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Outcomes of Bronchial Artery Embolization in Massive Hemoptysis of Various Etiologies

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Abstract

Massive hemoptysis characterized by the expectoration of 300 ml to 600 ml of blood in 24 hours, can be life threatening and without any regards to the etiologic factors, emergency management of this condition is crucial in restoring the health of the patient. Bronchial artery embolization has been gaining popularity in controlling massive hemoptysis and recurrent hemoptysis due to different etiologies. Along with its soaring use in interventional radiology, bronchial artery embolization definitely has proved itself to be useful in achieving hemostasis with minimal invasion and fewerpost-procedure complications. This has especially been evident in the patients with other comorbid conditions that render them unfit for a surgical approach to hemostasis. Nevertheless, the benefits of this procedure have not yet been solidified. Low sample size and lack of longer duration of follow-ups may have played a significant role in this. This review compares and summarizes the immediate and long-term benefits achieved in various studies conducted around the world to conclude that bronchial artery embolization is extremely effective in achieving immediate hemostasis with the least amount of complications. In addition, the long-term outcomes of the procedure are also overwhelmingly successful with a lesser number of recurrences and longer overall survival.

Introduction

Hemoptysis is regarded as a common, yet potentially life-threatening respiratory condition [1]. Massive hemoptysis, defined as expectoration of blood ranging from 300ml to 600 ml in a total duration of 24 hours [2-4], accounts for only 5% of hemoptysis. Nevertheless, it can especially be catastrophic to the patient due to the possibility of asphyxiation, regarded as the most common cause of death in massive hemoptysis [4-6]. It accounts for 80% of the morbidity and mortality in patients with massive hemoptysis [7]. Exsanguination and acute hypotension, although less common, are also some of the other reasons of fatality in massive hemoptysis [8, 9]. The etiology of massive hemoptysis is varied according to the developmental status of the countries. Tuberculosis is established as the most common cause in the developing countries whereas primary lung cancer, bronchiectasis, cystic fibrosis, aspergillosis, sarcoidosis are the common causes in developed countries. Bronchial artery embolization (BAE) is now a commonly opted procedure for the treatment of massive and life-threatening hemoptysis. Reported first hand by Remy et al. [10] in 1973, BAE has been suffering from comparatively fewer studies [9, 11] mainly due small sample size and shorter duration of follow-ups [12-15]. Here in this article, we are trying to review the outcomes of BAE in massive hemoptysis due to different causes.

Bronchial artery anatomy

Although, having a variable anatomy, bronchial artery most commonly arises from the level of T5 to T6. It usually comprises of single right intercostobronchial (ICB) trunk with single left bronchial artery (the most common combination). Other than that, it may arise as a single right ICB truck, and single left bronchial artery arising from a common trunk; or as a single right ICB trunk with two left bronchial arteries [16]. Bronchial arteries arising outside of T5–T6 are considered anomalous, with an incidence of 8.3% to 35% [17, 18]. Aberrant origins include the subclavian, thyrocervical, internal mammary, innominate, pericardiophrenic, superior intercostal, abdominal aorta, and inferior phrenic arteries [19-21].

Treatment of massive hemoptysis of bronchial origin with BAE

There are three major approaches for the treatment of hemoptysis: conservative medical treatment, bronchial artery embolization, and surgical approach. The treatment modality to be used mainly relies upon how severe the hemoptysis is and how urgent are the circumstances [22]. BAE is a minimally invasive procedure where the location of the selective bronchial artery is done via peripheral arterial access to catheterize and perform angiography for identification of any abnormal vessels which is then embolized to achieve hemostasis (Fig. 1) [14]. Before the procedure, a short neurological exam is done to establish a baseline. This will be repeated throughout the procedure of BAE [16].

