기관지동맥 색전술 후 객혈의 재발에 관한 연구

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Risk Factors of Recurrent Hemoptysis after Bronchial Artery Embolization

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서 론 : 대량객혈은 치료가 이루어 지지 않을 경우, 50% 이상의 사망률을 보이는 호흡기 영역의 가장 위급한 응급상황의 하나이며 여러 원인에 의해 발생 될 수 있다. 1973년 레미 등에 의해 처음 보고된 이후로 기관지동맥 색전술은 대량의 재발성 객혈의 치료로 확립되어 그 효과가 입증 되었다.
그러나 기관지동맥 색전술의 재발률은 10~52%로 보고되어 객혈의 재발을 예측 할 수 있는 위험 요소들에 대한 연구가 필요하다.
재료 및 방법 : 2000년 1월부터 2005년 1월까지 세브란스병원에 100 cc 이상의 대량 객혈로 내원하여 기관지동맥 색전술을 시행 받은 66명 환자들을 대상으로 하여 기관지동맥 색전술 후 재발의 빈도와 재발과 관련이 있는 위험 요인에 대해 분석하였다.
결 과 : 5년 간 기관지동맥 색전술을 시행 받은 환자는 75명이었고, 장기간 추적관찰이 되어 결과 분석이 가능했던 환자는 66명이었다. 이들의 평균 나이는 54.9 ± 15.9세이었고, 남자가 48명, 여자가 18명이었다. 원인 질환은 결핵 20명, 기관지 확장증 및 기타 양성질환 23명, 악성 종양 7명이었고, 평균 20.4개월 간의 추적 관찰 기간 동안 23명(34.9%)에서 치료가 필요한 대량 객혈이 재발되었다. 환자의 성별과 나이, 이전에 객혈로 시술 받은 과거력, 객혈의 원인 질환, 분포 혈관의 수 등은 대량 객혈의 재발과 유의한 관계가 없었으나, 병변의 양측성, 흉막 비후, 객혈의 양은 유의한 인자로 관찰되었고, 로그 회귀분석 결과에서도 동일하였다.
결 론 : 기관지동맥 색전술을 시행한 후 객혈의 재발을 예측할 수 있는 위험 인자로 흉막 비후, 병변의 양측성, 객혈의 양이 중요하게 작용하며, 이에 대한 대규모 임상 연구가 필요하다.
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Key words : 객혈; 기관지동맥 색전술; 위험 요인

Introduction

When massive hemoptysis is untreated, it has a mortality rate of over 50 percents. It is considered as one of most dreaded of all respiratory emergencies and can have a variety of underlying causes.

Bronchial artery embolization (BAE) was first reported in 1973 by Remy1 and it has become an established procedure in the management of massive and recurrent hemoptysis. Its efficacy is widely documented thereafter by number of articles[1-11]. An immediate control of hemoptysis is achieved in 73 to 98%, with a mean follow of less than one month[1-4]. Immediate success rates have increased recently because of the introduction of superselective embolization and the refinement of embolic agents and techniques[4]. However, the long-term success rate of BAE is known to be unfavorable. Long-term recurrence rates are reported to be 10 to 52%, with a mean follow up period ranging from one to 46 months[1-7].

The variety of factors influencing that control failure has been described.

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Bronchiectatic change on high resolution CT scan (HRCT)[4], broncho-pulmonary shunt[4], pleural thickening[5,7], underlying lung diseases[6], the amount of bleeding[8], multiple feeding vessels[9], incomplete embolization[10], and previous hemoptysis history[11] are possible risk factors of recurrent bleeding events. But these findings vary from article to article and there is not yet a proven condition to predict the recurrence.

This study is designed to survey previously documented possible risk factors of recurrence in those who underwent BAE in our hospital, during a long period. Furthermore, since all patients had taken HRCT, we focused on radiological findings such as pleural thickening to be possible risk factors of the recurrence.

Materials and methods

Seventy-five patients underwent bronchial artery embolization due to massive hemoptysis more than 100 cc amount of bleeding in Severance Hospital from Jan. 2000 to Jan. 2005. Among them, nine patients' data were not available and could not be contacted with. Finally 66 (48 males, 18 females) patients' medical records were analyzed retrospectively with a mean follow up period of 20.4 months (ranging from 1 month to 56 months).

The recurrence of massive hemoptysis after BAE was defined that a gross hemoptysis more than 100 cc amount of blood occurred again which needed to undergo treatments such as BAE or lung resection surgery.

Demographic characteristics such as gender, age, the duration of symptom, the amount of hemoptysis, previous history of treatment for hemoptysis, the main medical condition causing hemoptysis, bilaterality of pulmonary lesion, the number of feeding vessels, and the presence of pleural thickening were our parameters analyzed.

