Bronchial Artery Embolization for Severe Hemoptysis in Cystic Fibrosis*

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We studied the long-term outcome after BAE for life-threatening hemoptysis in patients with CF. Data from pulmonary function tests were available for 18 of the 25 patients followed. A case-control comparison revealed that these 18 patients died sooner than hemoptysis-free patients with CF matched for age, sex, and pulmonary function (p<0.02), with the excess mortality occurring within the first three months after BAE. Of all 25 patients followed, six died of cardiorespiratory failure within three months of BAE; in two of them, hemoptysis was a contributing cause of death. The 19 patients who lived more than three months after BAE had a mean survival after embolization of 3.5 years (five were still alive at the end of the study). Most patients experienced long intervals (>1 year) free of major hemoptysis. Extended follow-up (mean, 35 months) revealed a higher incidence of recurrent severe bleeding than previously reported for 13 of these patients followed a mean of 11 months. Repeat BAE for severe recurrence was performed successfully in eight of nine patients, without complication. (Chest 1990; 97:1322-26)

Hemoptysis is a common problem for patients with CF, especially as their disease progresses; however, massive life-threatening hemoptysis is not common in CF. Our large CF referral center may witness a few episodes in a given year. Bronchial artery embolization via percutaneous catheter, in conjunction with medical management (antibiotics, with vitamin K and blood transfusions as required), has been the treatment of choice at our institution for life-threatening hemoptysis in patients with CF for the past ten years. The present review of 25 patients followed for a mean of 35 months revealed a higher incidence of recurrent severe bleeding than our previous report of 13 patients with CF followed for a mean of 11 months after one or more bronchial arteries had been embolized. The extended follow-up permitted better assessment of the survival rate and of the results of repeat BAE for recurrent severe hemoptysis. Patients either died within three months of BAE (usually not due to bleeding) or else survived for a mean of 3.5 years with prolonged periods (generally >1 year) free of major hemoptysis. Survival after severe hemoptysis treated with BAE was decreased compared with control CF patients matched for age, sex, and FEV1, who had never bled massively. Nine patients received repeat BAE to good effect, without serious complications.

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Materials and Methods

Ten female and 15 male patients, aged 7 to 35 years (mean, 21 years) underwent BAE for severe hemoptysis. The indications for BAE and the technique used have been described. We no longer routinely submit patients to bronchoscopy before BAE to localize the source of bleeding. Attempts are made to occlude any abnormal, enlarged bronchial artery identifiable at angiography. Only patients with severe hemoptysis were considered; the 25 patients either had acute hemorrhage (immediately life-threatening or of at least 300 ml/day for three or more days) (16/25), or had recurrent bleeding of 100 to 200 ml/day persisting for a week or more (9/25). Most patients experienced a drop in hematocrit reading of at least 5 percent.

Patients were advised of possible complications of BAE, including bronchial necrosis, inadvertent embolization of abdominal or leg vessels, and paraplegia, and written informed consent for the procedure was obtained in all cases.

The embolic material in all cases was gelatin (Gelfoam), cut into pieces varying in size from 1 × 2 mm to 2 × 4 mm. These particles were injected selectively into bronchial arteries, as previously described, until 90 to 95 percent of distal flow had been occluded. In two patients, single Gianturco steel-coil emboli were placed in the proximal bronchial artery after gelatin embolization in an attempt to provide more complete and permanent occlusion. Following embolization, normal activities, including chest physiotherapy, were reinstated within 24 to 48 hours. Thereafter, no restriction of any activities was imposed by the procedure.

Hemoptysis following BAE was categorized as minor, moderate, major, or severe. Minor represents streaking to 5 ml/day, moderate was up to 60 ml/day, major was over 60 ml/day for three consecutive days or on five of seven consecutive days, and severe met the criteria for BAE.

The data reported herein were obtained primarily from review of the patients' charts at the Children's Hospital, Boston. For several patients, data were obtained from distant medical centers or the referring physicians. Patients were followed after initial BAE until death or the end of the study. All patients underwent BAE at least 20 months before the end of the study.

Eighteen subjects had pulmonary function tests in the six months prior to embolization. As assessed by their best FEV1, during that time, eight had severe airway obstruction (FEV1<40 percent of

BAE = bronchial artery embolization
predicted value), four had moderate (40 to 60 percent of predicted), three had mild (60 to 80 percent of predicted), and three had values within the normal range (>80 percent of predicted).

