Cardiovasc Intervent Radiol (2007) 30:638–643
DOI 10.1007/s00270-007-9034-5

CLINICAL INVESTIGATION

Bronchial Artery and Systemic Artery Embolization in the Management of Primary Lung Cancer Patients with Hemoptysis

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Published online: 28 April 2007

Abstract
Purpose To assess the safety and effectiveness of arterial embolization in lung cancer patients with hemoptysis.
Methods Nineteen primary lung cancer patients with hemoptysis underwent bronchial artery and systemic artery embolization from April 2002 to March 2005. There were 17 men and 2 women, with a mean age of 59 years. Histologic analysis revealed squamous cell carcinoma in 10 patients and poorly differentiated adenocarcinoma in 9 patients. The amount of hemoptysis was bleeding of 25–50 ml within 24 hr in 8 patients, recurrent blood-tinged sputum in 6, and bleeding of 100 ml or more per 24 hr in 5. Embolization was done with a superselective technique using a microcatheter and polyvinyl alcohol particles to occlude the affected vessels.
Results Arterial embolization was technically successful in all patients and clinically successful in 15 patients (79%). The average number of arteries embolized was 1.2. Bronchial arteriography revealed staining (all patients), dilatation of the artery or hypervascularity (10 patients), and bronchopulmonary shunt (6 patients). The recurrence rate was 33% (5/15) and 11 patients were alive with a mean follow-up time of 148 days (30–349 days).
Conclusion Arterial embolotherapy for hemoptysis in patients with primary lung cancer is an effective, safe therapeutic modality despite the fact the vascular changes are subtle on angiography.

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Keywords Bronchial arteries · Hemoptysis · Interventional radiology · Lung · Lung neoplasm · Therapeutic embolization

Introduction

Bronchial artery embolization has been widely demonstrated to be an important treatment option for the management of massive and recurrent hemoptysis [1–8]. Most reports describe hemoptysis caused by conditions other than primary lung cancer, such as tuberculosis, aspergillosis, cystic fibrosis, and bronchiectasis. Lung cancer is the leading cause of cancer death in the United States [9]: 172,570 new cases of lung cancer and 163,510 deaths from lung cancer were expected in 2005 [10]. About 10–30% of patients with lung cancer develop hemoptysis during the course of their disease and 10% of these patients have massive hemoptysis [11, 12]. Accordingly, theoretically thousands of patients who present with hemoptysis might prove candidates for bronchial arterial embolization in the United States alone every year. The purpose of this study was to report our experience with arterial embolization in a consecutive group of lung cancer patients with hemoptysis and to retrospectively evaluate the effectiveness and safety of the technique.

Materials and Methods

Included in this analysis are 19 consecutive patients with a histologically confirmed diagnosis of primary lung cancer who underwent arterial embolization in our institution between April 2002 and March 2005 (Table 1). There were 17 men and 2 women, with a mean age of 59 years (range

Table 1 Clinical data and outcome of lung cancer patients with hemoptysis treated with bronchial artery embolization

Patient no./Age (years)/Sex	Hemoptysis volume	Clinical outcome	Time to cessation of hemoptysis (days)	Time to recurrence (days)	Follow-up
1/67/F	Recurrent blood-tinged sputum	Failure			Died at 10 days
2/41/F	Recurrent blood-tinged sputum	Failure			Died at 5 days
3/60/M	Recurrent blood-tinged sputum	Complete success	0		Died at 55 days
4/59/M	Recurrent blood-tinged sputum	Partial success		15	Follow-up at 150 days
5/49/M	Recurrent blood-tinged sputum	Complete success	5		Follow-up at 51 days
6/55/M	Recurrent blood-tinged sputum	Complete success	3		Follow-up at 80 days
7/70/M	25 cm^3	Complete success	2		Follow-up at 77 days
8/48/M	30 cm^3	Complete success	4		Follow-up at 30 days
9/69/M	30 cm^3	Complete success	1		Follow-up at 205 days
10/63/M	30 cm^3	Failure		23	Died at 30 days
11/61/M	30 cm^3	Complete success	1		Follow-up at 91 days
12/67/M	50 cm^3	Complete success	4	60	Died at 62 days
13/66/M	50 cm^3	Partial success		5	Follow-up at 349 days
14/63/M	50 cm^3	Complete success	2		Follow-up at 275 days
15/48/M	100 cm^3	Partial success		14	Follow-up at 261 days
16/66/M	100 cm^3	Complete success	3		Follow-up at 59 days
17/51/M	140 cm^3	Complete success	10		Follow-up at 49 days
18/50/M	Massive	Failure			Died at 2 days
19/74/M	Massive	Complete success	2		Died at 200 days

