Bronchial Arterial Embolization for Hemoptysis :

Analysis of Outcome in Various Underlying Causes[1]

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Purpose : To clarify the short-term effect and long-term results of bronchial arterial embolization for hemoptysis in three groups with tuberculosis, idiopathic bronchiectasis and lung cancer.

Materials and Methods : This study involved 54 patients who underwent arterial embolization for the control of hemoptysis. Among 54, the causes of hemorrhage were; pulmonary tuberculosis(n= 32), idiopathic bronchiectasis (n= 15), and lung cancer(n= 7). In all patients, embolization was performed using Gelfoam particles and three underwent additional coil embolization. After the procedure, patients were followed up for between 1 and 95 (mean, 36.7) months. Short-term results were assessed on the basis of careful observation of patients for 1 month after arterial embolization and were classified as either; successful, indicating complete cessation of hemoptysis for 1 month, or failed, indicating continuing hemoptysis or recurrence within 1 month. Long-term results were evaluated in patients in whom the procedure was successful in the short term and who could be followed up for at least 6 months. Patients showed either complete remission(CR), indicating complete cessation of bleeding during the observation period; partial remission(PR), indicating complete cessation of hemoptysis with recurrent bloody sputum during the observation period; or recurrence, indicating recurrent hemoptysis, and were grouped accordingly.

Results : No serious procedure related complications occurred except for mild chest pain or fever, of which showed spontaneous relief within a few days. The overall short-term success rate was 79.6 %(43/54); individual rates were 84.4 % for pulmonary tuberculosis (27/32), 80 % for idiopathic bronchiectasis (10/15), and 57.1 % for lung cancer (4/7). Long-term follow-up showed that complete remission was achieved in 24 of 43 cases (55.8 %). The respective long-term remission and recurrence rates were 75 % and 25 % for bronchiectasis, 70.4 % and 29.6 % for pulmonary tuberculosis. While four lung cancer patients whose initial outcome was successful showed no recurrence of hemoptysis, three died within 3 months of embolization.

Conclusion : Embolization of bronchial arteries using a Gelfoam sponge is effective as initial treatment for moderate or severe hemoptysis caused by benign disease. During long-term follow up, high remission rates were achieved in pulmonary tuberculosis and idiopathic bronchiectasis patients, while the shortest bleeding control was in cases involving lung malignancy.

Index words : Lung, hemorrhage
Arteries, therapeutic blockade
Arteries, bronchial

Hemoptysis is a manifestation of pulmonary or tracheobronchial disease. Fortunately, most acute episodes involve only a small volume of blood, last less than 24 hours, and gradually subside without treatment. Massive hemoptysis, defined as 300 to 600 ml per 24-hour period, has a much worse prognosis, with a reported mortality rate of 50-60 % (1-2). Bronchitis, tuberculosis, and bronchiectasis have been cited as common causes of major hemoptysis(1). In recent years, however, while the incidence of bronchitis , bronchiectasis and tuberculosis is decreasing due to the development and widespread use of effective antibiotics including antituberculosis drugs, lung cancer has been added to this list. The reported incidence of cancer as a cause of pulmonary bleeding ranges from 3.2 % to 35.5 % (3- 7).

Bronchial artery embolization (BAE) has proved to be an effective, well established treatment for nonsurgical candidates and a palliative therapy in those requiring preoperative stabilization (1,2,8- 11). Among patients successfully embolized for hemoptysis, however, about 36 to 44 % rebled during long- term follow- up (11,12). A number of studies have investigated the long- term results of BAE for hemoptysis due to various underlying pulmonary disease including lung cancer (13,14).

The purpose of this study was to clarify the immediate and long- term effects of BAE on massive hemoptysis or continuing moderate hemoptysis resistant to medical treatment, both of which are attributable to pulmonary tuberculosis, idiopathic bronchiectasis, or lung malignancy.