In order to estimate the influence on long-term survival of severe hemoptysis leading to BAE, we constructed a “control” group from files of pulmonary function data. Patients with CF of the same sex as, and born within one year of, each studied patient were identified as candidates for “controls.” All candidates were free of major hemoptysis. From among these candidates, for each of the 18 studied subjects, we were able to identify one “control” who had FEV$_1$ values recorded during the six months immediately prior to BAE. “Controls” were chosen whose best FEV$_1$ (expressed as percent predicted value) during that time was closest to the subject’s best FEV$_1$, in the same six months. The survival of the “control” group was compared with that of the studied group.

RESULTS

Immediate Outcome

Twenty-one (84 percent) of 25 patients completely stopped bleeding immediately upon BAE (Fig 1). The other four (16 percent) continued to bleed, although less briskly than prior to BAE. Hemoptysis stopped after repeat BAE ten days later in one patient (case 7), two had ongoing, intermittent, spontaneously resolving minor (case 8) to moderate (case 19) hemoptysis, and the fourth (case 22) had moderate to severe hemoptysis which led to surgical removal of the bleeding right upper lobe.

Survival

Six patients, all of whom stopped bleeding promptly with BAE, died within three months of BAE. Two (cases 2 and 6) of the six had major rebleeding some time before death. Four died of cardiorespiratory failure within one month of their procedure (Fig 1).

Of patients who did not die within three months of initial BAE but did die within the study, the average survival after BAE was 3.5 years.

Most of the 20 patients who died succumbed to cardiorespiratory failure; however, major hemoptysis occurred at the time of death in two patients (cases 2 and 11) and hours before death in one (case 6). Major hemoptysis occurred in the weeks preceding death in another three patients (cases 5, 8, and 19), but these patients were not actively bleeding when they died, and hemoptysis was not believed to have contributed to their death. Thus, of all patients who died, hemoptysis was believed to be a contributory factor in three.

A comparison of survival in the 18 subjects who had pulmonary function data available with 18 “controls” matched for age, sex, and FEV$_1$, who were free of major hemoptysis revealed reduced survival in the embolized subjects (mean of 12 months vs mean of 46 months in the “controls;” p<0.02, by an analog of the Wilcoxon test for censored data). The excess mortality in the subjects with massive hemoptysis occurred during the three months immediately following BAE; thereafter, survival rates in the two groups were comparable (Fig 2).

Five of the 25 patients (20 percent) were still alive at the end of the study period, with an average survival of 63 months (range 20-101 months).

Clinical Course

Of the 15 patients who stopped hemorrhaging upon initial BAE and survived at least three months, one (7 percent) had major rebleeding in the first year after BAE. Of the nine patients from this group who survived two years after BAE, four (44 percent) had rebled in a major way by the end of the second year. It was unusual for a first major recurrence to happen after the end of the second year (Fig 1).
Overall, there was no recurrence of hemoptysis in eight of the 25 patients. Minor recurrences only were noted in four of the 25, and there was major repeat bronchial bleeding in 13 (52 percent), among whom the mean time from BAE to the first major recurrence was 20.5 months. Of the five patients alive at the end of the study, two have had no recurrence of bleeding, two were treated with repeat BAE, and one had spontaneous cessation of recurrent major hemoptysis.

Repeat BAE was necessary in nine (36 percent) of the 25 patients. Five required a second embolization, and four needed a third. The interval between the first and the second procedures ranged from five days to 24 months (average, 7.5 months). Of the nine patients requiring repeat procedures, bleeding was entirely controlled by BAE in five, was reduced to mild to moderate amounts in three others, and was uncontrolled in the ninth patient, leading to a lobectomy.

No neurologic or other major complication was observed. In over half of the group, mild fever or thoracic wall pain (or both) developed in the first 24 hours after BAE and persisted for one or two days. In all instances, these complications were self-limited and required short-term medical treatment only.

**DISCUSSION**

**Technique**

Gelatin (Gelfoam) has been our embolic agent of choice primarily because it is easily injected. We believe that it is necessary to inject a large number of small particles (usually 15 to 80 per artery) in order to occlude the bronchial vessels peripherally and completely. It is known that gelatin is not a permanent occluder and that resorption and recanalization take place over several weeks or months; however, the alternative material, polyvinyl alcohol (Ivalon), a more permanent occluder, is more difficult to handle. To inject multiple arteries with a large number of polyvinyl alcohol particles would considerably prolong what is already a lengthy procedure. The use of coil emboli in trunk bronchial arteries, after peripheral gelatin embolization, has been abandoned because the coils are likely to hinder, if not prevent, reembolization of these vessels in the future.

