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Value of bronchial artery embolisation with platinum coils in tumorous pulmonary bleeding

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Abstract

We performed bronchial artery embolisations (BAE) using platinum coils with Dacron^{TM} fibres in 30 consecutive patients with haemoptysis due to bronchial carcinoma. The aim of the study was to compare immediate results of bleeding cessation, recurrence and survival rates with a historical control group of 15 patients with tumorous pulmonary bleeding who were treated conservatively (non-BAE-group). Bronchial artery embolisation with platinum coils stopped active bleeding in all patients immediately. Comparing the BAE group and controls the cessation of first time haemoptysis (BAE 100% versus non-BAE 93%) and the rates of bleeding recurrence (BAE 50% versus non-BAE 47%) were similar in either group. In case of recurrent bleeding, repeated BAE led to a definite cessation of pulmonary haemorrhage in every case. In contrast, all patients with recurrent haemoptysis without a repeated BAE (8 patients, 27%) and all patients with bleeding recurrence in the non-BAE group died from pulmonary haemorrhage (8 patients, 53%). The mean survival time of the BAE group was significantly longer compared with the non-BAE group, 139 (range: 1–818) days versus 62 (range: 1–186) days ($P < 0.05$). We conclude that consistent BAE proved beneficial in tumorous pulmonary bleeding, particularly with regard to the permanent arrest of haemorrhage in case of recurrence.

Keywords: Platinum coils; Bronchial artery embolisations; Tumorous bleeding

1. Introduction

Severe pulmonary haemorrhage is an emergency which demands instant and effective treatment. A pulmonary bleeding with more than 600 ml of blood loss in 24 h is associated with a high mortality rate of more than 50%, but even moderate haemoptysis with up to 200 ml of blood loss and daily recurrence increases the risk of a fatal haemorrhage enormously [1–4]. Recently, the underlying causes of haemoptysis have shifted. Due to the decrease of tuberculosis, bronchitis and lung cancer have now become the most frequent causes of pulmonary haemorrhage [5–7]. Today, cancer is the cause of haemoptysis in approximately every third case [8]. The increasing incidence of bronchial cancer and, in turn, the growing prevalence of complications such as pulmonary bleeding required new therapeutic approaches such as bronchial artery embolisation (BAE).

Sources of pulmonary bleedings are normally bronchial or intercostal arteries with numerous anatomical varieties. The most common forms of aberrant origin are subclavian, internal thoracic, pericardiacophrenic, inferior phrenic, and thyreocervical arteries or branches of the abdominal aorta [9–11]. These anatomical features may complicate the catheter positioning in bronchial arteries.

In 1974, Remy and colleagues [12] published the first attempt of BAE using gelatin sponges for the treatment of pulmonary bleeding. The preliminary results were promising and were confirmed by others [11,13–15]. In 1992, Hayakawa and colleagues [16] reported a study of 12 patients with haemoptysis caused by lung cancer who were treated with BAE using, similar to Remy, gelatin sponge as the embolisation material. In patients

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with primary bronchogenic cancer and pulmonary metastases, the tumour feeding bronchial arteries are extended and enlarged and the small vessels within the tumour are irregular and tortuous to a variable degree [17]. The effects of embolisation were achieved by mechanical occlusion of the arteries, platelet aggregation and activation of the clotting system [18]. Complications are spinal cord injury or coil migration [19,20].

The aim of the study was to investigate the prospective outcome of patients with tumorous pulmonary bleeding who underwent BAE. Furthermore, we have retrospectively compared the results of bleeding cessation, rates of recurrence and the mean survival time with a historical group of patients with haemoptysis who were treated conventionally, without BAE.

2. Patients and methods

2.1. Patients

30 consecutive patients (26 male, 4 female; mean age 66±7 years) with moderate pulmonary haemorrhage ($\geqslant 20 \leqslant 200$ ml/day) caused by lung cancer underwent a prospective study of catheter BAE between 1992 and 1996. All patients suffered from advanced and inoperable tumours. The tumours were classified according to the TNM stage as follows, TNM IIIA ($n=12$), IIIB ($n=10$) and IV ($n=8$) [21]. The histology of these tumours was classified as squamous cell carcinoma ($n=21$), adenocarcinoma ($n=6$), small cell lung carcinoma ($n=1$) and metastasis of extrathoracic tumours ($n=2$).

