Review Article

A review of the modern, multidisciplinary approach to the management of massive hemoptysis

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Abstract: Massive hemoptysis was once considered a surgical emergency necessitating thoracotomy. Fortunately, technology has evolved to facilitate rapid localization and control of bleeding through minimally invasive diagnostic and therapeutic tools. Management of massive hemoptysis is now a multidisciplinary effort that requires input from interventional pulmonologists, interventional radiologists, and thoracic surgeons. In this comprehensive review, we discuss the complex management of massive hemoptysis, from initial stabilization to use of novel endoscopic and endovascular therapies to achieve hemostasis.

Keywords: Massive hemoptysis; interventional pulmonology; bronchoscopy; bronchial artery embolization (BAE)

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Overview

Massive hemoptysis is the life-threatening expectoration of large volumes of blood as a result of tumor, infection, or other cause. Historically, it has been managed with emergent thoracotomy, however, advancements in interventional pulmonology and interventional radiology have transformed the treatment algorithm for massive hemoptysis. Endobronchial and endovascular therapies are now often utilized as temporizing measures to control hemorrhage and bridge to more definitive therapies such as chemotherapy, antibiotics, or surgery. Management can be complex and is best handled by a well-trained, multidisciplinary team. In the following paragraphs, we review a detailed, modern approach to the management of massive hemoptysis.

Definition

Hemoptysis can range from blood-streaked sputum to substantial pulmonary hemorrhage, but massive hemoptysis accounts for only 5% to 15% of events (1,2). While rare, massive hemoptysis is deadly. Mortality rates can reach 80% if not appropriately managed (3). There is no consensus on the definition of "massive" hemoptysis. Proposed definitions include volumes ranging from 100 to 1,000 mL of blood over a 24-hour period. Others are based on rate of bleeding per hour over a 24-hour period (2). It can be difficult, however, for patients to accurately quantify hemoptysis, and under-reporting and exaggeration of blood loss are common. This has led to definitions based on "magnitude of effect" or "clinical consequence," whereby "massive" means the volume of blood that results in transfusion, hypoxemia, intubation, shock, or even death (1).

Anatomy

The lungs are supplied by both pulmonary and bronchial arteries. The pulmonary arterial system is a low-pressure system that accounts for only 5% of cases of massive hemoptysis (2). Blood is carried from the right ventricle to the pulmonary capillary bed where gas exchange

occurs. Blood is then returned to the left ventricle via the pulmonary veins. Mean pressures in this circulation are 15–20 mmHg systolic and 5–10 mmHg diastolic (1).

The majority (90%) of cases of massive hemoptysis can be localized to the bronchial circulation, a high-pressure system arising directly or indirectly from the aorta. It receives 1% to 2% of cardiac output and provides blood flow to the tracheobronchial tree. It also supplies the hilar lymph nodes, visceral pleura, pulmonary arteries and veins, vagus nerve, and esophagus (1). The bronchial arteries arise from the descending aorta between the third and eighth thoracic vertebral bodies, most commonly between T5 and T6. Nearly 40% of patients have a single right bronchial artery and two left bronchial arteries arising from T5/T6, but anatomical variations are common (2). The final 5% of cases of massive hemoptysis arise from the aorta itself or from the non-bronchial systemic circulation, which includes the intercostal, coronary, and thoracic arteries (1).

Etiology

The differential diagnosis for the etiology of massive hemoptysis is broad and varies by clinical setting and geography (*Table 1*). In the 1960s, *Mycobacterium tuberculosis*, bronchiectasis, and lung abscesses accounted for 90% of massive hemoptysis (1). Today, the most common causes include bronchiectasis, tuberculosis, mycetomas, necrotizing pneumonia, and lung malignancy (2). About 20% of lung cancer patients experience hemoptysis, but only 3% of patients present with massive hemoptysis (1). In cystic fibrosis, the annual incidence of massive hemoptysis is 1%, though prevalence increases in later stages of the disease (4). A recent retrospective cohort study looked at hemoptysis in adults over a 5-year period using the French nationwide hospital administrative database. The authors found that 18% of cases of hemoptysis are cryptogenic, despite advancements in diagnostics and therapeutics (5).