41–74 years). The interval between biopsy and hemoptysis was more than 1 month in all cases (range 44–300 days). Ten patients had squamous cell carcinoma (moderately differentiated in 5, poorly differentiated in3, and well-differentiated in 2) and 9 patients had adenocarcinoma (all poorly differentiated). There was hemoptysis in all, dyspnea in 16 patients (84%), and massive, intractable hemothorax in 3 patients (16%). The amount of hemoptysis was variable: bleeding of 25–50 ml within 24 hr in 8 patients, recurrent blood-tinged sputum in 6, and bleeding of 100 ml or more per 24 hr in 5. Six patients had been intubated and manually ventilated during the procedure. Twelve patients had multiple bleeding episodes. In 3 patients with both hemoptysis and hemothorax, arterial embolization was attempted to treat hemothorax also.

Eight patients had undergone radiation therapy (total dose 4000–8000 cGy, 20–35 fractions for 25–55 days) 6–12 months prior to the development of hemoptysis.

Bronchoscopy was performed in 5 patients on the day of arterial embolization but failed to depict the lesion in 1 of them.

A chest CT scan was performed in 16 patients 0–12 days (mean 3.5 days) prior to embolization. The possible bleeding focus and the origin of the bronchial artery or other bleeding vessel from the aorta was evaluated on this scan to determine the optimal approach during arterial embolization. A chest radiologist and two interventional radiologists interpreted the CT scans together.

All patients underwent bronchial, intercostal, and subclavian selective arteriography using a digital subtraction technique with a digital subtraction angiography unit (Integris V5000; Philips Medical Systems, Best, The Netherlands). A total of 6–9 ml of nonionic contrast material (Visipaque 270; Nycomed, Cork, Ireland) was injected at a rate of 2–3 ml/sec for selective arteriography with a 5 Fr catheter and a total of 3–4 ml at a rate of 1 ml/sec for superselective arteriography with a 2.8 or 3 Fr microcatheter. In 13 patients, a thoracic aortogram was performed before (n = 12) or during (n = 1) the embolization with injection of 30–50 ml of contrast material at a rate of 15–20 ml/sec for the detection of a missed vessel at selective arteriography.

Arterial embolization was done as follows. A 5 Fr catheter was inserted to the level of the origin or proximal segment of medium-sized vessels such as the bronchial, intercostal, internal thoracic or lateral thoracic arteries. We used a 2.8 or 3 Fr microcatheter in all cases to catheterize superselectively, through which embolization was performed with 355–500 μm polyvinyl alcohol particles (Ivalon, Nycomed Laboratories, Paris, France or Contour, Boston Scientific, Cork, Ireland). The end-point of infusion was stasis of contrast material in the feeding arteries.

Written informed consent was obtained from all patients before embolization. Since this study was retrospective, institutional review board approval was not required, in accordance with institutional review board policy.