For comparison of various risk factors between recurrent massive hemoptysis group and controlled hemoptysis group, Pearson's Chi-square test (for $n > 5$) and Fisher's exact test (for $n \leq 5$) were used. For continuous variables, Student's T-test was used. Statistical validity is defined if p-value is less

Table 1. Literature reviews of bronchial artery embolization outcomes

Author	No. of patients	Follow up (months)	Recurrence rate (%)	Risk factor for recurrence	Other variables
Osaki S[4]	22	46	50	Bronchiectatic change on CT scan, Pulmonary-bronchial artery shunt	Age, sex, underlying disease, morhphologic change, amount of hemoptysis, angiographic finding
Yeo DS[5]	146	6	63	Pleural lesion on chest X-ray	Embolic material, underlying disease, feeding vessel, shunt, bilaterality
Kim SO[6]	75	60	54.5	Underlying disease, amount of bleeding, extent of lung lesion	NR† ,
Tamura S[8]	40	20	60	Pleural thickening on chest X-ray	NR† ,
Kim BC[14]	47	72	40	None*	Age, sex, bilaterality, shunt, feeding artery, neovascularity, underlying disease,
Ko DS[15]	46	12	41.3	Multiple feeding vessel Incomplete embolization Previous history of hemoptysis	Hypervascularity, underlying disease, age, sex

* No statistically valid risk factor among candidate variables.
† NR = not reported

than 0.05.

To verify the compounding factors between the risk factors whose characters were diverse confounding variables, we did multivariate analysis using logistic regression analysis with 95% confidence interval.

Results

Among 66 patients whose data were available, 23 (34.9%) patients had recurred massive hemoptysis during a mean follow up period of 20.4 months (ranging from 1 month to 54 months). Eight out of 23 recurred patients had pneumonectomy or lobectomy of lung (3 pneumonectomies and 5 lobectomies) in following event, and remaining 12 patients had to undergo another BAE. Four patients died due to uncontrolled hemoptysis (one died after pneumonectomy).

Concerning the factors influencing relapse, age and sex did not play any role and duration of symptom had not any significance, but the amount of hemoptysis had a statistical significance (p =0.008 by T-test; Table 2).

As to the underlying diseases, we had 20 active tuberculosis, 19 benign diseases including 19 bron-

Table 2. Demographic features, duration, amount of hemoptysis and previous intervention history

		Relapsed group	Controlled group	p-value
Gender	Male	17	31	-
	Female	6	12	NS
	Total	23	43	-
Age (yrs)		56.5 ± 16.2	54.3 ± 16.2	NS
Duration of symptom (day)		6.3 ± 12.7	8.7 ± 19.5	NS
Amount of hemoptysis (cc)		217 ± 98	153 ± 94	0.008
Previous intervention				
Yes (n=9)		5 (55%)	4(45%)	
No (n=57)		18 (32%)	39(68%)	NS

NS = not significant

Table 3. Underlying diseases and previous history of bronchial artery embolzation intervention

	Relapsed group (n=23)	Controlled group (n=43)	p-value
Active tuberculosis	5(25%)	15(75%)	
Malignancies			
Primary lung cancer	2(50%)	2(50%)	
Metastais to the lung	2(67%)	1(33%)	NS
Other benign diseases			
Bronchiectasis	5(26%)	14(74%)	
Aspergilloma	8(57%)	6(43%)	
Others	1(17%)	5(83%)	

* Other diseases include 1 bronchial artery aneurysm, 2 lung abscesses, and 2 bronchitis
NS = not significant

Table 4. Radiologic findings and the recurred massive hemoptysis

		Relapsed group (n = 23)	Controlled group (n = 43)	p-value
Bilaterality of lesion				
	Yes	8(62%)	5	0.008
	No	15(28%)	38	
Pleural thickening				
	Present	12(75%)	4	0.001
	Absent	11(22%)	39	
Number of feeders				
	1	10(30%)	23(70%)	NS
	〉 1	13(39%)	23(61%)	

NS = not significant

Table 5. Multivariate analysis of different variables

Variables		Odds ratio	95% C.I	p-value
Gender	Male Female	1 0.59	0.53-4.37	NS
Age	〈50 ≥50	1 0.42	0.34-2.42	NS
Previous intervention	Yes No	1 0.51	0.28-2.76	NS
Underlying disease	Active tuberculosis	1		
	Malignancy	1.76	0.77-11.84	NS
	Other benign disease	0.62	0.80-4.86	NS
Duration of symptom	≤ 7days 〉7 days	1 1.14	0.16-1.73	NS
Amount of hemoptysis	≤ 200 cc 〉200 cc	1 10.21	10.08-50.23	0.008
Bilaterality of lesion	No Yes	1 13.93	1.41-138.32	0.018
Number of feeding vessel	1 〉1	1 2.20	0.36-13.39	NS
Pleural thickening	No Yes	1 20.84	3.38-128.45	0.001

NS = not significant

chiectasis, 14 aspergillomas, and 6 others (including 1 bronchial artery aneurysm, 2 lung abscesses, and 2 bronchitis), and 7 malignancies (4 primary lung cancer and 3 metastatic malignancies), we did not find any statistical significance between them (Table 3). Nine patients had a history of previous BAE treatments for hemoptysis, but they showed no increased risk of relapse of major hemoptysis (Table 3). Bilateral lesion on radiographic finding and pleural thickening on HRCT had increased risk of recurred major hemoptysis (p = 0.018 and 0.001, respectively, by Chi-square test and Fisher's exact

test; Table 4). Number of feeding vessels had not any statistical value concerning the relapse.