Diagnosis & management (*Table 2*)

Initial approach & stabilization

Massive hemoptysis is a medical emergency that requires a multidisciplinary approach to management. As is the first step in any emergency, the patient's airway and circulation must be stabilized. Large-bore peripheral IVs or large-bore central access need to be secured. Complete blood count, blood type, cross-match, and coagulation profile should

Table 1 A differential diagnosis for the etiology of massive hemoptysis

Etiologies of massive hemoptysis
Malignancy
Bronchogenic carcinoma
Endobronchial tumor
Pulmonary metastases
Sarcoma
Infectious
Lung abscess or necrotizing pneumonia
Endocarditis with septic emboli
Mycetoma
Mycobacteria
Parasitic disease
Cardiac/pulmonary vascular
Pulmonary artery aneurysm
Pulmonary hypertension
Pulmonary embolism/infarct
Congenital heart disease
Mitral stenosis
Left heart failure
Pulmonary veno-occlusive disease
Dieulafoy's lesion
Arteriovenous malformation
Bronchovascular fistula
Pulmonary
Bronchiectasis
Chronic bronchitis
Diffuse alveolar hemorrhage
Foreign body aspiration
Broncholithiasis
Lung transplantation
Idiopathic pulmonary hemosiderosis
Lymphangioleiomyomatosis
Vasculitis/collagen vascular disease
Granulomatosis with polyangiitis
Systemic lupus erythematosus
Behcet's disease

Table 1 (*continued*)

Table 1 (*continued*)

Goodpasture's syndrome
Other vasculitis or collagen vascular disease
Hematologic
Coagulopathy
Platelet disorder
Drugs & toxins
Crack cocaine
Penicillamine
Solvents
Nitrofurantoin
Bevacizumab
Iatrogenic/trauma
Catheter-induced pulmonary artery rupture
Blunt or penetrating chest injury
Secondary to biopsy, bronchoscopic procedure
Airway stent
Other
Cryptogenic
Endometriosis
Tuberous sclerosis

Table 2 An overview of the management of massive hemoptysis, including endobronchial and endovascular therapies

Overview of the management of massive hemoptysis
Initial approach & stabilization
Diagnosis & localization
Treatment
Endobronchial therapies
Thermal ablative techniques
Argon plasma coagulation
Electrocautery
Laser therapy
Bronchial-blocking balloon catheters
Silicone spigots
Endobronchial valves
Endobronchial sealing
Endovascular therapies
Bronchial artery embolization
Tranexamic acid
Surgery

be obtained to guide resuscitation. The patient should be positioned with the bleeding side down, if this is known, to allow gravity to isolate the bleeding lung.

An airway needs to be established as efficiently as possible to prevent asphyxiation. A large-lumen endotracheal tube (ETT) is the most accessible option in most settings. An appropriate ETT will have an internal diameter of 8.5 to 9 mm to facilitate use of fiberoptic bronchoscopy (FOB). FOB can guide the ETT through the vocal cords and into the non-bleeding mainstem bronchus. Disadvantages of single lung intubation include inability to intervene upon the bleeding lung and right upper lobe collapse with intubation of the right mainstem bronchus (2).

Another option for airway stabilization is a double-lumen ETT (DLETT), which consists of a long lumen and a short lumen bound together. The longer lumen is advanced into a mainstem bronchus while the shorter lumen remains in the trachea to ventilate the other lung (3). FOB confirms proper placement, as positioning can be difficult and time-consuming. A pediatric bronchoscope can be advanced through one of the lumens, but it is not large enough to remove blood rapidly and tends to clog. For these reasons, the DLETT is not recommended as a first-line approach in cases of massive hemoptysis.

