DOTS) regimen. Four patients had multidrug resistant tuberculosis (MDRTB), and one patient had atypical mycobacterial infection. Only seven (12%) patients were current smokers, and 13 (22 %) were ex-smokers. In total, 31 (53%) patients were nonsmokers. Smoking history was not available for seven (12%) patients.

A total of 208 arteries were embolized in 64 procedures. An average of four arteries was embolized per patient (range, 1–9 arteries). One patient who had 9 arteries embolized was a patient with post-tuberculosis sequelae with bilateral diffuse disease with cavities and cystic bronchiectasis. The following arteries were embolized in this patient: right D2, D3, D4 and D5 intercostal arteries; left D5 intercostal artery; a hypertrophied branch of the right internal mammary artery; two hypertrophied branches of the right subclavian artery; and the left bronchial artery.

Several agents were used for embolization: PVA particles (n=40); gel foam and PVA particles (n=10); gel foam (n=9); PVA and glue (n=2); PVA and coils (n=3). The size of the PVA particles ranged 150–1000 µm; the most commonly used particles ranged in size 355–710 µm. Glue was used in two patients who had rapidly forming systemic-to-pulmonary venous shunts. Coils were used in one patient with a bilobed saccular aneurysm of the right bronchial artery branch and in two patients to embolize the internal mammary artery.

Results of imaging

The chest radiograph was abnormal in 54 (93%) patients. The CT findings are summarized in Table 1. Tree-in-bud opacities, cavities with thick and irregular walls and cavities containing fluid were associated with active

Table 1. Summary of CT findings

Imaging feature	Number (%)
Extent:	
- Bilateral lung involvement	46/58 (79)
- Unilateral lung involvement	12/58 (21)
- Diffuse involvement	42/58 (72)
- Focal area of involvement	16/58 (28)
Cavity	38/58 (66)
Fungal ball in the cavity	12/38 (32)
Bronchiectasis	55/58 (95)
Pleural thickening >10 mm	36/58 (62)
Consolidation	14/58 (24)
Active tuberculosis with consolidation	9/14 (64)