BAE procedure

Femoral (most common) or bronchial route is generally preferred for the arterial access. The thoracic aortogram for the identification of origin, number, and course of bronchial and other non-bronchial systemic arteries are usually physician dependent [23]. Among the various catheter configurations, Cobra, Mikaelson, Simmons, or Judkins right catheters are the commonly preferred ones [24]. After selecting the target bronchial artery, a micro-catheter is forwarded coaxially to a more stable location (distal to the radicular and spinal arteries). Embolization under direct fluoroscopy is performed slowly until complete occlusion and near stasis of contrast medium is achieved. After selective catheterization of bronchial artery achievement, an angiogram is taken. Digital subtraction angiography and correct anatomical position of patient facilitate quick identification of spinal arteries and its course [23]. Osmolarity of contrast media for angiography and the size of the micro-catheter play a pivotal role in the causation of spinal ischemia. Low osmolar contrast media should be used for bronchial and intercostal angiography [23]. 2.4-2.8 French (F) micro-catheters [24], and

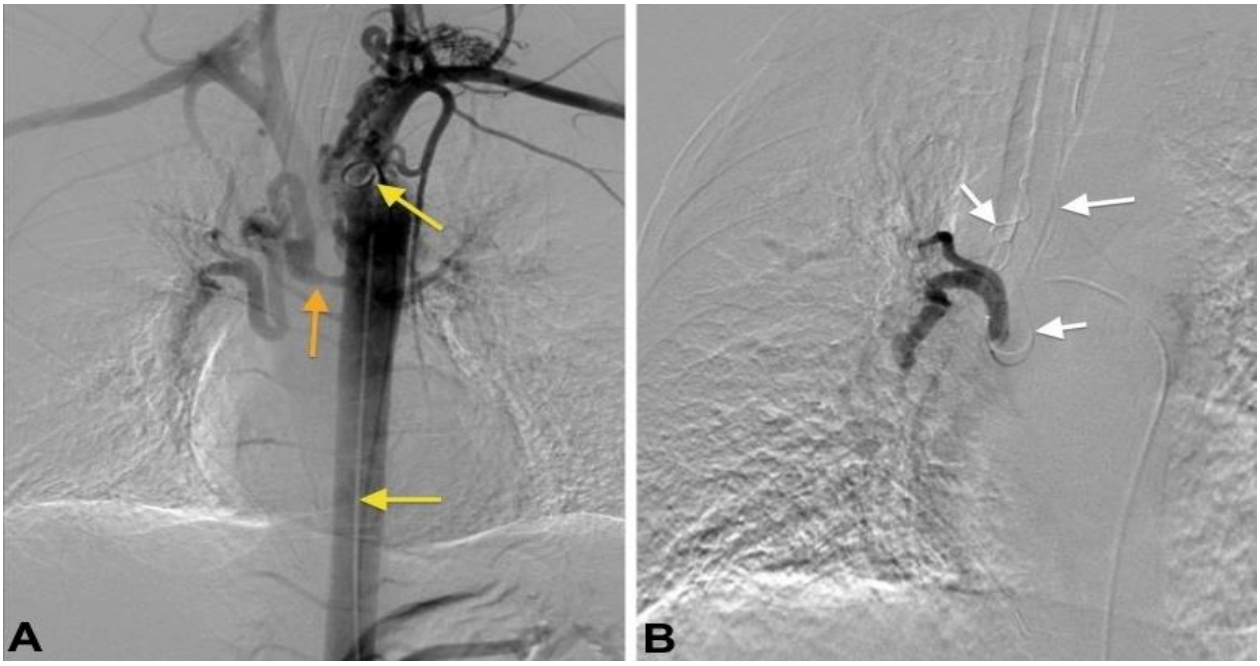

Fig. 1 Bronchial artery embolization procedure in a 31-year-old patient with cystic fibrosis who was presented with massive, life-threatening hemoptysis. (**A**) The catheter was inserted through the right femoral vein and positioned in the aortic arch (yellow arrows). The contrast was injected to determine the origins of the bronchial arteries and showed a hugely dilated right bronchial artery (orange arrow), which was presumed to be the source of the hemorrhage. (**B**) A microcatheter was then manipulated into this artery, taking a convoluted course through the tortuous vessel (white arrows). The artery was embolized and the patient's hemoptysis resolved. The figure was obtained from bronchial artery embolization Radiology St Vincent's University Hospital website and proper permission was obtained. (http://www.svuhradiology.ie/case-study/bronchial-artery-embolization/)

preferably 2.7F [22, 25] are found to be relatively safer for catheterization and embolization of the bronchial artery.