Rigid bronchoscopy offers the advantage of simultaneous visualization and ventilation. It also is the most efficient approach to airway stabilization. Blood and clots can be rapidly evacuated, and instruments can be exchanged quickly. The rigid scope can isolate a bleeding lung or core out tumor. FOB can be used concomitantly to localize the bleed without compromising ventilation or facilitate use of the endoscopic therapies described below (6). Unfortunately, not all bronchoscopists are trained in rigid bronchoscopy, and rigid scopes are not available in all bronchoscopy suites.

Once the patient's airway and circulation are stabilized, additional history can be obtained, including the patient's procedural history and current medication list. Coagulopathies should be corrected. The interventional radiology, interventional pulmonology, and thoracic surgery teams should be kept apprised of the patient's status so that

multidisciplinary decisions can be made.

Diagnosis & localization

While chest radiography can generally depict the site of bleeding in 45% to 65% of cases of massive hemoptysis, FOB or computed tomography (CT) are more likely to localize a bleed (3). Revel *et al.* reviewed chest X-rays and CT scans from 80 patients with "large" or "massive" hemoptysis. The site of bleed was identifiable on 46% of plain films compared to 70% of CT scans. FOB was performed in 73 of the 80 patients and identified the site of bleed in 73% of patients. When assessing diagnostic yield, however, the authors found that the cause of bleeding was identified on 35% of chest X-rays, 77% of CT scans, and only 8% of bronchoscopies, suggesting that CT is superior to bronchoscopy as a diagnostic tool (7). The authors did point out that bronchiectasis, post-tuberculous lesions, and aspergillomas accounted for more than half of the causes of bleeding in the study.

In another study looking at 40 cases of hemoptysis with normal bronchoscopy, abnormalities were seen on subsequent CT scan in 50% of cases (8). Similarly, in a prospective study comparing CT to bronchoscopy in 91 cases of hemoptysis, CT identified the 27 tumors seen on bronchoscopy plus seven additional lesions. CT also found 14 cases of bronchiectasis that were not detected on FOB (9). Unfortunately, CT requires the patient to be stable enough to travel to the scanner. In unstable patients or in patients with bilateral lung abnormalities, FOB with possible endobronchial management seems to be the optimal initial approach (2).

Treatment

Endobronchial therapies

Treatment of massive hemoptysis often begins with instillation of chilled saline or vasoactive agents through flexible or rigid bronchoscopes. Conlan and Hurwitz first described use of cold saline for the management of 12 cases of massive hemoptysis in 1980. Rigid bronchoscopy was used to clear the airway of blood and clot, then to intubate and ventilate of non-bleeding lung. Next, the scope was moved to the mainstem of the bleeding lung. The lung was irrigated with normal saline chilled to 4-degree C in 50-mL aliquots. Suction was applied 30 to 60 seconds after each instillation. Between each lavage, the rigid bronchoscope was returned to the mainstem of the non-bleeding lung for ongoing ventilation, though this is not necessary when using a scope with distal ventilating fenestrations. In all 12 patients, bleeding stopped during the bronchoscopy and lavage. Two patients required repeat bronchoscopy and lavage for rebleeding at three days and 10 days, and one patient had an episode of bradycardia during lavage. Three patients ultimately underwent surgery and several others were started on medical therapy. All were discharged free of hemoptysis (10).

Vasoactive agents, including vasopressin analogs, epinephrine, and norepinephrine, have been used to treat hemoptysis following transbronchial lung biopsies. Doses and dilutions of these agents vary, but doses as low as 0.1 mg of epinephrine have been associated with high drug plasma levels and cardiac arrhythmias (1,2,6). Fortunately, over the past two decades, advances in interventional pulmonology have led to safer alternatives and novel approaches to the endoscopic management of massive hemoptysis. Most of the treatment strategies described below have been introduced in case reports and series and have not yet been validated in large, randomized controlled trials. Many do, however, demonstrate promising results with minimal side effects.

