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The Factors Related to Recurrence after Transcatheter Arterial Embolization for the Treatment of Hemoptysis

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Objectives: *Massive hemoptysis is a major clinical problem associated with high morbidity and mortality. Transcatheter arterial embolization is widely used for the treatment of massive hemoptysis, but it was reported that the recurrence rate after embolization is 12-54% in the previous studies.*

We evaluated the therapeutic effect of transcatheter arterial embolization for the treatment of massive hemoptysis and the factors related to recurrence.

Methods: *We reviewed 51 patients (M:F=36:15) of trancatheter arterial embolization for the treatment of massive hemoptysis from Jan 1988 to Dec 1994, retrospectively.*

Results: *After arterial embolization, immediate successful control (<1wk) of massive hempotysis was achieved in 48 of 51 patients (94.1%) and recurrence of hemoptysis was observed in 17 of 51 patients (33.3%) during the follow-up period. The patients with non-bronchial artery hemoptysis and multiple artery bleeding had increased tendency of recurrence (77.7%). On the previous history of hemoptysis, the patients with massive hemoptysis (>400ml/24hr) or frequent history of hemoptysis had increased tendency of recurrence (87.5%, 72.7%).*

Conclusion: *Transcatheter arterial embolization is a useful and safe procedure for immediate control in massive hemoptysis. However, the patients with this procedure had a potentiality for recurrence. We suggest that close follow-up and caution will be needed in the patients with multiple artery bleeding or with large amounts of hemoptysis or with previous episodes more than 3 times.*

Key Words: *Bronchial artery embolization, Massive hemoptysis*

INTRODUCTION

Hemoptysis is a relatively common symptom of respiratory diseases. Most acute episodes of hemoptysis are not disaster, and they may subside gradually within 24 hours after bleeding. Massive hemoptysis, however, is a major clinical and surgical problem related to high morbidity and mortality.

The main causative diseases of massive hemoptysis are pulmonary tuberculosis, bronchiectasis, aspergilloma, paragonimiasis and bronchogenic carcinoma, respectively.

The operative intervention is the most attractive treatment, but it is not always feasible in some patients with diffuse pulmonary disease and markedly impaired pulmonary function that makes them poor candidates for thoracotomy.

Although the transcatheter arterial embolization is now well accepted in the management of massive and urgent hemoptysis, it was reported that recurrence rate after embolization is 12% to 54% in the previous studies[1-5] and relatively little has been described about the factors related to

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recurrence of hemoptysis after embolization.

The main goal of this study is to evaluate the therapeutic effect of transcatheter arterial embolization for the treatment of massive hemoptysis and to identify the factors related to the recurrence of hemoptysis after embolization.

SUBJECTS AND METHODS

1. Subjects

From January 1988 to December 1994, 51 patients with massive hemoptysis underwent transcatheter arterial embolization at Kyung Hee Medical Center. Massive hemoptysis was defined arbitarily as 400ml of pulmonary hemorrhage for a 24-hour period or more than 100ml of hemoptysis during one episode, or uncontrolled hemoptysis (more than 100ml/day) after more than 5 days of medical therapy. The patients were 36 men and 15 women, aged from 24 to 75 years (Table 1).

There were three degrees of hemoptysis severity; 1) up to 200ml of hemoptysis for 24 hours (n=24), 2) between 200ml and 400ml of hemoptysis for 24 hours (n=19), 3) more than 400ml of hemoptysis for 24 hours (n=8).

As for underlying diseases, thirty-six patients (71%) exhibited pulmonary tuberculosis, including 22 patients (43%) with active tuberculosis and 14 patients (28%) with sequelae to pulmonary tuberculosis. Eleven patients (22%) had bronchiectasis, three (3%) had aspergiloma, one had paragonimiasis and one had unknown cause (Table2).

Table 1. Age and Sex Distribution

Age	Male	Female	Total
21 - 30	2	5	7
31 - 40	6	2	8
41 - 50	12	2	3
51 - 60	11	4	5
61 - 70	5	1	6
> 71	0	1	1
Total	36	15	51

Table 2. Underlying Diseases with Hemoptysis

Cause	No. of Patient(%)
Pulmonary Tbc, active	22 (43.1)
Pulmonary Tbc, inactive	14 (27.4)
Bronchiectasis	11 (21.5)
Aspergilloma	2 (3. 9)
Paragonimiasis	1 (1.9)
Unknown	1 (1.9)

2. Arteriography and Embolization

The evaluation for site of bleeding began with chest radiography or bronchoscopy in patients, and confirmed with bronchial arteriography for the final diagnostic decision.