For comparison, we investigated retrospectively a group of 15 patients with lung cancer (12 male, 3 female mean age 62±8 years) and moderate haemoptysis ($\geqslant 20 \leqslant 200$ ml/day) who were treated conventionally at teaching hospitals of the Charité between 1990 and 1994 (historical non-BAE group). At these teaching hospitals BAE was not available. According to the TNM stage patients were classified as follows, TNM IIIA ($n=1$), IIIB ($n=3$) and IV ($n=11$). The tumours were characterised as squamous cell carcinoma ($n=10$), adenocarcinoma ($n=4$), and metastasis of oesophageal carcinoma ($n=1$).

All cases in the BAE group and in the historical non-BAE group were extensively discussed with experienced thoracic surgeons prior to any further treatment, especially prior to bronchial artery embolisation. All patients were rejected from surgery, most of them due to advanced tumour stage, elevated operational risk or in patients with stage IIIA tumour due to severe comorbidity. Tumour-specific therapies (radiotherapy/chemotherapy) were performed according to the usual protocols in the same way in all patients.

2.2. Methods

For evaluation of the tumour, chest radiographs and computed tomography (CT) scans were performed in all cases. Furthermore, every patient was examined by fibreoptic bronchoscopy (BF 30 D, OLYMPUS Europe) to determine the localisation and activity of bleeding. All patients gave their written informed consent and were premedicated according to our standard protocol (diazapam 10 mg intravenously (i.v.), atropine 0.5 mg i.v., 6 ml prilocain 2% for local anaesthesia).

BAE was performed using the Seldinger technique (Target Therapeutics®) via the femoral approach. In order to detect the tumour feeding vessels, a selective angiography of bronchial and intercostal arteries due to the endoscopic localisation of bleeding was performed. Within the BAE group, we performed selective angiograms of bronchial and intercostal arteries. Injections of contrast medium revealed the localisation, number and enlargement of tumour feeding vessels. Extravasation of contrast medium, hypertrophy of the feeding artery and hypervascularity of the involved area were direct and indirect signs of haemorrhage. We applied 1 to 6 platinum coils containing Dacron™ fibres (Fig. 1) depending on the vessel diameter (2×10 mm to 7×70 mm) and blood flow (Fig. 2).

To reinforce the results of embolisation, a microsuspension (aethoxysclerol and lipiodol) was applied, in addition to platinum coils, in 5 cases with extensive tumorous hypervascularisation.

All branches of the tumour feeding bronchial or intercostal arteries were occluded (supraselective embolisation). In 17 of the 30 patients (57%), one branch of the bronchial or intercostal artery was embolised. The occlusion of two artery branches was performed in 9 patients (30%) and of three artery branches in 4 patients (13%).

The patients without BAE received p-aminomethylbenzoic acid as an inhibitor of fibrinolysis ($n=7$ (47%), 3×500 mg/day), Vitamin C ($n=7$, (47%) 2×1000 mg/day)

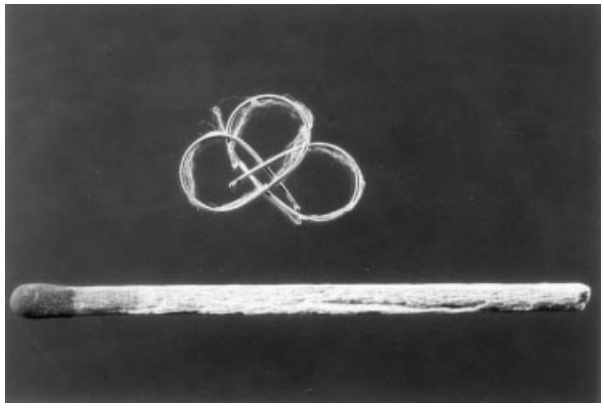

Fig. 1. Platinum coil with Dacron fibres.