Materials and Methods

The present study involved 54 patients (39 males and 15 females) aged from 19 to 72 (mean: 52.8) years who underwent, between November 1990 and November 1998, bronchial and other involved systemic artery embolization for massive or continuing moderate hemoptysis resistant to medical treatment. The amount of blood expectorated at the time of initial BAE was less than 300 ml/day in 35 patients, and more than 300 ml/day in 19 patients. Among this total of 54, the causes of hemorrhage were; pulmonary tuberculosis (n= 32, mean age 48.8 years), idiopathic bronchiectasis (n= 15, mean age 46.9 years), and lung malignancy (n= 7, mean age 65.1 years). We categorized a group of idiopathic bronchiectasis patients in whom bronchiectasis was not related to pulmonary tuberculosis (Fig. 1). In the lung malignancy group there were six cases of squamous cell carcinoma and one of small cell carcinoma. All these patients had inoperable advanced disease; radiation therapy was used in four, while two underwent chemotherapy (Fig. 2).

For logistical reasons, at our institution, patients with hemoptysis did not usually undergo bronchoscopy for the detection and treatment of bleeding sites before BAE. For those in whom hemoptysis was relatively extensive or in whom the condition was resistant to medical treatment, angiography and embolization were considered after discussion between respiratory physicians and radiologists. Chest radiographs and chest CT scans

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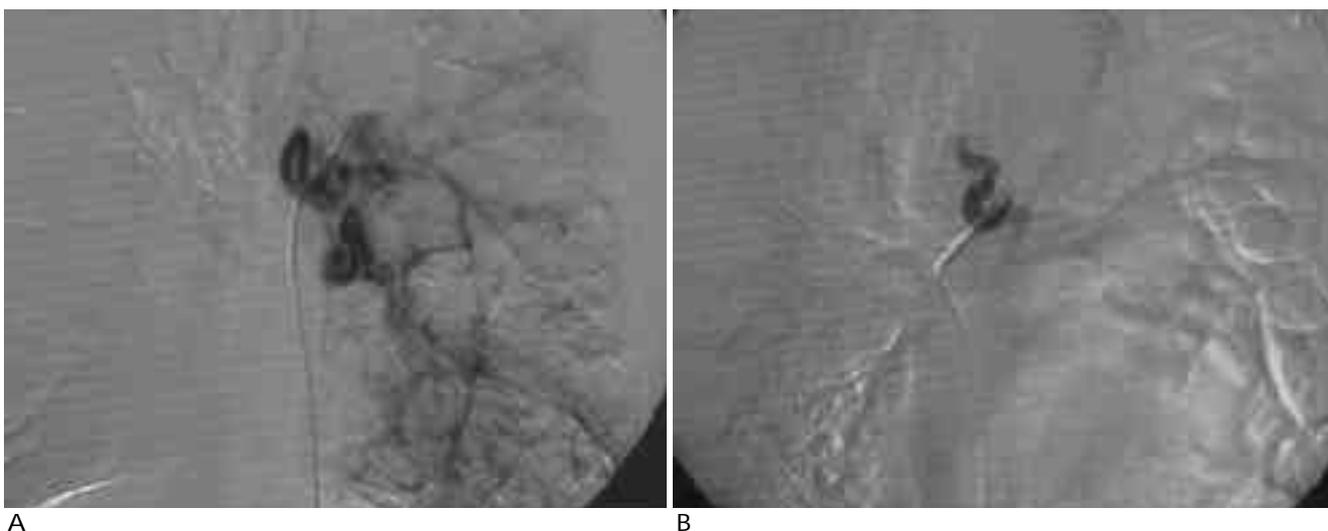
Fig. 1. A-60-year-old woman with idiopathic bronchiectasis.
A. Selective left bronchial arteriogram shows hypertrophic and tortuous bronchial arteries in lower lung zone.
B. After embolization with Gelfoam, complete occlusion of the bronchial artery at proximal level is noted. During follow up, she rebled within 1 month after arterial embolization.

were evaluated with regard to the site and extent of the lesion.