Transfemoral Seldinger technique was used for arteriography. Bronchial and nonbronchial systemic arteriographic studies were carried out to detect arterial abnormality in all patients. Embolization was performed to the vessel with hypervasculartity, interarterial broncho-pulmonary shunt, aneurysmal dilatation and extravasation or periarterial diffusion of contrast agent on arteriographic finding.

The embolic materials utilized were Gelform particles (absorptive material, Ferrosan A-S international, Soeborg, Denmark), Ivalon (nonabsorptive material, Ingenol, Paris, France), Contour (nonabsorptive material, International Therapeutics Corporation, San Francisco, U.S.A). Immediate successful embolization was defined when hemoptysis subsided within 1 week and clinical condition of patients improved. Recurrence of hemoptysis was defined as more than 100ml of hemoptysis for a 24 hour period after embolization. The follow-up period after embolization ranged from 7 months to 60 months in each patient. Retrospective analysis was done to evaluate the therapeutic effect of transcatheter arterial embolization to control massive hemoptysis and to identify the factors related with recurrence of hemoptysis, such as underlying diseases, previous history of hemoptysis, amount of hemoptysis, target arteries for embolization and embolic material used.

3. Statistics

Chisquare test was used to compare the recurrence rate according to factors related to hemoptysis.

RESULTS

In 42 patients (82.3%), bronchial artery was em-

Table 3. Target Arteries for Embolization

Target Artery	No. of Patients(%)
Bronchial	42 (82.3)
Bronchointercostal trunk	1 (1.9)
Intercostal	3 (5.8)
Bronchial & Intercostal	4 (7.8)
Bronchial & Internal mammary	1 (1.9)

Table 4. Complications of Embolization

Complication	No. of Complications / Total No. of Patients (%)
Chest pain	7/51 (13.7)
Abdominal pain	5/51 (9.8)
Shoulder pain	1/51 (1.9)
Fever	1/51 (1.9)
Headache	1/51 (1.9)

bolized. Broncho-intercostal trunk in one patient (1.9%) and intercostal artery in 3 patients (5.8%) were emboliged. Bronchial and intercostal artery were emboliged in 4 patients (7.8%) and bronchial and intercostal mammary artery in one patient (1.9%) (Table 3).

Complications of embolization occurred in 15 out of 51 patients (29.4%), which included chest pain in 7 patients, abdominal pain in 5 patients, shoulder pain in one patient, fever in one patient and headache in one patient. These symptoms, however, subsided within 3 days (Table 4). Immediate successful control of massive hemoptysis was achieved in 48 of 51 patients (94.1%) and recurrence of hemoptysis was observed in 17 of 51 patients (33.3%), during the follow-up period. Recurrence of hemoptysis occured in 17 patients (33.3%), and the interval between embolization and recurrence of hemoptysis was less than 1 week in 2 patients, from 1 week to 1 month in 1 patient and more than 1 month in 14 patients. So, most recurrence occurred after 1 month of embolization (Table 5). Medical therapy was done in 9 re-bleeding patients and repeated emobolization and operation performed in 6 and 2 patients (Aspergilloma), respectively.

Recurrence of hemoptysis was 56.2% (9 out of 16 patients) in Gelform, 35.7% (5 out of 14 patients) In ivalon and 28.5% (2 out of 7 patients)

Table 5. Outcome of Embolization

Outcome	No. of Patients(%)
No recurrence	34 (66.6)
Recurrence	17 (33.3)
Interval between embolization and recurrence	
< 1 week	2
1 week-1 month	1
> 1 month	14

Table 6. Embolic Materials

Material	No. of Recurrences(%)
Gelform	9/16 (56.2)
Ivalon	5/14 (35.7)
Contour	2/ 7 (28.5)
Gelform & Ivalon	1/ 3 (33.3)
Gelform & Contour	4/11 (36.3)

in contour according to used material.

Recurrence of hemoptysis of combined gelform and ivalon was 33.3% (1 out of 3 patients) and that of gelform and contour was 36.3% (4 out of 11 patients) (Table 6).

Recurrence of hemoptysiss according to underlying diseases was 22.7% (5 out of 22 patients) in active pulmonary tuberculosis, 42.8% (6 out of 14 patients) in inactive pulmonary tuberculosis, 27.2% (3 out of 11 patients) in bronchiectasis and 100% in patients with aspergillosis and paragonimiasis.

Recurrence of hemoptysis of emobolized arteries was 26.1% in bronchial arterise (11 out of 42 patients), 66.6% in intercostal arteries (2 out of 3 patients), 75.0% in concomitant bronchial and intercostal artery (3 out of 4 patients). Concomitant bronchial and internal mammary artery embolization recurred in all patients. Recurrence of hemoptysis was high in embolization of nonbronchial systemic artery and that of 2 or more arteries ($p < 0.025$).