Thermal ablative techniques

Argon plasma coagulation (APC)

APC is a non-contact form of electrocoagulation that allows for rapid coagulation of target tissue. It was first used for bleeding in open surgery, laparoscopy, and in gastrointestinal endoscopy. APC uses electrically conductive gas (argon plasma) to deliver a high-frequency current from a flexible probe to the desired tissue, ablating it and promoting hemostasis. It works on tissues with high water content and low electrical impedance. Once bleeding has stopped, the bronchial wall is less conductive, and deeper tissues are not penetrated (2) (*Figure 1*).

In 2001, Morice *et al.* published a review of the efficacy of APC in the bronchoscopic treatment of hemoptysis. The study included 60 patients who underwent 70 FOB procedures to treat hemoptysis and/or neoplastic airway obstruction. Only six patients had severe bleeding of more than 200 mL per day. Bleeding in all cases stopped after APC with no recurrence for a mean of 97±91.9 days (11). Additional investigation is needed to determine if APC is as successful in larger volume hemoptysis. When APC is applied, we recommend forced mode, 20–40 W, 0.8–1.4 LPM via 2.3 mm straight fire, though a pulsed mode also can be utilized.

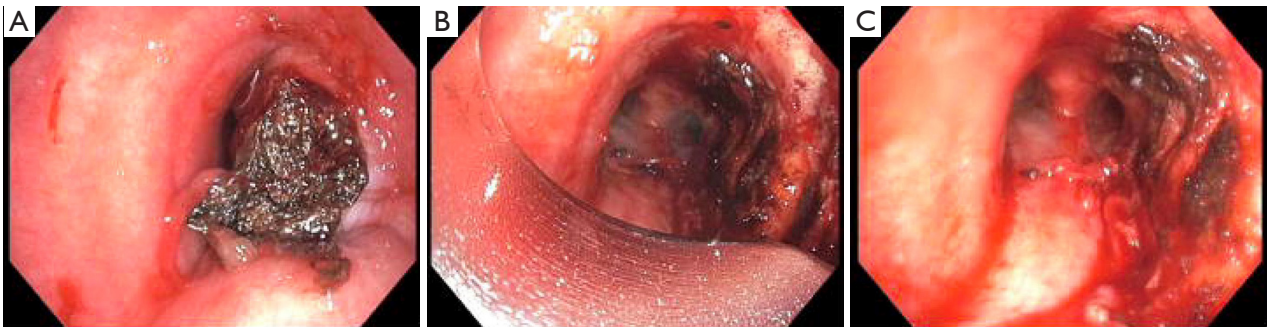

Figure 1 Images from the application of APC. (A) A patient presented with hemoptysis from a large tracheal mass. APC and mechanical debulking were performed to clear the airway and control bleeding. (B,C) The same patient after therapy. APC, argon plasma coagulation.

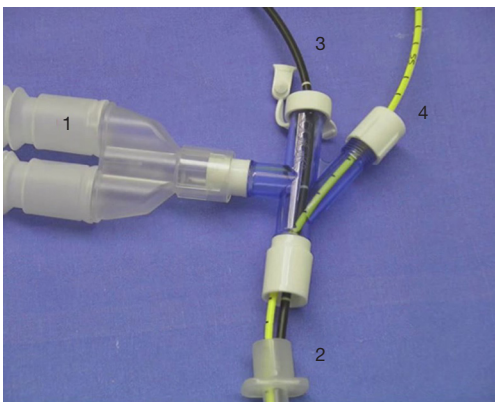

Figure 2 Endobronchial blocker. Image guide: [1] ventilator connector; [2] endotracheal tube adapter; [3] bronchoscope; [4] endobronchial blocker.

Electrocautery

Electrocautery is an ablative method used to debulk endobronchial tumors and treat related bleeding. It applies direct electrical energy to the target tissue, producing heat, coagulation, and necrosis. There are no large studies to date describing its use as a bronchoscopic tool in massive hemoptysis (1,2).