Materials used for embolization

There are several agents that can be used for embolization of arteries. Polyvinyl alcohol (PVA) particles-both spherical and non-spherical, gelatin sponge pledgets, PVA hydrogel, tris-acryl gelatin microspheres, acrylic glue and steel coils are commonly used [12, 26-28].The most popular one is PVA particles and gelatin sponge pledgets [23, 29]; preferably PVA particles as the gelatin pledgets are reasonable and thus less durable than PVA particles [22,30]. Steel coils should refrain from its use as it can occlude the arteries proximally and thus access to the re-bleed site [9, 23, 24]. However, coils are used for embolizing proximal/mediastinal bronchial artery aneurysms and for occlusion of abnormal broncho-systemic arterial shunts to prevent the non-target embolization [23].The particle size generally used is between 300µm to 700 µm [23, 24]. Smaller particles size and liquid embolic agents are also not favored in BAE, because of the possibility of non-target embolization distally increasing the risk of aortic, esophageal, pulmonary, and bronchial wall necrosis, including spinal, the most dreaded spinal cord ischemia [9, 23]. Recent studies, on the other hand, contradict with it where 94% patients had a successful outcome post-BAE using liquid embolic agent ethylene vinyl alcohol (EVOH) copolymer. The result was satisfactory with the fairly good outcomes, minimal complications, and recurrences [31].

BAE as a treatment of choice

Although there are scarce data regarding the use of bronchial artery embolization, it has been reported by many as one of the safest interventional procedure [8, 11, 12, 32]. Most of the patients needing BAE present themselves with other comorbid conditions due to which they are not a good candidate for surgical intervention [2]. The advancements in techniques and the availability of various embolizing materials indeed have played a significant role in

establishing success rates of BAE at a higher note [33, 34]. Several studies have shown that whatever, the cause of massive hemoptysis, BAE has always been the treatment of choice. BAE has also been found as the ultimate treatment choice in rare diseases like sarcoidosis [35], and cystic fibrosis [36].

Complications of BAE procedures

Considered comparatively safer procedure, BAE nevertheless has its own complications. Besides, the most common complication, chest pain was found to occur in 24%-91% cases [37], other complications following BAE that have been reported, includes bronchoesophageal fistula, fatal ischemic colitis, renal and splenic infarctions [38]. Although rare, the most dreaded complication of BAE is coined spinal cord ischemia caused by the non-intended occlusion of spinal arteries occurring in 1.4%-6.5% of cases [37, 38]. The reports suggest that 25 out of 30 (83.3%) patients complained of mild to moderate chest pain post-BAE [39]. Minor complications were reported to be 9 out of 34 (26.4%) patients in a research conducted by Rasciti et al. [40]. In another study, it was found that there were mostly minor complications that were managed conservatively. Out of 69successful BAE procedures, only 6 (8%) had a mild dissection, 2 (3%) had hemomediastinum, 1 (1%) had a perforation of the vessel and 1 (1%) had chest pain [14]. There are also reports of transient cortical blindness as one of the complications of the BAE procedure [45]. Vascular complications, having a notoriously bad prognosis of cortical blindness due to infarctions of occipital and cerebellar arteries can be accounted for about <10% of BAE cases [46].

Immediate outcomes of BAE

Overall immediate outcomes

The immediate success rate of bronchial artery embolization has been found exceptionally great in most of the research reports accounting for 90% success rate in controlling the bleeding immediately [38]. All the cases achieved immediate control of bleeding post-BAE in the research conducted by Ghanaati et al. [39]. These results are comparable to the studies done by Ustonsoz et al. [41] who had 100% success rate in controlling the hemoptysis immediately. In another study, 205 patients out of 209 (98%) achieved immediate control of bleeding after the procedure [42]. In a study conducted by Rabkin et al. [43], a total of 278 out of 306 cases (91%) accomplished hemostasis acutely. There was no procedure-related complication in a study of 47 patients that underwent a cumulative of 109 BAE procedures [44]. All of these 47 cases had a successful BAE except for 2 cases which had to undergo repeat BAE for the recurrent hemoptysis within a period of two months.