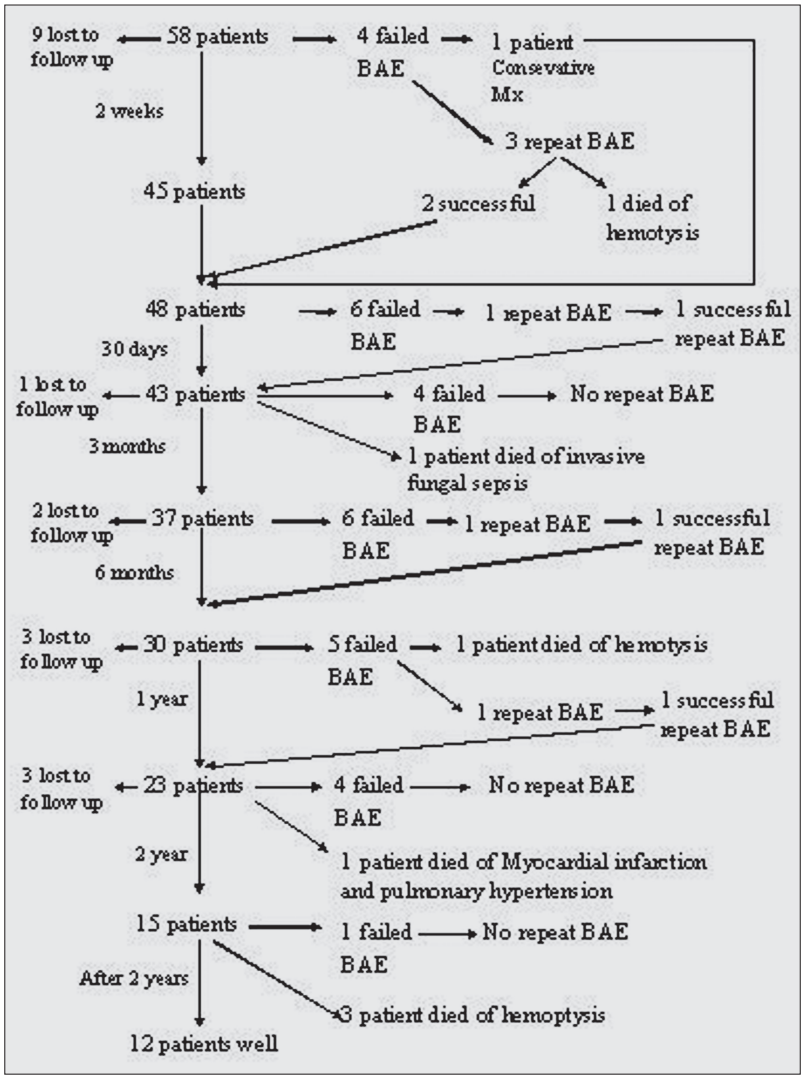

Figure 1. The distribution of follow-up periods in 58 patients who underwent bronchial artery embolization (BAE) for massive hemoptysis due to tuberculosis or post-tuberculosis sequelae.

tuberculosis. Volume loss, fibrosis with traction bronchiectasis, calcification and pleural thickening were seen in patients with tuberculosis sequelae.

Angiograms showed multiple abnormalities in 43/58 patients and a single abnormality in 15/58 patients. Abnormal hypertrophied tortuous arteries were seen in all 58 patients; 41 (72.4%) patients showed hypervascularity and parenchymal blush; 11 (19%) showed systemic–to-pulmonary venous shunts; two had bronchial artery aneurysm; and one patient had active contrast extravasation. None of these patients displayed a bronchial or intercostal origin of the spinal artery. The right bronchial artery was abnormal in 49 (84.5%) patients; the left bronchial artery was abnormal in 31 (53.4%) patients; the intercostals were abnormal in 20 (35%) patients. Accessory bronchial arteries were found in seven patients (12%); nonbronchial systemic artery collaterals from the subclavian artery or intercostal arteries were seen in 36 (62.1%) patients.

Results of outcome analysis

Data from all 58 patients were available for analysis of the immediate outcomes of the procedures. Immediate control of hemoptysis was achieved in 54 patients. Among the four patients who had immediate recurrence, one patient with modest hemoptysis was managed conservatively, and the other three patients underwent repeat BAE. Two cases were successful, and one patient died. Therefore, a total of 57 patients were eligible for follow-up. Nine patients were lost to follow-up after being discharged from the hospital, so 49 patients (40 males, 9 females) were included in the analysis of outcome. The median follow-up period was 438 days (range, 11–1789 days). The number of patients at each follow-up interval is shown in Fig. 1. Three-quarters (37/49) of the patients were followed up for at least one year.

Out of the 49 patients with complete follow-up information, 27 patients (55%) had recurrence of hemoptysis after a median interval of 110 days after BAE (range, 1–959 days). Table 2 and Fig. 2 summarize the outcomes of the 49 patients who were followed up. The Kaplan–Meier curve describing the cumulative probability of survival without recurrent hemoptysis after BAE in patients with tuberculosis and post-tuberculosis sequelae shows that the hemoptysis control rate was 93.1% at the end of two weeks, 85.7% at the end of one month, 79.5% at 90 days, 63.2% at 180 days, 51% at one year and 38.7% at the end of two years (Fig. 3).

Outcome after a repeat BAE

Six patients had a repeat BAE for recurrence of hemoptysis between 4 and 273 days following the first BAE. Out of the six patients, one had active tuberculosis and five had post-tuberculosis sequelae. A repeat BAE due to recurrence of hemoptysis was observed in four patients within one month, in one patient within four months, and in one patient at nine months after the first BAE. After the second BAE, one patient with active tuberculosis was completely symptom free at last follow-up

Table 2. The outcomes of 58 patients who underwent bronchial artery embolization (BAE) for tuberculosis and post-tuberculosis sequelae

Outcome	N	Success	Failed BAE	Repeat BAE	Death	Successful repeat BAE	Cause of death	Hemoptysis control rate	Lost to follow-up
Immediate (<2 weeks)	58	54	4	3	1	2	Hemoptysis	93.1%	9
30 days	48	42	6	1	0	1	-	85.7%	0
3 months	43	39	4	0	1	0	Invasive fungal sepsis	79.5%	1
6 months	37	31	6	1	0	1	-	63.2%	2
1 year	30	25	5	1	1	1	Hemoptysis	51%	3
2 years	23	19	4	0	1	0	Respiratory failure	38.7%	3
After 2 years	15	12	1	0	3	0	Hemoptysis (n=2) multidrug resistant tuberculosis and hemoptysis (n=1)	24.5%	0