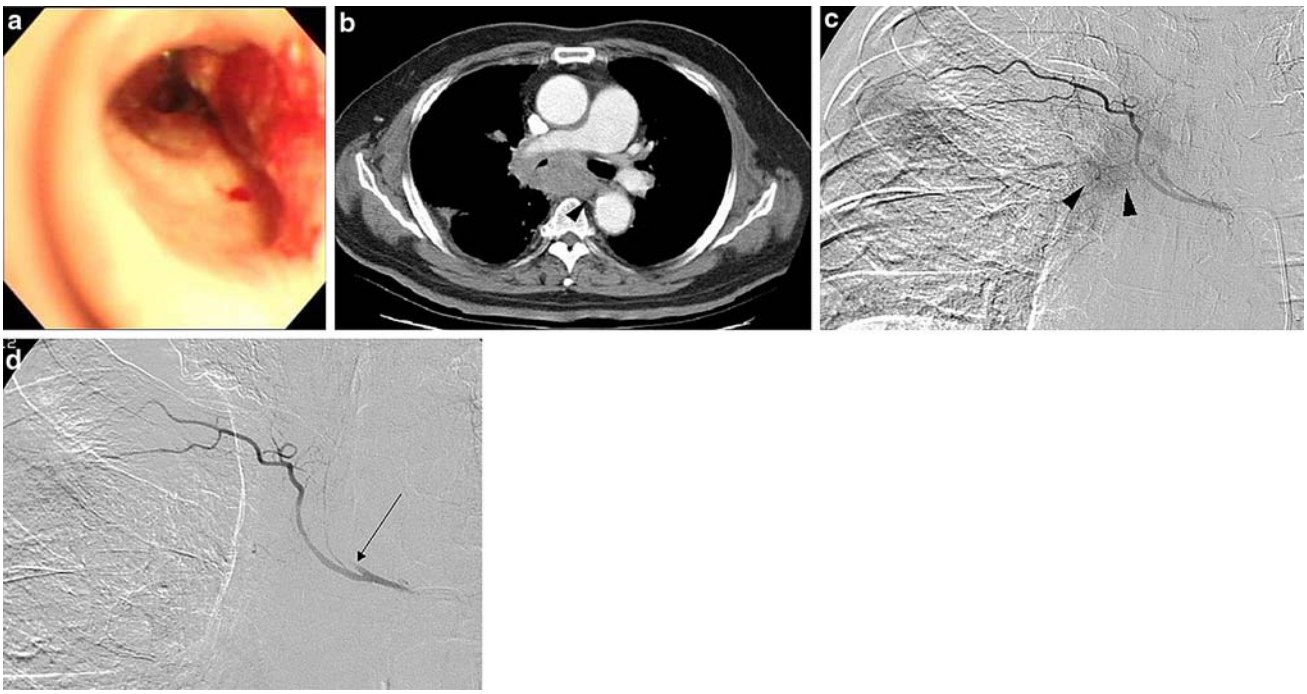

Fig. 1A–D Images obtained in a 61-year-old man with well-differentiated squamous cell carcinoma who had suffered hemoptysis 1 day previously. **A** Bronchoscopy on that day reveals bleeding from the tumor in right upper lobe bronchus. **B** CT scan obtained just before arterial embolization shows tumor surrounding the right bronchus and right intercostobronchial artery (arrowhead). **C** There is faint staining (arrowheads) in superselective right intercostobronchial arteriography with a microcatheter. We embolized this vessel with small amount of polyvinyl alcohol particles. **D** Completion angiogram shows complete occlusion of the right bronchial artery (arrow). Hemoptysis stopped 1 day later

Technical success was defined as an immediate result evaluated with completion angiography. Clinical success was assessed by close follow-up of patients for 30 days immediately following arterial embolization; complete clinical success was defined as the resolution of hemoptysis and partial clinical success as a significant decrease in hemoptysis after embolization with a positive impact on the clinical course of the patient [13].

Results

Technical success was achieved in all patients (Fig. 1). Clinical success was achieved in 15 patients (79%): complete in 12 (63%) and partial in 3 (16%). The mean interval between embolization and cessation of the symptoms was 3.1 days (range 0–10 days) in 12 patients with complete clinical success.

Eight patients died (3 of disease progression and superimposed pneumonia, 3 of hemothorax, 1 of rebleeding, and 1 of unknown cause) 2–200 days (mean 52 days) after embolization. There was no improvement after embolization in the hemothorax of 3 patients with both hemoptysis and hemothorax, and they died 2, 5, and 10 days after embolization. Eleven patients were alive after a mean follow-up of 148 days (range 30–349 days).

A small amount of hemoptysis recurred within 1 month in 4 patients, 5–23 days (mean 14 days) after embolization, which disappeared with conservative management. In 1 patient recurrent hemoptysis developed 2 months after embolization and he died 2 days later. The overall recurrence rate was 33% (5/15).

Pre-embolization chest CT scans showed bronchial artery dilatation in 8 of 16 patients evaluated and intercostal artery dilatation in 1 patient. These findings were confirmed at angiography and these vessels were embolized. Based on the findings of chest CT and angiography, the tumor itself was thought to be directly related to bleeding in 12 patients and radiation fibrosis and the resultant bronchiectasis in 4 patients (Fig. 2) who had radiation therapy (total dose of 5000–6300 cGy, 20–35 fractions for 25–55 days) 7–12 months prior to the development of hemoptysis.

On bronchial arteriography, abnormal staining was seen in all cases, and dilatation of the artery or hypervascularity in 10 patients and bronchopulmonary shunt in 6 patients. In 3 patients, dilatation of the bronchial artery was equivocal. On thoracic aortography of 13 patients, potential feeding vessels were delineated in 10 and abnormal stain was suspected in 5.