To provide a road map, a descending thoracic aortogram was performed prior to selective catheterization using a 5-Fr Pigtail catheter (Cook, Bloomington, Ind.). Bronchial arteries were selected for embolization on the basis of all relevant clinical, radiographic, endoscopic, and arteriographic information. Selective arteriography of the bronchial arteries and collateral vessels was usually performed using cobra-head type (Cook, Bloomington, Ind.), shepherd's crook (Sooho, Seoul, Korea), or Yashiro (Therumo, Tokyo, Japan) 5-6 Fr catheters. In some cases, a selective bronchial arteriogram was followed by subselective catheterization of the bleeding vessel with a 3 Fr microcatheter using the coaxial technique (Fig. 3). Eight to 10 ml of 305 mgI/ml meglumine diatrizoate

(Angiografin, Schering AG, Germany) was manually injected into the bronchial artery and 3 to 7 ml into the intercostal artery. When abnormal bronchial arteries were not identified, bilateral selective subclavian arteriograms were performed to locate bronchial arteries with aberrant origins and to identify any transpleural collaterals that might have arisen from branches of the subclavian and axillary arteries.

Signs of bleeding were the extravasation of contrast medium, hypertrophy of the supply artery, hypervascularity of the involved area, bronchial artery to pulmonary artery shunt, bronchial artery to pulmonary vein shunt, and any combination of these findings. Embolization was performed using a gelatine sponge (Gelfoam, Upjohn, Kalamazoo, U.S.A.) which was cut into 0.5-1.0 mm cubes and soaked in contrast medium. To avoid over-
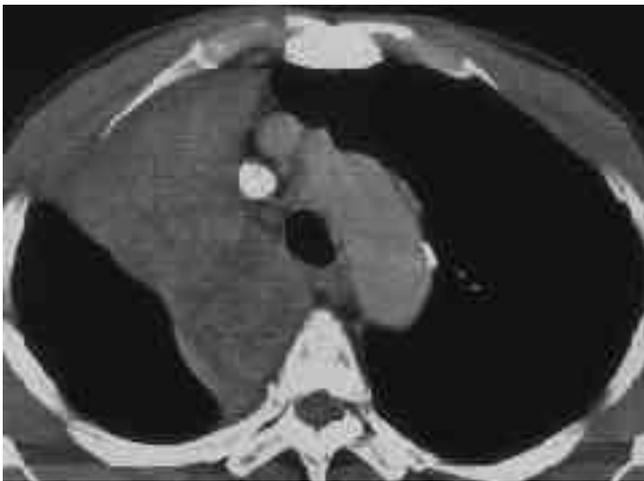
Fig. 2. A-64-year-old-man with lung cancer.
A. An axial CT scan at the level of aortic arch shows complete atelectasis of right upper lobe due to central mass. Massive hemoptysis occurred during receiving radiation therapy.
B. Selective right bronchial angiography shows hypertrophy of the bronchial branch and hypervascularity toward the upper and lower lobes.
C. Arteriogram after embolization of the intercostobronchial trunk shows that the proximal bronchial branch and intercostal branch are occluded.
D. Follow-up right bronchial arteriogram that obtained on second BAE shows recanalized bronchial and intercostal branches.
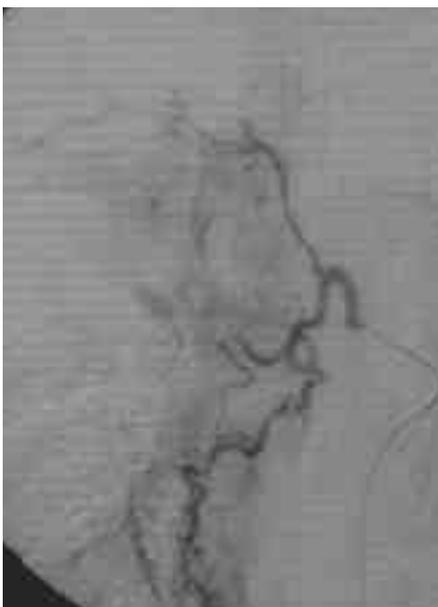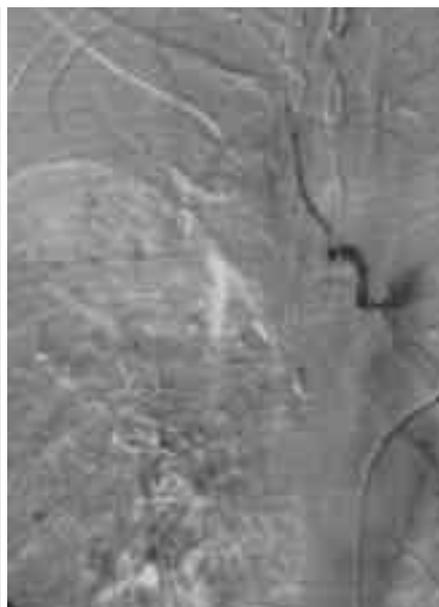
flow into the aorta, the sponge particles were slowly and carefully injected under fluoroscopic guidance. Additional coil embolization was performed in three cases (Fig. 1). Finally, postembolization arteriography was used to ascertain the extent of embolization. If this was insufficient, the embolization procedure was repeated until complete blockage of the feeding artery was achieved.