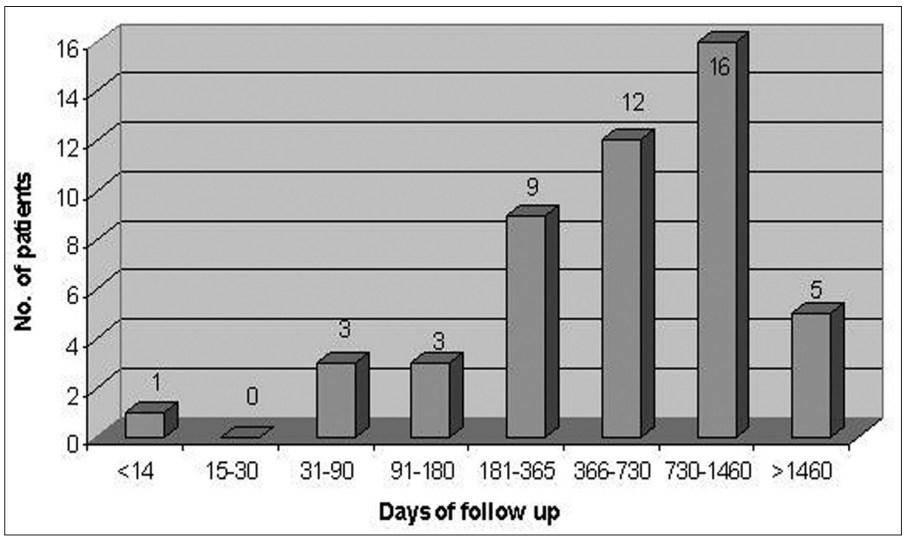

Figure 2. A flow chart depicting the follow-up duration of the patients.

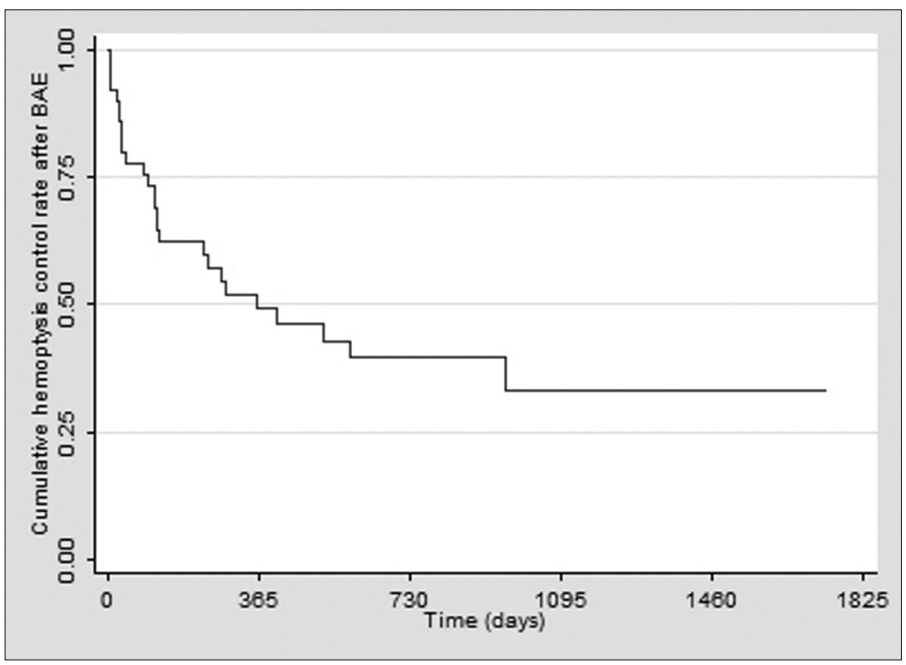

Figure 3. The cumulative hemoptysis control rate as depicted graphically by the Kaplan-Meier method.

(at 281 days), and another patient with post-tuberculosis sequelae was symptom free at 1154 days. Four others with tuberculosis sequelae had recurrence of hemoptysis at 7 days, 62 days, 63 days and 281 days after the second BAE. One patient who had recurrence of hemoptysis at day 7 after the second BAE died. Other patients who had recurrence of hemoptysis were advised to undergo BAE, but they declined a repeat procedure because of the high cost.