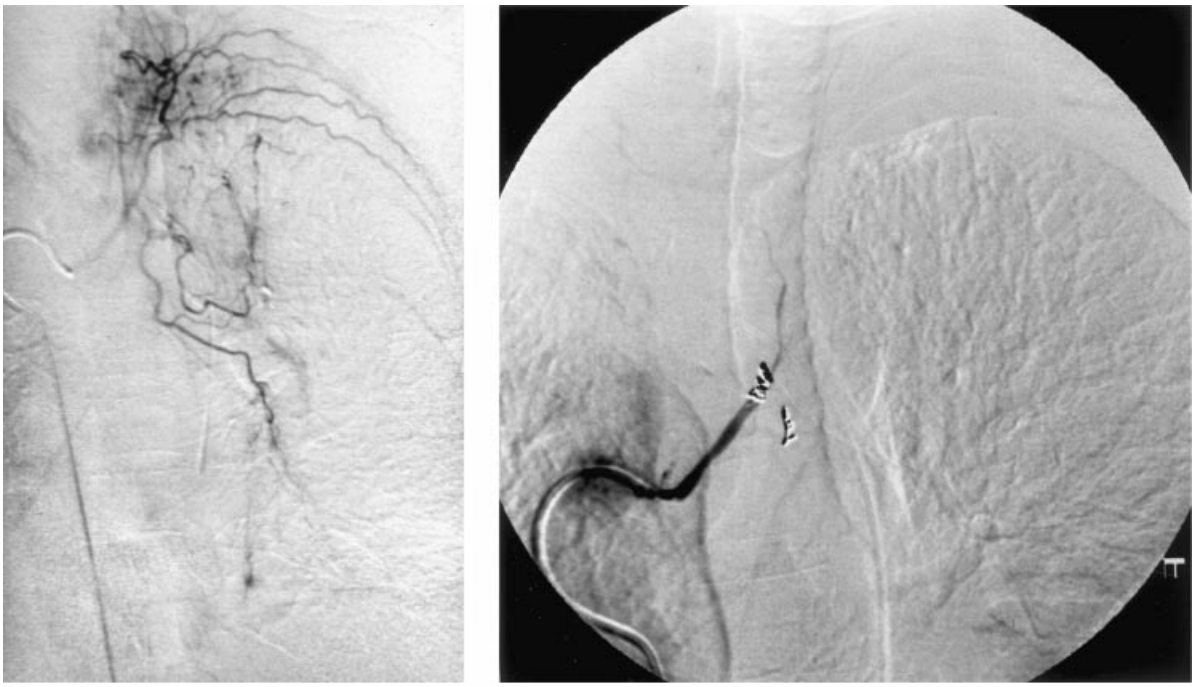

Fig. 2. (a) Selective bronchial aretriography demonstrates hypervascularisation. (b) Bronchial arteriogram shows vessel occlusion after successful bronchial artery embolisation with fibred platinum coils.

and antitussive drugs ($n=15$ (100%)). Endpoints of the study were immediate cessation and recurrence of bleeding and lethal haemorrhage.

Survival rates were compared using the log-rank test. The values are expressed in Kaplan–Meier Life Tables of Survival.

3. Results

In the BAE group pulmonary bleeding ceased immediately following embolisation in all patients (100%) (Fig. 3). In 3 of the 30 patients the BAE treatment reduced the haemoptysis to a minimal oozing which ceased within 24 h.

After initial BAE treatment, 13 of the 30 patients (43%) experienced no further bleeding until they died of tumour progression (mean survival time: 166 days). 2 patients (7%) left the trial and were therefore not followed-up.

However, 15 patients (50%) suffered from recurrent pulmonary bleeding after initial embolisation after a mean interval of 34 days (range: 1–69 days). 6 of these patients (20%) were immediately re-embolised resulting in stable cessation of the pulmonary bleeding (mean time of survival: 159 days). One patient (3%) was referred to thoracic surgery for pneumonectomy as an ultimate treatment approach which became necessary after massive pulmonary blood loss during a recurrent bleeding. Owing to bad clinical conditions 8 patients of the BAE group (27%) with a recurrent pulmonary bleeding could not undergo a second BAE treatment and died from pulmonary haemorrhage (mean survival time: 49 days). In the 5 patients with extensive tumorous hypervascularisation in whom BAE was followed by injection of aethoxysclerol and lipiodol, permanent bleeding cessation was achieved after the first ($n=2$) or second BAE ($n=2$). The fifth patient died from recurrent bleeding without additional BAE.

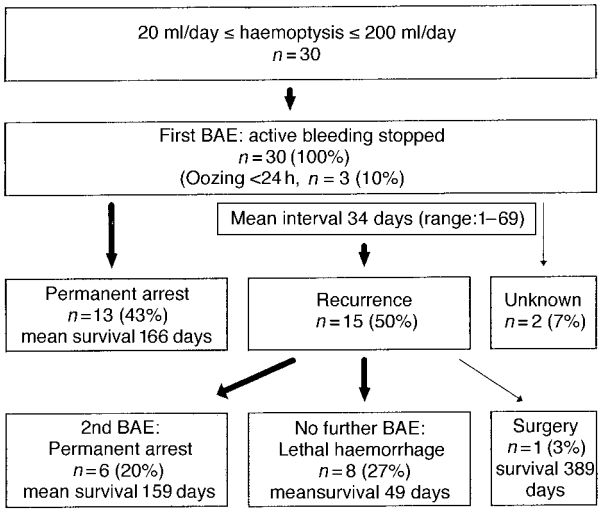

Fig. 3. Follow-up after bronchial artery embolisation (BAE) with platinum coils in tumorous pulmonary haemorrhage (mean survival 139 days, range: 1–818).