A total of 65 embolization procedures were performed in 54 patients; once in 45 patients, twice in 7 patients, and three in two patients. The arteries embolized were the bronchial artery only in 42 patients, nonbronchial systemic arteries in four, and both bronchial and non-

bronchial systemic arteries in eight. Nonbronchial systemic arteries embolized included intercostal arteries(n= 6), the internal mammary artery(n= 5), and branches of the subclavian artery(n= 2). Angiography revealed various, clearly defined findings in relation to the lesions. These are detailed in Table 1.

Investigation of underlying disease and the extent of hemorrhage, and follow- up, were conducted by reviewing the patients' medical records and by telephone interview. Where medical records indicated the recurrence of hemoptysis, observation was terminated at the point at which the most recent notation was entered. For those with repeated BAE, observation continued.

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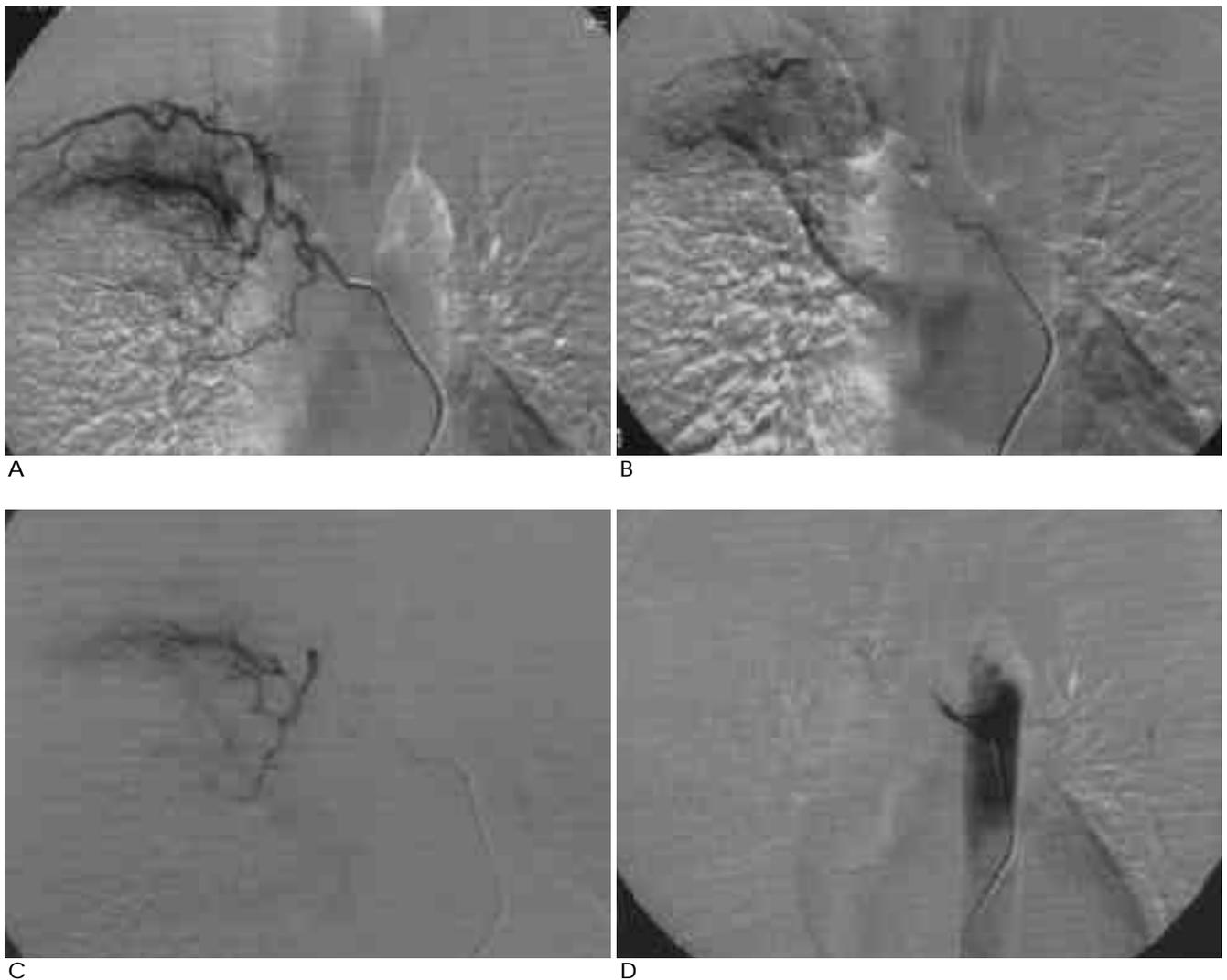
Fig. 3. A-31-year-old man with pulmonary tuberculosis.
A. Early selective digital subtraction arteriogram of right intercostobronchial artery shows increased vascularity.
B. Late phase shows considerable amount of shunting into the pulmonary vein.
C. Subselective arteriogram of upper bronchial branch with 3 Fr microcatheter shows hypertrophied vessels and systemic pulmonary shunt.
D. Postembolization bronchial arteriogram shows complete occlusion of bronchial intercostobronchial artery. Note microcoils were seen in branches of intercostobronchial trunk.