Recurrence rates according to volume of hemoptysis were 12.5% (3 out of 24 patients) in less that 200ml of hemoptysis, 87.5% (7 out of 8 patients) in massive hemoptysis (more than 400ml) ($p < 0.005$). Recurrence rates according to past history of hemoptysis were 10.6% in patients without history of hemoptysis (3 out of 28 patients) and 72.7% in patients with more than 3 times of

Table 7. Factors related to Recurrence of Hemoptysis

	No. of Recurrences / Total No. of Patients (%)
Cause	
Active Tbc	5/22 (22.7)
Inactive Tbc	6/14 (42.8)
Bronchiectasis	3/11 (27.2)
Aspergilloma	2/ 2 (100)
Paragonimiasis	1/ 1 (100)
Embolized vessel	
Bronchial artery	11/42 (26.1)
Nonbronchial & multiple artery	7/ 9 (77.7)*
Bronchointercostal trunk	0/ 1 (0)
Intercostal	2/ 3 (66.6)
Bronchial & Intercostal	3/ 4 (75.0)
Bronchial & Internal mammary	1/ 1 (100)
Amount of Hemoptysis	
<200ml/24hrs	3/24 (12.5)
200ml~400ml/24hrs	7/19 (36.8)
>400ml/24hrs	7/ 8 (87.5)**, +
Previous History of Hemoptysis	
None	3/28 (10.7)
1~2	6/12 (50.0)
more than 3	8/11 (72.7)***

*: $p<0.025$ as compared with patients with bronchial artey embolization
**: $p<0.005$ as compared with patients with < 200ml/ 24hrs
+: $p<0.025$ as compared with patients with 200ml~400ml/24hrs
***: $p<0.005$ as compared with patients without history of hemoptysis

hemoptysis (8 out of 11 patients) ($p<0.005$). It is suggested that volume and past history of hemoptysis are related to recurrence (Table 7).

DISCUSSION

Hemoptysis is a disastrous manifestation of tracheobronchial or pulmonary disease.

Fortunately, most acute episodes of hemoptysis last less than 24 hours and gradually subside. Massive hemoptysis, however, is associated with high mortality, usually from rapid flooding of the tracheobronchial tree and asphyxiation[6-8].

Massive hemoptysis is defined as pulmonary hemorrhage of more than 300ml to 600ml within 24 hours and it carries a mortality rate of 50% to 80% in medically treated patients[9, 10].

Surgical intervention has been the procedure of choice in patients with massive hemoptysis, but surgery during an episode of massive hemoptysis carries high morbidity and mortality.

Since Remy introduced the embolization of bronchial arteries in 1974, bronchial artery embolization is well accepted and widely used for treatment of massive and urgent hemoptysis, especially in patients with chronic diffuse pulmonary disease who are poor candidates for surgery[11].

Main causes of hemoptysis are pulmonary tuberculosis, bronchiectasis, pneumoconiosis, aspergilloma, chronic bronchitis, sarcoidosis, pulmonary cyst, bronchopleural fistula and lung caner[12-14]. Pulmonary tuberculosis is the most common cause of massive hemoptysis in Korea, and the pathophysiologic mechanisms of hemoptysis in pulmonary tuberculosis are rupture of the artery, which has elevation of pulmonary artery pressure by anastomosis between bronchial artery and pulmonary artery in the peribronchial inflammatory tissue, and erosion of pulmonary artery around the pulmonary cavity or rupture of the pulmonary artery by arteriovenous fistula[12-15].

Causes of hemoptysis after treatment of pulmonary tuberculosis are colonization of microorganisms in the remaining cavity, formation of malignant cancer in the scar, associated blood dyscrasia, and bronchiectasis, aspergilloma, chronic bronchitis as a sequelae of pulmonary tuberculosis[16, 17].

Fiberoptic bronchoscopy is essential for diagnostic procedure in the evaluation of bleeding site and the accuracy of bronchoscopy to localize the site of hemoptysis has been reported as 29.4% to 75%[18, 19]. However, in patients with massive or active bleeding, bronchoscopic examination should be avoided, because bronchoscopic procedure may increase the risk of hemorrhage in these patients.