Laser therapy

Laser photocoagulation was introduced by Dumon *et al.* in the early 1980s (12). While most often used to debulk tumors, it also has been applied in the treatment of hemoptysis (13,14). The Nd:YAG and Nd:YAP lasers are most commonly used in bronchoscopy and have wavelengths of 1,060 and 1,340 nm, respectively. The lasers use light energy to produce heat in target tissues, resulting in photocoagulation, vaporization, and necrosis (3). While APC can more rapidly ablate a larger area, laser photocoagulation can penetrate deeper into tissues. Han *et al.* conducted a retrospective review of laser photocoagulation use in patients with central airway tumor. Of 110 patients, 52 presented with hemoptysis. Following laser treatment, bleeding completely resolved in 77% of patients and partially resolved in 17%. No procedure-related mortality was reported (13). For the Nd:YAG laser, we utilize 20 W/30 Hz with a pulse duration of 0.5–1 as a starting setting.

With each of the ablative methods described above, the patient's FiO2 must be reduced to 40% prior to use to minimize the risk of airway fire. Therefore, these therapies are not recommended in patients unable to tolerate a decrease in oxygen delivery.

Bronchial-blocking balloon catheters

Balloon catheters have been used for decades to tamponade bleeding in the lung and prevent asphyxiation. Large Foley catheters can be inserted into a mainstem bronchus to isolate a bleeding lung, but smaller transbronchoscopic catheters allow for more targeted blockade of segmental bronchi (2) (*Figure 2*).

In the early '90s, Freitag *et al.* developed and tested a dual-lumen balloon catheter that could be inserted through the working channel of a fiberoptic bronchoscope. The second lumen was added to allow for ongoing administration of topical agents (2). They utilized 30 catheters in 27 patients over a 36-month period. Underlying diagnoses included malignancy, tuberculosis, aneurysm or vascular deformity, silicosis, and bronchiectasis. All patients had lost at least 100 mL of blood prior to balloon deployment. Blockers were left in place for 15 minutes to 7 days, until more definitive treatment (chemotherapy, radiation, surgery, embolization, antibiotics) could be

pursued. Bronchial blockade was successful in all but one case, in which balloon placement was not possible due to tumor location (15).

Silicone spigots

The Endobronchial Watanabe Spigot (EWS) was first used for bronchial occlusion in cases of intractable pneumothorax and bronchopleural fistula (16). It has now been reported as an effective bronchial blocker in cases of massive hemoptysis. The EWS is an endobronchial plug with studs on the outside to prevent migration. It comes in three sizes: small (5 mm), medium (6 mm), and large (7 mm) (17). EWS is most typically employed as a temporizing measure until BAE or surgery can be performed, but there are case reports detailing its use as definitive therapy (18,19).

Sakaguchi *et al.* recently used an EWS in a patient who was not a candidate for surgery or BAE. The patient was status post aortic valve replacement and coronary artery bypass grafting and developed massive hemoptysis while being weaned from venoarterial extracorporeal membrane oxygenation (ECMO) in the post-operative setting. The bleed was localized to B3, B4, and B5 bronchi via emergent FOB. Three silicone spigots were inserted into each of the bronchi using forceps. Bleeding was controlled, and he was able to be weaned from the vent and from ECMO just days later. The spigots were removed six weeks later, and hemoptysis never recurred (19).

In most reported cases, silicone spigots are inserted into the bronchus using forceps. However, other insertion techniques have been described, including insertion by curette. In a retrospective review, Morikawa *et al.* studied EWS-based bronchial occlusion procedures performed in 18 consecutive patients. In each case, the bronchoscopist used a Cytology Curette (Olympus Medical Systems) to position the spigot in the target bronchus. Time to EWS occlusion ranged from 65 to 528 seconds, and 93.5% were completed within 5 minutes. All EWS insertions were successful (17). The authors proposed that insertion by curette improves bronchoscopic flexibility and efficiency. Using a curette, the spigot can be easily turned, while forceps can be difficult to navigate into the targeted bronchus (17). Others have raised concern that a silicone spigot inserted by curette may not be able to withstand the pressure of bronchial bleeding and may be difficult, if not impossible, to remove later (20).