The observation of patients who underwent pneumonectomy after embolization was terminated at the time of surgery. Patients with no recurrent hemoptysis according to their medical records responded to a telephone questionnaire regarding the presence/absence of recurrent hemoptysis, and, if applicable, its severity and timing. Among the 54 patients, the shortest observation period was that of a patient who died due to recurrent hemoptysis two days after embolization. The longest observation period was 95 months, and the mean observation period was 36.7 months.

Short-term results were assessed on the basis of careful observation of patients for 1 month post-BAE and were classified as either successful , indicating complete cessation of hemoptysis during 1 month, or failed, indicating continued hemoptysis or recurrence within 1 month. Patients with residual or occasional blood-streaked sputum within 1 month but not hemoptysis, which was defined as an expectoration of blood, were considered controlled.

Long-term results were evaluated in patients who could be followed up for at least 6 months and in whom the procedure had been successful. Patients showed either complete remission(CR), indicating complete cessation of bleeding throughout the observation period; partial remission (PR), indicating complete cessation of hemoptysis with recurrent bloody sputum during the observation period, or recurrence(R), indicating recurrent hemoptysis (13).

The hemoptysis control period is defined as the time from initial BAE to the first incident of recurrent hemoptysis, regardless of whether any episode of bloody sputum occurred. For all 54 patients as well as for each disease group, cumulative hemoptysis control and survival rates were assessed using the Kaplan-Meier method. In addition, the relationship between long-term results and various affecting factors such as the extent of hemoptysis or numbers of arteries embolized were analyzed.

Results

Short-term results were analyzed in 54 patients (Table

Table 1. Clinical Data, Arteries Embolized and Angiographic Findings, According to Disease Process.