The use of absolute alcohol injections in the bronchial arteries as treatment for hemoptysis has been described. Serious complications (eg, fatal bronchial infarction) associated with this technique render it unacceptable.

**Clinical Issues**

Bronchial artery embolization combined with medical therapy offers several advantages over surgical (lobectomy) or supportive medical management alone (parenteral antibiotics, with vitamin K and transfusions as required). Cessation of hemorrhage is achieved more rapidly with BAE (immediately in 21 [84 percent] of 25 in this series) than by medical means only. In patients with massive life-threatening hemoptysis, achieving hemostasis promptly may be desirable to minimize transfusion requirements and to reduce morbidity and possibly mortality (but see subsequent discussion). There are major psychologic benefits for the massively bleeding patient and his family from immediate resolution of this most frightening of symptoms. Embolization has been performed safely and
effectively in patients who were poor surgical candidates. The BAE permits the reinstitution of vigorous chest physiotherapy sooner than with either surgery or medical treatment. The patients are up and about within 24 hours. The time to resumption of full activity and the length of hospitalization are shortened by BAE.

Two different groups were identified based on survival after BAE: (1) those who died within three months; and (2) those who lived longer (mean survival, 3.5 years). Even in the first group, BAE was well tolerated, and prompt relief from symptoms was believed to be beneficial.

Repeat hemoptysis may occur if some dilated bronchial arteries remain inadequately embolized after the first attempt. We prefer to embolize all abnormal, enlarged bronchial arteries which it is technically possible to identify and occlude safely. It is not necessary routinely to subject patients to the risks bronchoscopy involves, although bronchoscopy prior to BAE can be helpful in localizing the lung or lobe from which the major bleeding is coming. The anatomic site of bleeding is not localized, as a rule, during angiography. It is generally impossible to determine if recurrent hemoptysis originates from the same site as the initial bleeding.

Severe hemoptysis treated with BAE predicted reduced survival in our subjects with CF, when compared to controls with CF matched for age, sex, and pulmonary function status who never bled massively. Patients with CF who have severe hemoptysis not treated with BAE have been so rare at our institution in the last ten years that it has not been possible to compare the results of medical management alone with those of BAE and medical management combined, nor to compare the survival of patients with CF and severe hemoptysis treated solely by medical means with survival in patients with CF who have never bled profusely but are otherwise similar from a pulmonary point of view. Further studies, perhaps involving multiple CF centers, are needed to address these questions.

Stern et al12 reported that the survival rate of their patients with CF who had massive hemoptysis treated medically is comparable to that of a group of patients with CF who had equally severe pulmonary disease but who never bled profusely; however, their assessment of severity of pulmonary disease (the total Shwachman-Kulczycki score) differed from ours, and their control group was not individually matched for age, sex, and pulmonary status. Their criteria for massive hemoptysis also differed from ours, such that their population was less severely affected.

In 1970, Holscaw et al13 from our institution, using solely medical treatment, reported a high mortality (six of 19 patients; 32 percent) within 48 hours of the onset of hemoptysis, and a high morbidity rate. In the present series the mortality within four days of BAE was two (8 percent) of 25; however, Stern et al12 followed 38 patients with CF who expectorated 300 ml or more of blood in 24 hours, all of whom survived the acute episode with medical treatment alone.

Stern et al12 followed their patients a mean of 55 months after their first massive hemoptysis. The reported incidence of repeat major bleeding, 45 percent, was similar to that observed in our patients who were followed for two or more years after BAE, suggesting that BAE may not reduce the long-term recurrence rate of major hemoptysis. On the other hand, the observed incidence of rebleeding is much lower than this in the first year after BAE, especially in patients who survive more than three months after their embolization. If major bleeding does recur after BAE, the BAE can be repeated safely and, as noted in eight of nine patients, with good results.

Although associated with known serious risks (related to inadvertent compromise of arterial supply to vital structures, such as the spinal cord or intestines), BAE can be performed safely. The only complications attributable to BAE in our patients have been transient fever and chest wall pain, both responsive to short-term symptomatic treatment.

In view of the advantages of BAE outlined previously, it has been our belief that we should not withhold BAE from those in whom it is indicated. The BAE should only be done by experienced angiographers familiar with thoracic vascular anatomy and only where the risk to the patient from ongoing bronchopulmonary hemorrhage is deemed to outweigh the risk (especially of spinal cord injury) of the procedure itself.

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