It is unclear how long silicone spigots should remain in place once hemostasis is achieved, but, as with any foreign body, they pose a risk of infection. Studies looking at permanent EWS and rates of infection in cases of fistulous lung disease have been conflicting (20). Studies are needed to investigate the risk of infection associated with long-term EWS use.

Endobronchial valves (EBVs)

EBVs were initially designed to reduce lung volume in severe emphysema, but they also have been effectively utilized in the management of bronchopleural fistulas. The one-way endobronchial valve allows air to flow out of a segment of lung during exhalation without allowing air to flow back in during inhalation, leading to atelectasis of an isolated lung segment (21). There are now a handful of published case reports describing successful application of EBVs in persistent or massive hemoptysis.

Lalla *et al.* recently described a case of massive hemoptysis in a young, HIV-positive male with pulmonary tuberculosis and a left upper lobe (LUL) cavitary lesion. The source of bleeding could not be identified by angiography, and he was deemed a poor surgical candidate. After days of conservative management, massive hemoptysis recurred during a spontaneous breathing trial. On repeat angiography, two abnormal vessels were identified, one of which was embolized. His hemoptysis continued, so the decision was made to intentionally collapse the LUL. A Zephyr EBV was implanted into the LUL bronchus distal to the lingula. Chest X-ray showed an atelectatic LUL with preservation of aeration in the lingula. The patient was extubated 48 hours later with no further hemoptysis. The valve was electively removed at six months with no complications (22).

There are at least three other published cases of EBV use in the management of persistent hemoptysis, however, this appears to be the only case to date describing an application in massive hemoptysis. Proposed mechanisms for the efficacy of EBVs in hemoptysis include the bronchial blockade achieved by the valve itself, the pro-thrombotic effect of the valve, the tamponade effect of lobar atelectasis, and the hypoxic vasoconstriction caused by lobar atelectasis. It is likely some combination of these mechanisms that slows or stops the bleeding (21).

Endobronchial sealing

Endobronchial sealing using biocompatible, quick-drying glue to control hemoptysis has been reported (23-25). In 2002, Bhattacharyya *et al.* described the use of n-butyl cyanoacrylate glue in six patients with persistent hemoptysis. In each case, FOB was performed under mild sedation, and a polyethylene catheter was passed through

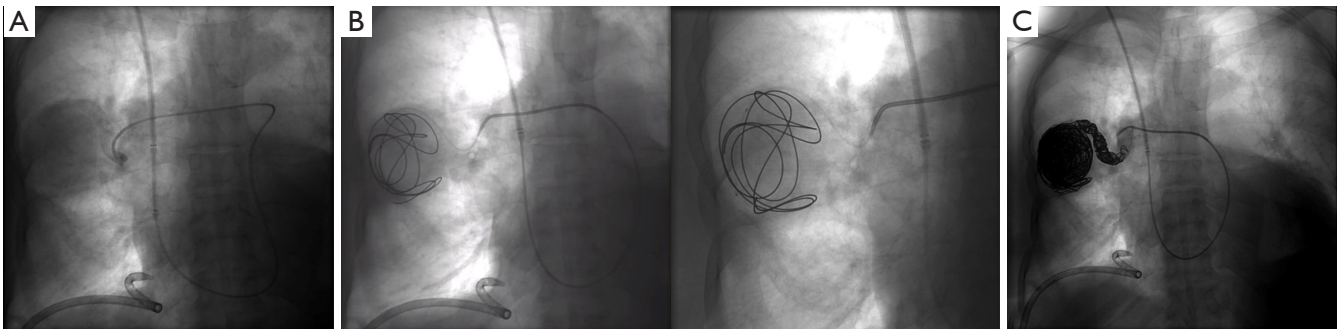

Figure 3 AVM embolization by interventional radiology. (A) An 86-year-old female presented with massive hemoptysis and underwent embolization of a large AVM. In this case, the right internal jugular vein was accessed, and a catheter was advanced to the right upper lobe branch of the pulmonary artery. A chest tube, used to treat an iatrogenic hemothorax resulting from a prior embolization attempt, is in place on the right. (B) Multiple detachable coils were used to coil the AVM. (C) A post-embolization arteriogram showed no antegrade flow in the AVM. AVM, arteriovenous malformation.