	Tuberculosis(n= 32)	Bronchiectasis(n= 15)	Lung Malignancy(n= 7)
Mean Age(years)	48.8	46.9	65.1
Extent of bleeding			
Massive	11(34.4%)	3(20%)	6(85.7%)
Moderate	21(65.6%)	12(80%)	1(14.3%)
Numbers of arteries that were embolized			
Single	23(71.9%)	13(86.7%)	7(100%)
Two	5(15.6%)	2(13.3%)	0(0%)
More than three	4(12.5%)	0(0%)	0(0%)
Angiographic Findings			
Hypervascularity	32	15	7
Enlargement of arteries	32	15	5
Systemic to pulmonary shunt	8	2	0
Extravasation	3	1	0

Table 2. Short-term and Long-term Results of Bronchial Artery Embolization According to Each Disease Group.

	Tuberculosis(n= 32)	Bronchiectasis(n= 15)	Malignancy(n= 32)	Total(n= 54)
Short-term Results				
Successful	84.4%(27/32)	80%(12/15)	57.1%(4/7)	79.6%(43/54)
Failed	15.6%(5/32)	20%(3/15)	42.9%(3/7)	20.4%(11/54)
Long-term Results				
Complete remission	51.9%(14/27)	66.7%(8/12)	50%(2/4)	55.8%(24/43)
Partial remission	22.2%(6/32)	16.7%(2/12)	25%(1/4)	20.9%(9/43)
Recurrence	25.9%(7/32)	16.7%(2/12)	25%(1/4)	23.3%(10/43)
Hemoptysis Control Period				
Mean± SD(mos)	28± 14.8	24± 19.2	6.5± 5.75	24.4± 16.5
Median	27	10	3	12
Range	1-95	1-72	0-18	0-95
Mortality Rate	3.1%(1/32)	6.7%(1/15)	100%(7/7)	16.7%(9/54)

2). BAE was successful in 43 patients but failed in 11. The overall short-term success rate was 79.6 %(43/54); individual rates were 84.4 % for tuberculosis (27/32), 80 % for bronchiectasis (12/15), and 57.1 % for lung malignancy (4/7). The underlying pulmonary diseases of patients with failed BAE included lung cancer (n= 3) and bronchiectasis (n= 3). The outcome for patients with failed BAE included death from bleeding or asphyxia (n= 3), death from causes other than hemoptysis (n= 2), repeated embolization with survival (n= 2), or chronic intermittent and mild hemoptysis with conservative treatment (n= 4). While one of three patient who died from asphyxia expired on the day of BAE, two others died on the 24th and 28th day after the procedure due to recurrence of massive hemoptysis. The mortality rate of patients with failed BAE was 45.5 %(5/11).

In this series, complications arising from the embolization were relatively minor and included temperature elevations of 37-38 in 12 patients, and/or mild chest and shoulder pain for several days in 25 patients. Following embolization, neither spinal cord injury nor acute impairment of pulmonary function was noted.

Among 43 patients in whom BAE had initially been evaluated as successful, the duration of follow-up was as follows: in 17 patients, from 1 to 12 months; in 18, from 1 to 3 years; in six, from 3 to 5 years; in two, more than 5 years. The mean hemoptysis control period was 24.4 ± 16.5 months, and the median period was 19 (range 1-95) months. Twenty-four patients(55.8 %) were rated as showing complete remission, nine (20.9 %) as showing partial remission, and ten (23.3 %) as showing recurrence.

Of the nine patients who underwent 11 repeat embolization procedures, seven patients underwent one, and two underwent two procedures. The results of these 11 embolization procedures were as follows: in the short term, 81.8 % were successful (n= 9),18.2 % failed (n= 2); in long term, CR 55.6 % (5/9), PR 44.4 % (4/9), and recurrence 22.2 % (2/9). Repeat embolization thus showed short-term and long-term results similar to those of the initial embolization procedure.