Mortality

There were a total of seven deaths during the follow-up period. Five patients died because of hemoptysis on follow-up days 11, 294, 801, 902, and 1432, respectively. One of these patients who died of hemoptysis had active MDRTB. One patient died of invasive fungal septicemia on day 76 after the procedure; this was unrelated to his disease and was not associated with hemoptysis. One patient died of chronic pulmonary hypertension and myocardial infarction on follow-up day 379.

Complications

Procedure-related complications were not uncommon and, when encountered, were mostly minor (Table 3).

Factors affecting outcome

Of all the clinical and radiological features of patients, there was no statistically significant difference between those who experienced recurrence and those who did not. There was a trend favoring the group with recurrence in the following areas: cavitations in the lung as seen upon HRCT/ CT thorax ($P = 0.08$), nonbronchial systemic artery collaterals (P =

Table 3. Postprocedure complications

Complication	Number %	Consequence
Chest pain	20 (34.5)	6 have chronic pain
Dysphagia	3 (5)	Transient
Dissection (bronchial and intercostals)	2 (3.4)	No consequence
Fever	1 (1.7)	-
Contrast reaction	1 (1.7)	Mild reaction was treated with chlorpheneramine injection
Transient ischemic attack (weakness of left upper limb)	1 (1.7)	Resolved completely one day after the procedure
Paraplegia	0	-
Mortality	0	-

0.081) and systemic-to-pulmonary venous shunts on angiogram ($P = 0.053$). There was no significant difference in the number of patients with cavities containing fungal balls ($P = 0.939$). The outcome was not significantly different as the result of the type of embolic agent used ($P = 0.238$), the size of PVA particles used for embolization ($P = 0.262$) or the number of vessels embolized ($P = 0.852$). There was also no significant difference in the outcome among patients with active tuberculosis compared with those with post-tuberculosis sequelae ($P = 0.282$).

Discussion

BAE is a well-established procedure used to control massive hemoptysis (5, 10, 11). However, few reports have addressed the outcomes in the control of hemoptysis due to tuberculosis. Even in the larger series found in the literature, patient follow-up after BAE only lasted up to 6 months (5, 6, 12–14). There are only a few studies that have assessed possible prognostic factors that determine outcome in patients who have undergone BAE (15, 16). Thus, we intended to assess the long-term outcome and the factors influencing the outcome of BAE in these patients and to review the available literature.

Various definitions of life-threatening hemoptysis are available; these are based on the amount of hemoptysis per 24-hour period. However, we used the functional definition used by Mal et al. (8, 17, 18). We limited embolization to abnormal arteries seen in aortograms, so the anatomy of bronchial arteries could not be assessed in our study. Selective catheterization of abnormal arteries was technically not difficult because tuberculosis is a chronic disease that causes hypertrophy and dilation of the bronchial arteries.

According to our protocol, visualization of the spinal artery origin coming from the bronchial or abnormal intercostal artery was considered as an absolute contraindication to embolize that vessel; we did not visualize the anterior medullary artery in any of these patients. Spinal arteries are reported to arise from the intercostal branch of the right intercostobronchial trunk in 5%–10% of cases, but it is generally believed that the true prevalence is considerably lower (19). Pulmonary angiography was done only when no systemic artery abnormality was seen. Thus, only three patients underwent pulmonary angiography in addition to bronchial angiography; these individuals showed no abnormality.

Recurrence of hemoptysis within 2 weeks after embolization is usually due to incomplete embolization of nonbronchial systemic artery collaterals. Recurrence during this period usually necessitates a repeat BAE, and the outcome of such a procedure is generally good. Immediate control of bleeding was achieved in 93% of cases. This result is similar to the immediate results reported in the literature (6, 8, 11, 20, 21).

Hayakawa et al. (19) have reported two peak times of bleeding recurrence. The first is from 1 to 2 months after BAE, which may reflect incomplete embolization. The second peak for recurrence is from 1 to 2 years after the patient underwent embolization. This appears to reflect the recruitment of blood supply and revascularization due to underlying pulmonary inflammation or progression of the underlying disease (22). However, we did not observe similar peak times for recurrence in our series.