The number of vessels embolized was one in 17 patients, two in 1 patient, and three in 1 patient. The

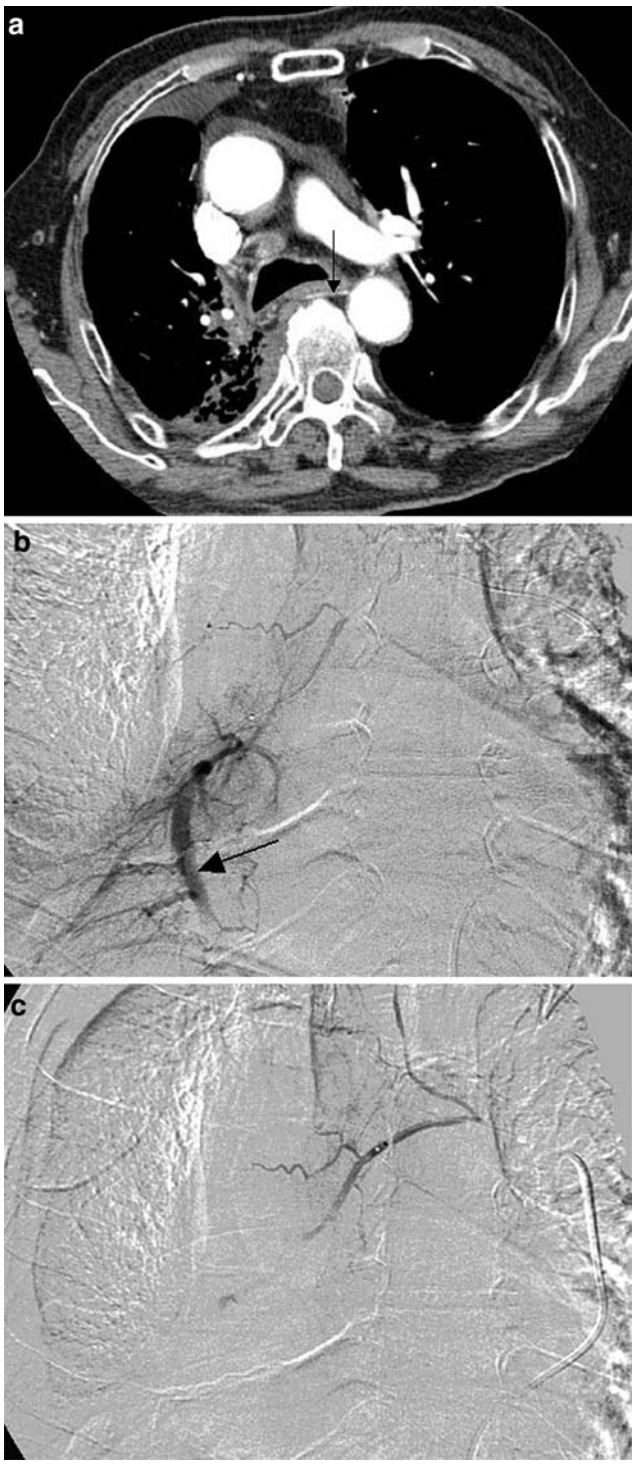

Fig. 2A–C Images obtained in a 66-year-old man with moderately differentiated squamous cell carcinoma who had undergone radiation therapy 8 months previously. **A** CT scan obtained just before arterial embolization shows radiation fibrosis and bronchiectatic change. Note the right bronchial artery arising from the aorta (arrow). **B** In the delayed phase of superselective bronchial arteriography, there is faint staining and bronchopulmonary shunt (arrow). **C** Completion angiogram shows occlusion of the bronchial artery. Hemoptysis stopped 3 days later

embolized arteries were as follows: right intercostobronchial trunk ($n = 7$), intercostal artery ($n = 6$), right bronchial artery ($n = 5$), left bronchial artery ($n = 3$), and lateral thoracic artery ($n = 1$). The stasis of blood flow in feeding vessels was easily achieved with a relatively small amount of polyvinyl alcohol particles in all patients except 1, in whom embolization with additional gelatin sponge (Gelfoam, Upjohn, Kalamazoo, MI, USA) was needed. There was no major complication requiring further management and only 2 minor complications occurred: 1 transient chest pain and 1 puncture site hematoma.