the scope's working channel. Next, 0.5 mL of glue was injected through the catheter with a water column behind. The patients required a total of 0.5 to 1.5 mL of glue to achieve hemostasis. While patients reported expectoration of glue particles in the days following the procedure, no major complications occurred, and no rebleeding was noted during the follow-up period (70 to 250 days) (23).

Coiffard *et al.* used cyanoacrylate-based glue to occlude the site of bleeding in a patient who had already failed two attempts at BAE and EWS placement. The authors injected 2 mL of glue mixed 50-50 percent with iodinated contrast to facilitate fluoroscopic guidance. A flush of saline was used to advance the glue into sub-segmental bronchi. The bleeding stopped and did not recur during her hospitalization (24).

Ryu *et al.* applied endobronchial sealing to treat massive hemoptysis resulting from a silicone Y-stent complication. Following airway stabilization and stent removal, the authors placed oxidized regenerated cellulose to achieve hemostasis, then applied polyethylene glycol polymers over top as surgical glue. The bleeding stopped and had not recurred two years after removal of the stent (25).

Endovascular therapies

Bronchial artery embolization (BAE) was introduced as a diagnostic and therapeutic tool for the management of massive hemoptysis in the mid-1970s (26). Since that time, BAE has been routinely used by interventional radiologists as a temporizing measure or as definitive treatment for massive hemoptysis.

First, a descending thoracic aortogram is used to map the bronchial arteries. In CF, ascending aortography or selective subclavian/innominate arteriography may also be needed to identify apical collaterals that have formed over time (4). Bronchial artery selection is performed by injecting iodinated contrast through a 4- or 5-French catheter. Active extravasation of contrast is seen in only 10% to 15% of cases (6,27). Other targets for embolization include tortuous or hypertrophied vessels, hypervascularity, aneurysms, and arteriovenous malformations (AVMs). Next, a "superselective" 3-French microcatheter is inserted through the initial catheter to advance distally and catheterize target vessels. Embolization is performed using gelatin sponge, microspheres, polyvinyl alcohol particles, liquid embolic agents like cyanoacrylate glue, or metallic coils (1,28) (*Figure 3*).

In 2017, Panda *et al.* published a systematic review of 22 studies reporting on BAE use in hemoptysis. They found that BAE resulted in immediate clinical success (complete cessation of bleeding within 24 hours) 70% to 99% of the time. The preferred embolization agent was polyvinyl alcohol particles (size 300–600 micrometers), a permanent occluding agent. Unfortunately, rebleeding occurred in 10% to 57% of cases. Higher rates of rebleeding were seen in cases of aspergillomas and reactivated or multidrug-resistant tuberculosis (29). Recurrence was attributed to incomplete embolization, recanalization of previously embolized arteries, and development of new collaterals. Risk factors for recurrence included presence of nonbronchial systemic collaterals and bronchopulmonary shunting, which are commonly seen in patients with chronic hypoxia and bronchial inflammation (4).

Han *et al.* looked specifically at the safety and efficacy

of BAE in primary lung cancer-related hemoptysis. In a retrospective review of 84 cases of hemoptysis, technical success, or the ability to successfully embolize the abnormal vessel, was achieved in 98.8% of patients. Clinical success, defined as complete or partial resolution of hemoptysis, was achieved in 82.1% of patients. The median hemoptysis-free survival period for patients was 61 days, however, massive hemoptysis was a risk factor for reduced hemoptysis-free survival post-BAE (HR, 1.83; P=0.12). The authors proposed that massive hemoptysis in patients with lung cancer may be related to neovascularization and new, friable bronchial arteries with higher likelihood of rebleeding (26).