The long-term results were also analyzed according to disease group (Table 2). For bronchiectasis, the remission rate was 75 % (CR 58.3 %, PR 16.7 %), and for tuberculosis, 70.4 % (CR 48.2 %, PR 22.2 %). Of four lung cancer patients in whom the procedure was successful in the short term, three showed no recurrence of hemoptysis but died within 3 months of embolization, and in one, hemoptysis recurred during follow-up, 18 months after the
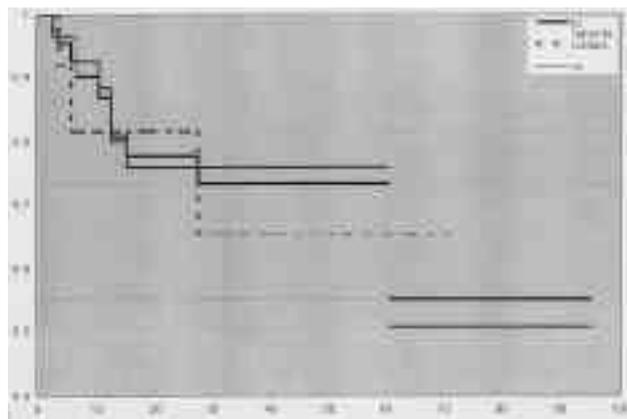

Fig. 4. Cumulative hemoptysis control rates for all patients, tuberculosis group and bronchiectasis group calculated by the Kaplan-Meier method. No plot can be drown in cancer group since there is only one valid survival function value.

Table 3. Cumulative Hemoptysis Control Rate According to the Each Disease Group.

Disease	Control Rates(%)		
	< 1year	< 3year	< 5year
Tuberculosis	88.4	75.8	60.5
Bronchiectasis	81.5	65.2	65.2
Lung malignancy	100.0	0.0	
Total	86.9	73.4	55.0

procedure.

In addition, long-term results were analyzed according to the extent of hemoptysis. The massive hemoptysis group showed a shorter hemoptysis control period (49.8 months) than the moderate group (54.3 months) (p< 0.05). Long-term results showed a 55.3 % remission rate in the massive hemoptysis group and 78.8 % in the moderate group.

The overall cumulative hemoptysis control rate (CHCR) after initial embolizations was 86.9 % at 1 year, 77.5 % at 2 years, and 55.0 % at 5 years (Table 3, Fig. 4). In the tuberculosis and bronchiectasis groups, the one-year CHCR remained at 75.8 % and 65.2 %, respectively. There was, however, no statistically significant difference between the two groups (P < 0.05, generalized Wilcoxon test). In addition, one-year CHCRs differed significantly according to the extent of hemoptysis and the number of hypertrophied vessels embolized. The massive and the moderate hemoptysis group showed 56.2 % and 88.1 % one-year CHCRs, respectively (P< 0.05). The one-year CHCR remained at 87.3 % in patients with a single feeding vessel, and 54.5 % in patients with multiple feeding vessels (P< 0.05).

Discussion

Transcatheter embolization of bronchial and other systemic pulmonary arteries has proved to be an effective method of accomplishing temporary or permanent hemostasis in various benign, chronic inflammatory disease states such as tuberculosis, bronchitis, and bronchiectasis (1,2,8-12). Only scattered reports are found in the literature in English about the effectiveness of BAE including its use in cases of lung cancer (3,13,14).

Regarding the immediate effect of BAE on hemoptysis, previous studies have reported bleeding control rates of 76.6% to 90.8% (1, 11-13). A relatively worse rate (76.9%) was obtained in our study, and we believe that this discrepancy in short-term results is due to the stricter criteria for success we adopted: to be considered successful, the effect of BAE had to last at least 1 month. The mortality rate of patients in whom BAE failed was 45.5% (5/11), which was higher than that previously reported (4). We believe that this discrepancy was due to the high proportion of lung cancer patients in this study.