Discussion

In our series, clinical success was achieved in 79% of patients, which is lower than the 85% achieved in various diseases [7] or the 95% and 84% in cystic fibrosis [14, 15]. The incidence rate of vascular abnormalities such as dilatation of the artery and bronchopulmonary shunt was much lower (53%, 32% each) than the 100% in benign disease [16] and the 78% in various diseases [17]. The artery to be embolized is usually small and the flow is slow, so great care should be taken in superselective catheterization and the injection rate must be reduced cautiously to that necessary for embolic agent delivery.

We usually use one or more bottles of polyvinyl alcohol particles for the treatment of hemoptysis in tuberculosis, but a much smaller amount was used for lung cancer patients. We wondered whether this kind of embolization (in a relatively hypovascular lesion with only faint staining) would be as effective as in a hypervascular lesion. Given this limitation, the success rate of 79% is very encouraging.

The cause of hemoptysis in lung cancer is generally local necrosis and inflammation of blood vessels within the tumor bed rather than direct tumor invasion of blood vessels [11]. That is not very different from the mechanism in an inflammatory lesion, such as tuberculosis or abscess. The extent and severity of these changes is much less in lung cancer; therefore the angiographic changes and symptoms are not so severe. Most patients in our study had trivial hemoptysis. According to the report by Hirschberg et al. [18], lung cancer patients with hemoptysis were associated with mild to moderate bleeding in 90%, but had a higher mortality rate (8/39, 21%) than that of benign disease (8/161, 5%). The indication for embolization has been expanding and even mild hemoptysis is considered [19]. In our series, 16 patients (84%) had dyspnea which had aggravated or developed after hemoptysis and we thought that embolization was needed.

Arterial embolization was ineffective in the treatment of massive, recurrent hemothorax in our study. A possible

reason for this is that hemothorax in these patients was caused by an accumulation of minor bleeding from multiple collaterals that could not be visualized or embolized.

The recurrence rate of 33% in our study is not high, and is comparable with the 14–42% recurrence rate reported in the literature [2, 3, 4, 7, 20]. Recurrence rate is influenced by the underlying disease [6], and this applies also to patients with lung cancer. There may be a reciprocal relationship between the stage or extent of disease, the survival time, and the risk of rebleeding.

The staining on angiography is an important sign of hemoptysis. Without this finding, in 9 patients bronchial arteriography would have been negative and there would have been no attempt to treat the lesion. Therefore, careful evaluation of staining, however faint, is very important in the detection of the bleeding focus.

According to the report by Revel et al. [21], CT is more efficient than bronchoscopy in identifying the cause of hemoptysis and the two methods have a similar rate in localizing the site of bleeding. Performing both CT and bronchoscopy takes too much time and most treatment was conducted on emergency basis. The interventional radiologist and referring physician agreed that bronchoscopy was not necessary. We performed bronchoscopy in the first 5 patients in our series, but not subsequently. We were able to localize the site of bleeding with CT and angiography in all those cases.

Hemoptysis tends to disappear gradually over several days, not promptly. Thus, other treatment options ought to be delayed to allow for the effect of arterial embolization to appear, as long as the condition of the patient permits.

All the patients in our study developed hemoptysis more than 1 month after biopsy; therefore, there is no relation between biopsy and hemoptysis.

Thoracic aortography was not performed in all cases, because we thought there may be a limitation in detecting subtle abnormalities in lung cancer. We first tried to catheterize the bronchial and intercostal artery, supplying the suspected area with a 5 Fr catheter on the basis of anatomic landmarks. In cases where these arteries could not be catheterized, we performed thoracic aortography only to provide a road map of these arteries, not to detect the bleeding focus.

The average number of arteries embolized was 1.2, which was much fewer than the 2.5–2.6 in various diseases from other reports [7, 22]. This can be explained by the relative subtlety of the vascular abnormality in lung cancer.

There was no major complication in our series. Complications are uncommon in arterial embolization, but have been reported; the most serious one is spinal cord injury [6, 23]. The artery of Adamkiewicz and the anterior spinal artery were not visualized on angiography in our patients. When there was an arterial branch running toward the vertebral body, we catheterized more distally beyond that branch and embolized carefully, watching for the reflux of the embolic material.

The limitations of this study are the small number of patients studied, its retrospective nature, and the lack of a control. Further study of a large number of patients in a prospective manner may be needed to confirm our findings.