Major complications from BAE are rare with a median incidence of 0.1% (28). These include stroke and spinal cord ischemia from accidental embolization of an anterior medullary spinal artery (27). Additional complications to consider are femoral access site complications and contrast nephropathy.

Tranexamic acid (TXA)

TXA is a synthetic antifibrinolytic agent approved for the treatment or prophylaxis of bleeding in patients with hemophilia and perioperative bleeding associated with major surgeries (3). In these settings, TXA is given orally or intravenously. In 2009, Solomonov *et al.* published a case series describing the use of topical TXA in six patients with massive hemoptysis. Two patients developed bleeding after biopsy and received a single bolus of 500 mg/5 mL through the working channel of the bronchoscope. The other four bled spontaneously (lung cancer, diffuse alveolar hemorrhage, idiopathic, metastatic thyroid cancer) and received 500 mg/5 mL by inhalation three to four times daily. In all patients, bleeding stopped with the first dose, and no adverse events were reported (30).

Hankerson *et al.* reported on the use of a nebulized TXA in a patient with an invasive laryngeal tumor. A 10 mg/mL nebulized TXA solution was delivered continuously to his mouth and tracheostomy via facemask. Bleeding stopped within 15 minutes, and the patient experienced no side effects (31).

Recent studies have demonstrated a role for the early use of TXA in trauma patients and in postpartum hemorrhage to decrease mortality (32). A prospective study published in *Chest* in 2018 also found TXA to be safe and effective in controlling non-massive hemoptysis. Wand *et al.* conducted a double-blind, randomized controlled trial comparing the use of nebulized TXA (500 mg three times daily) versus placebo (normal saline) in patients admitted with hemoptysis. Patients with massive hemoptysis, defined as more than 200 mL in 24 hours, were excluded. A total of 47 patients were randomized to receive TXA (n=25) or normal saline (n=22). TXA was associated with a significantly reduced volume of expectorated blood by hospital day two, and its use was associated with shorter hospital length of stay and fewer invasive procedures. No side effects were reported (33).

Al-Samkari *et al.* developed and tested a clinical treatment pathway for systemic antifibrinolytic agent use in CF patients in the inpatient and outpatient setting. Seventy-two episodes of hemoptysis in a total of 21 adult patients with CF were treated according to the pathway. Two-thirds of episodes were considered moderate or massive hemoptysis. Outpatient treatment resulted in a 50% reduction in annual hemoptysis-related admission rate (32).

In studies to date, the use of topical/inhaled TXA for hemoptysis has generally been associated with few adverse events and positive outcomes. However, we recommend its use only in cases of mild to moderate hemoptysis without any imminent threat to airway stability. This includes, for example, patients with mucosal oozing and mild hemoptysis in the setting of thrombocytopenia.

Surgery

Surgical management is an option for most patients with massive hemoptysis, but it is less commonly first-line therapy. Surgery is still the treatment of choice in cases of iatrogenic pulmonary artery rupture, chest trauma, and aspergillomas resistant to other therapies (1). Mortality rates associated with emergency surgery can approach 50% (1,34,35), but rates are significantly lower when surgery is scheduled or planned. Risk factors for poor surgical outcome include advanced age, pleural adhesions, complete pneumonectomy, bronchiectasis, and broncholithiasis (36). The endovascular and endoscopic interventions described above often serve as temporizing measures to bridge to definitive operative management.

Conclusions

Over the past several decades, the management of massive hemoptysis has evolved to include innovative endovascular and endoscopic therapies that, either alone or in conjunction with well-planned surgical interventions, can achieve hemostasis and save lives. We anticipate that the safety and

efficacy of these tools and others will be evaluated by large-scale studies as the fields of interventional pulmonology and radiology continue to grow.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to disclose.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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