As reported in the literature, the hemoptysis control rate at one month varies between 51%–85% (6, 8, 10, 20, 23, 24). Uflacker et al. (21) and Ramakantan et al. (6) report their experience predominantly in patients with tuberculosis and its sequelae (91% and 100%, respectively). The authors report a hemoptysis control rate of approximately 50% at one month. However, we report an 86% hemoptysis control rate at one month; this rate is much higher than that reported by the studies described above. This could be explained by the fact that we undertook limited embolization in an attempt to embolize the visualized nonbronchial systemic artery collaterals, even though we did not search extensively for collaterals. The number of patients with active tuberculosis in our series was smaller: 24% (14/58) of our patients compared with approximately 35% (51/140) of the patients in the Ramakantan et al. (6) series. Information on the number of patients with active tuberculosis was not available for the Uflacker et al. (21) series.

Though immediate control of hemoptysis was satisfactory in the patients in our study, the long-term outcomes were not good. The hemoptysis control rate decreased progressively to 51% at the end of one year and to 39% at the end of two years, after which the condition stabilized. Thus, BAE is palliative rather than curative in patients who present with massive hemoptysis due to tuberculosis. However, BAE may be the only life-saving treatment option for patients with massive hemoptysis due to tuberculosis and with bilateral diffuse disease that is not amenable to definitive surgical treatment. BAE may also be the only option for patients who are unfit for surgery because of poor lung function from extensive tuberculosis or other lung diseases, such as chronic obstructive pulmonary disease. It is reasonable to assume that patients who experience a relapse of symptoms are more likely to return for follow-up. If so, we may have underestimated the success of this approach.

A total of 27 (55 %) patients experienced recurrence of hemoptysis after BAE. Cavitating lung lesions, nonbronchial systemic artery collaterals and

systemic-to-pulmonary venous shunts appeared more commonly among patients who had recurrence of hemoptysis than among those who did not. Similar findings were obtained in a study by Shin-ichi et al. (23). However, cavities with fungal balls and pleural thickening of >10 mm did not influence the incidence of recurrence in our series, which is in contrast to previous reports (5, 9). There are conflicting reports on the association between active tuberculosis and recurrence. While Lee et al. (22) demonstrated a significant association between active tuberculosis and recurrence after BAE, van den Heuvel et al. (24) has shown that the presence of active tuberculosis amenable to treatment is protective. However, our series shows no such association; this could be due to fewer active tuberculosis patients or it could mean that the type of lung pathology rather than the presence of active tuberculosis may influence outcome. The type of agent used for embolization did not influence the chance of recurrence, as was also shown in studies published by other authors (6, 8, 20).

Though repeat BAE was indicated in many, only six patients underwent repeat BAE because the others could not afford this expensive treatment. The recurrence-free period after the second BAE ranged from 62 to 1154 days.

Procedure-related complications were common; however, most were minor. The only major complication in our series was transient ischemic attack in one patient causing weakness of the left upper limb because of patent foramen ovale; however, this patient recovered completely the following day. There were no spinal cord–related complications in our series; this is probably related to the use of DSA, superselective catheterization of the abnormal vessel and the use of a microcatheter for the particle embolization.

On follow-up, there were five patient deaths directly related to hemoptysis, i.e., 10.2% (5/49). This is similar to a previous report (25). Two deaths were due to other causes. Our study is limited by the nine patients who were lost to follow-up. Furthermore, a larger number of patients may be needed to assess factors influencing outcome.

As a conclusion, BAE is a relatively safe procedure, and most complications related to the procedure are minor. We believe the use of microcatheters for superselective catheterization and embolization may minimize serious complications related to spinal cord injury. Embolization of visualized abnormal nonbronchial systemic collaterals increases the hemoptysis control rate achieved at one month; an exhaustive search for nonbronchial systemic artery collaterals is not necessary. The long-term outcome in these patients is not good, but BAE may be the only life-saving treatment option in patients who are poor surgical candidates. Repeat BAE in patients with early recurrence improves outcome. Although the trends were not significant, cavitating lung lesions, nonbronchial systemic artery collaterals and systemic-to-pulmonary venous shunts were more common in patients with recurrence of hemoptysis.

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Conflict of interest

The authors declared no conflicts of interest.

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