Immediate outcomes in tuberculosis (TB) and post-TB sequelae

Kim and his team found that around 25% of the total tuberculosis patient (n = 190) that had undergone BAE procedure had to undergo repeated BAE and among those, 26% had to undergo repeated BAE in less than a month time interval [47]. This is analogous to the study done by Pei et al. [48] who also had a lower success rate for the immediate control of hemostasis in the tuberculosis patients. A total of 97 out of 112 patient accounting for about 86.6%, including both active and passive diseases, had achieved hemostasis immediately after the procedure. However, Anuradha et al. [49] reported an immediate success rate of 93% (54 out of 58 cases) with the patients having tuberculosis and post-tuberculosis sequelae.

Immediate outcomes in various other etiologies

A study of BAE procedure in pulmonary hypertension patients showed that 19 out of 22 pulmonary hypertension patients (86%) achieved complete embolization [40]. This was significantly impressive when compared to the control group which had only 9 out of 12 (75%) patients that were able to achieve complete embolization post-BAE. The 30-day relapse, however, was higher in the patients with pulmonary hypertension (26%) when compared to the control group (9%).

The BAE procedure done in patients with aspergillosis reveals that the immediate success rate was 64%,whereas post procedure complications were seen in 6% patients [50].BAE has also been successfully used in the treatment of massive life-

threatening hemoptysis associated with sarcoidosis. A case report of Andrew et al. [35] suggested that the outcome of the BAE procedure was remarkably good as revealed by a repeat CT done at two years follow-up that showed marked alleviation in the size and thickness of the pulmonary cavity walls. Further, BAE has been reported successful in achieving hemostasis in patients with cystic fibrosis. A case report revealed an uneventful BAE procedure in a 16-year-old girl suffering from cystic fibrosis. There were no complications and recurrences till 9 months of follow-up [36].

Long-term outcomes of BAE

Overall long-term outcome

In a study of 46 patients, it was found during follow-ups that the proportion of relapse was 7 cases within 30 days; 1 case between 30 to 90 days and 3 cases beyond 90 months period [12]. Lee et al. [14] in a study with 70 patients, mentioned that the recurrence rates were 26% for the acute major group and 47% for the chronic recurrent group of patients with hemoptysis. The interval from the BAE to repeat BAE ranged from 60 days to 4.6 years (median = 1 year). In another study, Out of 41 patients treated with BAE, 17/21 (81%) patients with massive hemoptysis and 16/20 (80%) patients with recurrent hemoptysis had a successful control of bleeding immediately. Over the long term, 8 patients were not followed and 13/17 (76.5%) patients with massive hemoptysis and 11/16 (68.7%) patients with recurrent hemoptysis were found to have good long-term results [51]. Pathak et al. [52] reported that fifty patients undergone BAE due to different etiologies achieved 100% immediate hemostasis. During follow-ups, 24/50 (48%) had recurrences. In the long term, there were 15 deaths. Out of these, seven were with-in the first month, one after two months, one after four months, and then after 2, 4, and 5 years post BAE. The early mortality was found to be in patients having cystic fibrosis and small cell lung carcinoma. Patients were followed for a median duration of >2 years (longest up to 13 years).

Osaki et al. [53] observed recurrence, incorporating minor hemosputum, in 11/22 (50%) of the patients during a follow-up period of 25 to 88 months. Among those, one case (4.5%) recurred within one month, nine cases (41%) recurred in 1–36 month period and one case (4.5%) recurred >3 years after BAE. However, a recurrence of hemoptysis (excluding hemosputa) was observed in 6/22 (27.3%) cases in the same follow-up period. Out of these, six cases, recurrence within one month was seen in one case (4.5%), while the other five (22.7%) cases recurred within 36 months. According to Kaplan-Meier's method, 75% of the recurrent cases were within 1.5 years and none recurred after 3 years of the initial BAE.