Bronchial arteries arising from the thoracic aorta around 3th to 8th thoracic spine supply trachea, brounchus, vagus nerve, posterior mediastinum and eosphagus. These arteries are the first goal for arterial embolization. Rabink categorized the

angiographic signs of pulmonary bleeding as direct or indirect. Direct signs of bleeding included extravasation of contrast agent-enhanced blood (the pathognomonic sign of bleeding) and thrombosis of branches of the bronchial artery. Indirect signs of bleeding included pathologic hypervascularzation, chronic occlusion of bronchial artery branches, capillary stasis and interarterial bronchopulmonary shunts. Such signs are reliable indicators of the source of bleeding in unilateral pulmonary disease[12]. In this study, patients showed mostly hypervascularization, peribronchial diffusion of contrast agent, and a few patients showed interarterial bronchopulmonary shunt, formation of bronchial aneurysm. Extravasation of contrast agent or thrombosis of branches of the bronchial artery was not shown in our patients. Gelform is commonly using for arterial embolization due to its availability and low risk of reflux to aorta, but it was reported that bronchial infarction or necrosis with patients used ivalon or contour could occur, and peripheral vessel for effect of hemostasis need not to be occluded in the previous study[21-23]. Tomashefski reported that recurrence rate of embolization with ivalon developed in about 20%[24].

Combined method of proximal embolization with absorptive material and distal embolization with nonabsorptive material had been tried in a previous study, but Katoh reported that recurrence rate of patients with this method was about 21%, and suggested no difference between the use of ivalon or contour only and combined method.

Kang reported that 7 patients who used gelform and coil, metallic compound, achieved successful control of hemoptysis and did not recur after embolization, so he recommended this method for permanent bronchial artery embolization[3]. In this study, there was increasing tendency of recurrence of hemoptysis in embolizaiton with nonabsorptive material (ivalon or contour) and embolization with combination (ivalon or contour and gelform) method. Target arteries for embolization are mostly bronchial artery and nonbronchial systemic artery. By Keller's study, nonbronchial systemic collateral arteries contributed significantly to areas of pathologic pulmonary tissue and frequently were the major arterial supply in 45% of patients with hemoptysis[25-27]. These nonbronchial systemic collaterals included branches of subclavian and axillary arteries intercostal arteries and phrenic arteries, internal mammary arteries, and lateral thoracic arteries.

The patients with nonbronchial systemic artery hemoptysis and multiple artery hemoptysis had a more increased tendency of recurrence (77.7%) than patients with only bronchial artery bemoptysis in this study. This result showed that occlusion of nonbronchial systemic collaterals providing blood to hypervascular pulmonary lesions is essential for successful percutaneous embolotherapy of hemoptysis.

In this study, the amount of hemoptysis and previous history of hemoptysis are related to recurrence after embolization. The patients with large amount of hemoptysis (>400ml/24hours) or frequent history of hemoptysis had an increased tendecy of recurrence (87.5%, 72.7%) than small amount of hemoptysis (<200ml/24hours) or no history of hemoptysis (12.5%, 10.7%). Complications after embolization are paraplegia, severe respiratory infection, esophagobronchial fistula and ischemic colitis. To avoid these complications, the catheter should be advanced selectively into the bleeding vessel and gelform particles injected very slowly in order to prevent inadvent embolization of other organs. The presence of a major spinal artery is an absolute contraindication for an embolization procedure because of the high risk of spinal infarction[1-4, 12, 14, 16, 28, 29].

In this study, mild complication of chest pain, abdominal pain, shoulder pain and fever developed in 15 patients (29.4%), but these complications disappeared within 3 days mostly.

In a previous study, immediate control of hemoptysis after embolization was achieved in 70% to 100%[1-4, 28, 30]. In this study, immediate successful control after embolization was achieved in 48 of 51 patients (94.1%). The important causes of initial failure of embolization are the following: 1) extensive and bilateral disease, which is more common in patients who have repeated episodes of massive hemoptysis 2) technical failures include inability to catheterize or achieve a secure catheter position in the bronchial artery for safe embolization: small bronchial arteries, tortuous aorta and anomalous or aberrant origins of the bronchial

arteries are some of the other reasons 3) pulmonary artery origin of the bleeding[5].

The most important causes of recurrence are incomplete embolization, progression of underlying disease, and recanalization of the embolized vessel[1, 12].

The incidence of recurrent hemoptysis after embolization varies from 12% to 21% in English literature, otherwise, 30% to 50% in Korea[1-5, 28]. The cause of this discrepancy may be due to pulmonary tuberculosis which is the most common cause of hemoptysis in Korea. We think that the patients with pulmonary tuberculosis are susceptible to re-bleeding, because a lesion can be aggravated after embolization and rapid formation of collateral circulation.

In conclusion, transcatheter arterial embolization is a useful and safe procedure for immediate control of massive hemoptysis. However, the patients with this procedure had a potentiality of recurrence. The recurrence rate has an increasing tendency in patients with large amounts of hemoptysis frequent history of hemoptysis, and various or complexed angiographic finding.

We suggest that meticulous embolization and close follow-up will be needed in patients with factors related to recurrent hemoptysis after embolization.

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