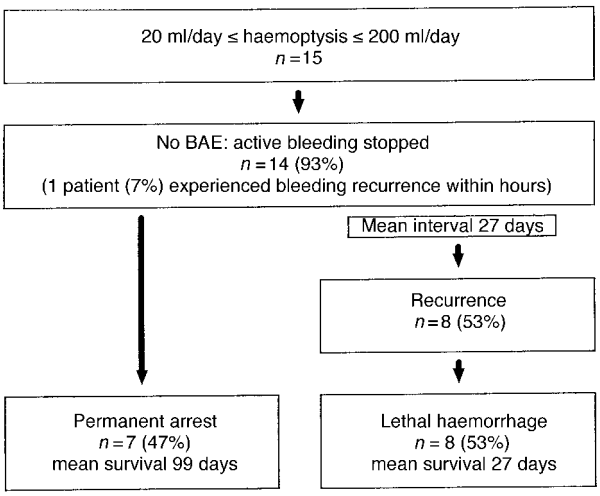

Fig. 4. Follow-up in tumorous pulmonary bleeding without bronchial artery embolisation (BAE) treatment (mean survival 62 days, range: 1–186).

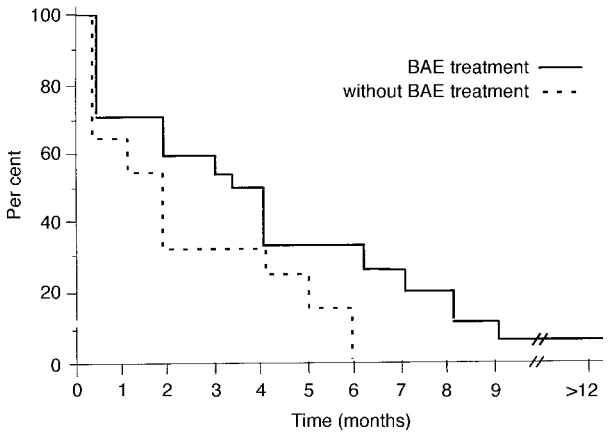

Fig. 5. Rates of survival with BAE treatment and without BAE treatment (historical control group) in tumorous haemoptysis.

Technically, BAE could be performed in all patients. We have not seen any treatment-related complications such as spinal cord injury or coil migration.

The analysis of the patient group which was treated conventionally showed a cessation of the pulmonary bleeding in 14 of 15 patients (93%) after an average of 6 h on average (Fig. 4). 7 of the 15 patients (47%) without BAE treatment did not show recurrent bleeding. They died from tumour disease progression (mean survival time: 99 days).

Furthermore, 8 of 15 patients (53%) suffered from recurrent haemoptysis and died from massive pulmonary haemorrhage as a severe complication of lung cancer (mean survival time: 27 days).

Regardless of treatment, a primary cessation of the pulmonary bleeding was reached in all patients, except one who died within hours from a pulmonary haemorrhage. The rate of permanent bleeding arrest was similar in both treatment groups (47% without BAE treatment, 43% with BAE treatment). All patients who suffered from a recurrent bleeding and were not treated with BAE died. An additional BAE led to a permanent arrest of the pulmonary bleeding.

The mean survival time of all patients with BAE treatment was 139 days (Fig. 5). The follow-up of the control group showed a mean survival time of 62 days which was significantly different from the BAE group ($P < 0.05$) (Fig. 5).

Comparing the endpoint of the study lethal pulmonary haemorrhage in both groups we found a significantly lower incidence in the BAE group (BAE group: 8/30 (27%) versus control group: 8/15 (53%) and a significant prolongation of mean survival (BAE group: 49 days versus the control group: 27 days).

After approximately 15 days 71% of the BAE group patients were alive compared with 66.6% of patients without BAE treatment. After a period of 2 months, 60.7% of the patients treated with BAE had survived, compared with 33.3% of the control group. At 4 months, 35.7% of the BAE patients and 20% of the patients of the conservative treatment group were alive. After 6 months, 28.5% of BAE-treated patients were alive, and all patients in the control group had died. 2 patients left the follow-up and were therefore excluded from the survival analysis.