Long-term outcome in TB and post-TB sequelae

Kim and his team found that 47 (25%) of the total 190 tuberculosis patients that had undergone BAE procedure had to undergo repeated BAE in the time interval range of 0.7 to 81.6 months (median 7 months). Among those, 12 patients (26%) had to undergo repeat BAE in less than a month time interval [47]. In another study, 27 out of 49 (55%) TB and the post TB sequel followed up patients had a recurrence of hemoptysis (median = 110 days, range 1–959 days) after the BAE procedure [49].

Long-term outcome in various other etiologies

BAE done for patients with pulmonary hypertension (n=19) had 5 (26%) patients with 30-day relapse and 6 (31%) in 90-day relapse category. The death frequencies were 3 (13%) in both 30days and 90-day relapse [49]. Aspergillosis, chronic pulmonary aspergillosis and simple aspergilloma combined, had 12/19 (63.1%), 4/22 (63.6%) and 7/11 (63.6) patients with <1 month, 1 month to 1 year, and >1-yearrelapse incidents, respectively [50]. BAE has been a treatment of choice in the life-threatening hemoptysis caused by rare diseases like sarcoidosis and cystic fibrosis. The outcome of BAE was found to be immensely successful in a patient with a life-threatening hemoptysis caused by sarcoidosis, which was confirmed with a CT imaging after two years that revealed a substantial decrease in the size of the pulmonary cavity along with the thinning of their walls [35]. Similarly, the outcome in the case of cystic fibrosis was also found to be satisfactory although the case was only followed for nine months [36].

Factors affecting long-term outcomes of BAE

In tuberculosis patients, many factors were found to be associated with re-bleeding post-BAE. Kim et al.[47]evaluated suspected factors, namely tuberculous destroyed lungs, the presence of the fungal ball, increased pre-BAE CRP levels, underlying chronic liver disease, and the use of anticoagulant agents and/or anti-platelet agents. There was nosignificant association found with the age, gender, activity of PTB, need of ICU admission, use of mechanical ventilation and other medical problems in their study. On the other hand, Pei et al. [48] in his study with 112 TB patients revealed that patients with active TB had a significantly higher recurrence-free period than the patients with inactive TB. The study, however, is complimentary to the insignificance of age and gender. This difference in results may be due to the difference of sample size, but further studies should be done to come to a conclusion.

Bronchiectatic findings in chest CT and the pulmonary-bronchial shunt in chest angiography are also regarded as a risk factor for recurrences of hemoptysis. Recurrent infection in bronchiectasis is associated with inflammation and progressive extermination of the lung along with angiogenesis leading to pulmonary-bronchial shunt [53]. Baseline respiratory function status was attributed as the main factor causing the mortality due to hyperbaric respiratory failure in the patients that had undergone BAE for massive hemoptysis due to cystic fibrosis. If these patients had severely reduced baseline pulmonary function, the risk of BAE outweighed the risks from the disease itself [54]. The amplified bronchial circulation [55, 56] and the size of the embolizing particle (if <300 μm) are found to be the culprits for precipitation of stroke and bronchial artery embolism in end-stage cystic fibrosis patients resulting in high risk of mortality [57, 58]. In addition, incomplete embolization, recanalization, collateralization by other arterial vasculature, missed culprit vessel identification, inadequate causal therapy or progression of the underlying pulmonary disease are also found to be other factors that can influence recurrence post-BAE [59]. There have been reports stating that aspergilloma, diabetes mellitus and the presence of shunt in angiographic finding were the most significant risk factors for recurrence after BAE [13].

Conclusions

In conclusion, it is obviously clear that the bronchial artery embolism is one of the safest and least invasive procedures which is highly efficient in immediate control of the hemoptysis and has proved itself to be one life-saving measure in case of massive and life-threatening hemoptysis. Although enough studies are not conducted for a long follow-up period, even then long-term outcomes still have been tremendously successful with a lesser number of recurrences. More studies are yet to be done with the malignant cases like squamous cell lung carcinoma, aspergilloma, and cystic fibrosis to improve its overall long-term outcomes and survival.

Conflict of interest

The authors declare no conflict of interest.

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