As for the long-term effects of hemoptysis, the cumulative non-recurrence rates in patients who underwent a single BAE were 86.9% for 1 year, 73.4% for 3 years, and 55.0% for 5 years. These results were similar to those reported by others (11-13). However, by performing additional BAE for those with recurrent hemoptysis, these rates increased to 92.5% for 1 year, 80.8% for 3 years, and 61.8% for 5 years. These results suggest that by repeating BAE, the outcome of the treatment can be improved even in patients with recurrent hemoptysis. This improvement can probably be achieved when the reembolization gives the chance to compensate for technical insufficiency at initial BAE, such as overlooking the feeder vessels.

Our results revealed a high incidence of early recurrent hemoptysis and low cumulative hemoptysis control rates in the massive hemoptysis group and in the group with angiographically multiple hypertrophied feeder vessels. Therefore, the amount of hemoptysis and numbers of feeder vessels as well as the underlying disease, might have a significant impact on long-term effects.

The malignancy group showed the highest failure rate and the shortest hemoptysis control period. This result was similar to those of the previously reported (13). Hayakawa et al. (13) noted that these poor results in the lung neoplasm group were related to the BAE procedure as well as to the treatment for the underlying pulmonary disease. In this regard, patients with malignancy were the most difficult to manage, as most neoplasms were advanced. The neoplasm received its blood supply not only from the bronchial artery but from multiple sources and had invaded the vascular structures aggressively. In patients with a bronchogenic tumor, fatal hemoptysis was frequently associated with necrotic squamous cell carcinoma, arising in either the right or left main bronchus (15). Previous investigators have shown that in this cell type there is an increased tendency to tissue necrosis and subsequent hemorrhagic infarction. A proposed mechanism for the development of necrosis in squamous cell carcinoma is tumor invasion of vascular structures leading to ischemia and vascular necrosis (16,17). The lung malignancy group showed the worst short-term results and the shortest bleeding control time. Despite this, for three such patients in whom the initial procedure was successful, adequate bleeding control was achieved up to the time they died. In addition, while BAE failed in three patients in the short term, the procedure stopped the bleeding immediately and controlled bleeding in two of them until massive rebleeding resulted in their death within one month. Only one patient died of asphyxia on the day of BAE. Therefore, embolization had in each case been of some benefit, at least transiently. The question of how far to go in trying to stop bleeding in patients with far-advanced lung cancer, however, is a difficult one: most patients died within three months despite successful hemostasis by BAE. This is simply a matter of the best available judgement of physicians, surgeons, patients and patients' families at the time of decisions.

As an embolic agents, all procedures employed Gelfoam sponge cut into fragments 1-3 mm in size. The material most commonly used for BAE at the present time include Gelfoam (12,13,18) and polyvinyl alcohol (PVA) particles (19,20). Other embolic materials such as bucrylate (21), steel coils, detachable coils (22,23) and ethanol (24) have previously been used. Gelfoam is a readily available, slowly resorbable material that can be used as individual pledgets, torpedoes, or as part of slurry. A theoretical disadvantage of Gelfoam is that its resorption may lead to more rapid recanalization and recurrent bleeding (25). PVA is a particulate embolic material that is available in several particle sizes (19,20) and because of its permanent nature has advantages over Gelfoam. Recanalization is thus less likely to occur (11).

In three of nine patients (33.3 %) who underwent repeated BAE, bronchial arteriograms demonstrated recanalization of the bronchial artery responsible for hemoptysis and subsequent successful embolization after repeated BAE. We believe, therefore, that for BAE, the use of permanent embolic material such as PVA or bucrylate might show better results. Kim et al. (26), however, reported that the rebleeding rate did not depend on the embolic materials used for BAE.

BAE is a safe and effective procedure that can be used in the short term to stop bronchial bleeding due to a benign, chronic inflammatory process such as tuberculosis or bronchiectasis. Recurrence rates at more than 20 %, were rather high, however. To decrease recurrence, continuing treatment of the underlying problem, be it cancer or an inflammatory disease, is needed. Even though BAE showed the worst results in the short term and the shortest bleeding control time in the lung malignancy group, it successfully stopped hemoptysis immediately in most cases.

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80.0% (12/15),   57.1% (4/7)   .   75%
25%   ,   70.4%   29.6%   .   4
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