4. Discussion

In the majority of previous BAE studies the focus of interest was patients with haemoptysis caused by benign lung diseases such as inflammation, bronchiectasis and arteriovenous malformations [11,12,22]. Following the increase in incidence of pulmonary bleeding caused by lung cancer our investigations focused on malignant lung diseases.

Bronchial artery embolisation with platinum coils and Dacron™ fibres could stop active bleeding in all patients immediately. In cases where bleeding recurred, repeated BAE led to a definite cessation of pulmonary haemorrhage in every case. To date, larger series of embolisations in malignant conditions with this device have not to our knowledge been reported. As randomised controlled trials cannot be performed for ethical reasons we compared embolisation results retrospectively with a historical non-BAE group treated at teaching hospitals.

Pulmonary bleeding is also an established indication for surgical intervention when there is no contraindication for thoracotomy. A comparison between bronchial artery embolisation and palliative lung resection in pulmonary bleeding was not done in our study and data comparing outcome after these different approaches are awaited. We believe that the less

aggressive strategy of BAE in comparison with thoracotomy might be advantageous in palliation of patients with advanced tumour and severe concomitant diseases.

The comparison of BAE with non-BAE patients showed similar results of the primary bleeding cessation in either treatment group. Even the rate of bleeding recurrence was similar in both treatment groups as well as the period of bleeding cessation. However, all patients from the non-BAE group and all patients of the BAE group without a second embolisation died from a recurrent pulmonary bleeding. These results imply that the prognosis of patients with recurrent bleeding can be improved by an additional BAE. Bronchial arteriography must be repeated to detect recanalisation of previously embolised vessels, development of collaterals, and neovascularisations in the region of the tumour. Re-embolisation should be attempted in such cases [14]. Our results suggest that BAE is more indicated in patients with recurrent pulmonary bleeding. However, we do not know whether the first BAE did contribute to the final result. Interestingly, recurrence of haemorrhage was lethal in all patients of the non-BAE group but in only half of the patients who have had BAE. We interpret this as an effect of the first BAE on neovascularisation within the tumour. However, the significant prolongation of survival time in the BAE group can certainly partially be attributed to differences in tumour stage. We nevertheless believe that part of this improvement is due to a consistent embolisation strategy.

Hayakawa and colleagues reported the outcome of patients ($n=12$) with pulmonary haemorrhage caused by lung cancer who were treated by BAE within a study of non-malignant pulmonary bleeding [16]. The patients were embolised with gelatin sponge material and in 58% (7 of 12) of the treated patients the pulmonary bleeding ceased immediately. Mean survival time in Hayakawa's study was approximately 90 days, compared with our result of 139 days. The follow-up of BAE-treated patients revealed in our study a bleeding recurrence rate of 50% which was higher compared with the results obtained by Hayakawa and colleagues (14% recurrence). The reasons for these differences in bleeding arrest, recurrence rate and survival time may be the use of different embolisation materials. Application of platinum microcoils with fibres may be of more benefit for patients with widespread and inoperable lung cancer and severe haemoptysis. Histological investigations have shown that these platinum coils lead to a lasting thrombus in the arteries [23,24]. Following instillation the radiopaque coil expands and wedges itself against the vascular wall and leads to blood clotting [25] followed by vessel embolisation. Despite this effective mechanism of embolisation a spontaneous revascularisation of embolised arteries and neovascularisation in close vicinity of the tumour due to the dynamics of tumour growth is possible. Angiography before second BAE revealed that in 2 of our 6 cases of recurrent bleeding the vessel, which had been occluded in first BAE, was still perfused. In the 4 remaining patients, neovascularisation led to recurrent tumoral bleeding, whereas the initial embolised vessels were still completely blocked. As a subject for further trials, it should be investigated whether tumour-specific therapies such as radiotherapy and chemotherapy can stabilise the effects achieved by BAE. Multimodal strategies in tumour therapy including both tumour-specific and non-specific treatments offer interesting possibilities like intermediate stenting and tumour-specific therapy [26].

In conclusion, tumour patients suffering from bronchogenic haemorrhage benefit from bronchial artery embolisation with fibred platinum coils. Primary results and recurrence rates are comparable in patients with BAE treatment and without BAE treatment. Prolongation of mean survival time and a lower rate of lethal recurrence can be partially attributed to BAE and re-embolisation. BAE, however, proved predominantly beneficial, particularly with regard to the permanent arrest of haemorrhages.

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