In conclusion, bronchial artery and systemic artery embolization is an effective and safe technique in the treatment of hemoptysis in lung cancer patients, as it is in other, benign diseases. The recurrence rate is similar to the rate in other studies. The vascular changes are subtle and the number of vessels involved and the formation of collateral vessels is less than in other diseases.

Acknowledgments The authors thank Siunna Baek for her editorial assistance.

Reference

1. Uflacker R, Kaemmerer A, Picon PD, et al. (1985) Bronchial artery embolization in the management of hemoptysis: Technical aspects and long-term results. Radiology 157:637–644
2. Rabkin JE, Astafjev VI, Gothman LN, et al. (1987) Transcatheter embolization in the management of pulmonary hemorrhage. Radiology 163:361–365
3. Knott-Craig CJ, Oostuizen JG, Rossouw G, et al. (1993) Management and prognosis of massive hemoptysis. J Thorac Cardiovasc Surg 105:394–397
4. Ramakantan R, Bandekar VG, Gandhi MS, et al. (1996) Massive hemoptysis due to pulmonary tuberculosis: Control with bronchial artery embolization. Radiology 200:691–694
5. Fernando HC, Stein M, Benfield JR, et al. (1998) Role of bronchial artery embolization in the management of hemoptysis. Arch Surg 133:862–866
6. Mal H, Rullon I, Mellot F, et al. (1999) Immediate and long-term results of bronchial artery embolization for life-threatening hemoptysis. Chest 115:996–1001
7. Swanson KL, Johnson M, Prakash UB, et al. (2002) Bronchial artery embolization: Experience with 54 patients. Chest 121:789–795
8. Goh PY, Lin M, Teo N, et al. (2002) Embolization for hemoptysis: A six-year review. Cardiovasc Intervent Radiol 25:17–25
9. Alberg AJ, Samet JM (2003) Epidemiology of lung cancer. Chest 123:21S–49S
10. Jemal A, Murray T, Ward E, et al. (2005) Cancer statistics, 2005. Cancer J Clin 55:10–30
11. Winter SM, Ingbar DH (1988) Massive hemoptysis: Pathogenesis and management. J Intens Care Med 3:171–188
12. Lung Cancer Symptoms. Available at http://www.lungcancerinfo.net/content/symptoms. Accessed August 24, 2005
13. Drooz AT, Lewis CA, Timothy EA, et al. (2003) Quality improvement guidelines for percutaneous transcatheter embolization. J Vasc Interv Radiol 14:S237–S242
14. Cohen AM, Doershuk CF, Stern RC (1990) Bronchial artery embolization to control hemoptysis in cystic fibrosis. Radiology 175:401–405
15. Sweezey NB, Fellows KE (1990) Bronchial artery embolization for severe hemoptysis in cystic fibrosis. Chest 97:1322–1326

16. Katoh O, Yamada H, Hiura K, et al. (1987) Bronchoscopic and angiographic comparison of bronchial arterial lesions in patients with hemoptysis. Chest 91:486–489
17. Hsiao EI, Kirsch CM, Kagawa FT, et al. (2001) Utility of fiberoptic bronchoscopy before bronchial artery embolization for massive hemoptysis. AJR Am J Roentgenol 177:861–867
18. Hirshberg B, Biran I, Glazer M, et al. (1997) Hemoptysis: Etiology, evaluation, and outcome in a tertiary referral hospital. Chest 112:440–444
19. Mauro MA, Burke CT, Jaques PF (2006) Transcatheter bronchial artery embolization for inflammation (hemoptysis). In: Baum S, Pentecoast MJ (eds) Abram's angiography: Interventional radiology. Philadelphia: Lippincott Williams & Wilkins, pp 909–919
20. Marshall TJ, Jackson JE (1997) Vascular intervention in the thorax: Bronchial artery embolization for haemoptysis. Eur Radiol 7:1221–1227
21. Revel MP, Fournier LS, Hennebicque AS, et al. (2002) Can CT replace bronchoscopy in the detection of the site and cause of bleeding in patients with large or massive hemoptysis? AJR Am J Roentgenol 179:1217–1224
22. Wong ML, Szkup P, Hopley MJ (2002) Percutaneous embolotherapy for life-threatening hemoptysis. Chest 121:95–102
23. Saluja S, Henderson KJ, White RI (2000) Embolotherapy in the bronchial and pulmonary circulation. Radiol Clin North Am 38:425–448