Univariate analysis showed that reliable risk factors for recurrent hemoptysis after BAE were amount of hemoptysis, bilaterality of lesion, and pleural thickening on HRCT. To verify the compounding factors between the risk factors whose characters were diverse confounding variables, we did multivariate analysis using logistic regression analysis with 95% confidence interval. Multivariate analysis showed same results as univariate analysis (Table 5).

Discussion

We analyzed the result of BAE in our institution during a long period. In previous literatures, long-term recurrence rate have been reported to be 10 to 52%, with a mean follow up period ranging from one to 46 months[1-11].

Remy et al.[1] reported that of 49 patients treated for hemoptysis, an immediate arrest was achieved in 41, but 34 patients had experienced re-bleeding in follow up period beyond the 18 months. Ulfacker et al.[3] reported that an immediate control of hemoptysis was achieved in 33 out of 41 patients (80.5%) while hemoptysis recurred in 9 of 33 patients (27.3 %) in the long-term follow up (mean 24.8 months). In our analysis, BAE effectively controlled 65.1% of life threatening massive hemoptysis (23 re-bleedings in 66 cases) in a mean follow up period of 20.4 months.

Regarding the factor of recurrence after BAE, Osaki et al.[4] concluded that bronchiectatic change on CT scan and pulmonary-bronchial shunt had some statistical significance. Kim et al.[6] described the underlying lung disease and amount of bleeding as reliable risk factors for the recurrence, in a study involving 75 patients with a result estimating 54.5 % of re-bleeding rate after 3 years. But in the study of Kim et al[14] published 5 years earlier, those factors had no significant impact on the recurrence of hemoptysis. The former used Caplan-Mayer survival analysis with each variable and the latter used Chi-square univariate analysis. The diversity of previously proposed risk factors may be explained by variability of their criteria on recurrence, sample size, underlying diseases, follow-up time, and statistic tool used.

In this study, the amount of hemoptysis had some statistical relation with the recurrent event. Though the analysis of underlying disease had no statistical significance, active tuberculosis tended to have more control rate compared to aspergilloma and cancer. The effective anti-tuberculosis drug therapy must have reduced the recurrent hemoptysis but its relatively modest prevalence in our series (30% compared to 43-52% in other domestic studies)[5,6,12,14] lead to overall no statistical significance.

The fact that bilaterlity of lesion on initial chest X-ray was higher in relapse group can be explained by the extent of the lung disease accounts for more serious pathology as it was commented by Kim et al.[6]

In 1993, Tamura et al.[8] described pleural thickening as a risk factor for recurrent bleeding after BAE. According to them, in the presence of pleural thickening, non-bronchial systemic feeder vessels that originate from various arteries (e.g., intercostals artery, branches of the subclavian and axillary arteries, internal mammary artery and inferior phrenic artery) may develop along the pleural surface and become enlarged as a result of the inflammatory process. In our study 16 cases showed pleural thickening on chest radiography and 12 (75%) of them experienced recurrent massive bleeding, which was significantly higher than 22% of no pleural thickening group.

This study is a retrospective review of medical records, which often should underestimate strength of variable. But the presence of pleural thickening which had the highest odds ratio can be a reliable risk factor for the recurrence of hemoptysis after BAE, and this should be verified in a prospective study with larger number of patients because this study has the limitation caused by small size population involved with various underlying diseases.

Summary

Background :

Hemoptysis, when massive and untreated, has a mortality rate of over 50 percents, is considered as one of most dreaded of all respiratory emergencies and can have a variety of underlying causes.

Bronchial artery embolization (BAE) has become an established procedure in the management of massive and recurrent hemoptysis, and its efficacy is widely documented thereafter by number of articles.

However, the long-term success rate of BAE is known to be unfavorable. Risk factors influencing that control failure are inevitably needed.

Materials and methods :

Seventy-five patients underwent bronchial artery embolization due to massive hemoptysis in Severance Hospital from Jan. 2000 to Jan. 2005. Nine patients' data were not available and could not be contacted with. Finally 66 patients' (48 males, 18 females) medical records were analyzed retrospectively during a mean follow up period of 20.4 months (ranging from 1 month to 54 months).

Results :

Among 66 patients whose data were available, 23 (34.9%) patients had recurrent major hemoptysis. Patients' age, sex, underlying disease, previous intervention history, and number of feeding vessels had no statistical validity as risk factors of recurred major hemoptysis. But bilaterality of lesion, amount of hemoptysis, and pleural thickening were revealed as meaningful factors for predicting relapse (p = 0.008, 0.018, and 0.001, respectively).

Conclusion :

According to our series, patients presenting with larger amount of hemoptysis, pleural thickening of chest radiography and bilateral lesion are associated with increased risk of major hemoptysis in patients treated with BAE.

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