

Managing Massive Hemoptysis

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Massive hemoptysis is a medical emergency with high mortality presenting several difficult diagnostic and therapeutic challenges. The origin of bleeding and underlying etiology often is not immediately apparent, and techniques for management of this dangerous condition necessitate an expedient response. Unlike hemorrhage in other circumstances, a small amount of blood can rapidly flood the airways, thereby impairing oxygenation and ventilation, leading to asphyxia and consequent cardiovascular collapse. Of paramount importance is early control of the patient's airway and immediate isolation of hemorrhage in an attempt to localize and control bleeding. A coordinated team response is essential to guarantee the best chances of patient survival. Prompt control of the airway and steps to limit the spread of hemorrhage take precedence. Bronchial artery embolization, rigid and flexible bronchoscopy, and surgery all serve as potential treatment options to provide definitive control of hemorrhage. Several adjunctive therapies described in recent years may also assist in the control of bleeding; however, their role is less defined in life-threatening hemoptysis and warrants additional studies. In this concise review, we emphasize the steps necessary for a systematic approach in the management of life-threatening hemoptysis. CHEST 2019; ■(■):■-■

KEY WORDS: bronchial artery embolization; bronchoscopy; hemoptysis; life-threatening hemoptysis; massive hemoptysis

Massive or life-threatening hemoptysis is among the most ominous clinical presentations in medicine and was feared since antiquity as a harbinger of impending demise because of TB or cancer.¹ Patients presenting with massive hemoptysis present an immediate diagnostic and therapeutic challenge. Historically, few therapeutic options were available, with mortality > 75% with conservative management alone; therefore, surgery gained a prominent life-saving role.^{2,3} In 1978, Garzon and Gourin³ published outcomes for a series of patients with massive hemoptysis over a decade

demonstrating an improvement in mortality to 17% with early operative intervention. Q8

Over the last 50 years, advances in medical imaging, fiberoptic technology, and interventional radiology have improved patient outcomes and reduced mortality. Whereas historical management was conservative with an emphasis on emergent surgery, bronchial artery embolization (BAE) has emerged as an effective minimally invasive means to control massive hemoptysis.^{4,5} The literature reveals an improvement in mortality for massive hemoptysis to 13% to 17.8%.⁶⁻⁸ Critical to

ABBREVIATIONS: BAE = bronchial artery embolization; ETT = endotracheal tube; TXA = tranexamic acid

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the successful management of patients with hemoptysis is a knowledge of the precipitating causes of hemoptysis and the importance of a prompt and coordinated response to synchronize efficient care for these patients.

Massive hemoptysis was previously defined as a specific volume of expectorated blood within a particular period of time. However, approximating the amount of hemoptysis is challenging, and frequently over- or underestimated. Prior definitions for massive hemoptysis ranged quite widely from 200 to 1,000 mL/24 h and were an ongoing source of debate.^{9,10} Instead, additional clinical factors such as the briskness of bleeding, ability of a patient to maintain a patent airway and expectorate blood, the swiftness of available therapeutic options, and the patient's underlying physiological reserve are far more important. These more significant variables underscore the concept of the magnitude of effect definition for massive hemoptysis. Within this context, any degree of hemoptysis causing clinical consequences such as respiratory failure from airway obstruction or hypotension is considered life-threatening hemoptysis.¹ This definition relies on the main clinical consequence of hemoptysis—hemoptysis resulting in aspiration of blood to the contralateral lung, airway obstruction, hypoxemia requiring mechanical ventilation, transfusion, and death.^{1,11,12} One limitation of this definition is that it excludes a population with optimal respiratory reserve who can efficiently expectorate large volumes of blood, and remain clinically stable during the initial stages of life-threatening hemoptysis. Such instances should be managed with equal efficiency, assuming that clinical instability will follow if management is not expedited.

Among cases of fatal hemoptysis, the inciting cause of death is not hemorrhagic shock, but asphyxiation from inability to oxygenate or ventilate because of hemorrhage flooding the airways. The total volume of the conducting airways averages 150 mL in adults.¹³ Therefore, a given hemorrhage that may be regarded as mild from another location can briskly become life threatening in the airways.

The existing literature on hemoptysis spans over a century. Most studies are retrospective, single-centered, and include a heterogeneous population of patients, including combinations of different etiologies and different categories of hemoptysis while often including both minor and massive hemoptysis in the same cohort. Selection bias, small sample size, and limited internal and external validity are among the major limitations of

most studies in this area. This, in addition to the changing prevalence of hemoptysis in different regions of the world, should be taken into account when reviewing the literature on massive hemoptysis.

Epidemiology and Prognostic Factors

Although hemoptysis is a common cause of outpatient pulmonary clinic visits and hospital admissions, massive hemoptysis is relatively uncommon.¹¹ TB, bronchiectasis, mycetoma, and cancer are the leading etiologies of massive hemoptysis.^{11,14} Among regions of the world with a high endemic burden of TB, it is the dominant cause of hemoptysis and remains the most common cause of massive hemoptysis worldwide.¹⁵ Iatrogenic hemoptysis occurring from procedures is reported in 0.26% to 5% of diagnostic bronchoscopies; however, massive hemoptysis complicates only a minute fraction of these procedures.¹⁶ Although 20% of patients with lung cancer are estimated to experience hemoptysis at some point in their clinical course, massive hemoptysis affects only 3% of this population.^{17,18} Up to 80% of patients with malignancy-related massive hemoptysis present with episodes of sentinel bleeding during the weeks prior to their event.¹⁹ Table 1 lists etiologies of life-threatening hemoptysis.

Mortality in patients with hemoptysis is higher in several groups. In a study of 1,087 patients with hemoptysis, a mortality risk score was developed based on factors independently associated with increased mortality.¹² One point was assigned for chronic alcoholism, pulmonary artery involvement, or hemorrhage affecting two or more quadrants on chest radiograph, whereas 2 points were assigned for aspergillosis, cancer, or need for mechanical ventilation. The cumulative total score predicted increasing mortality ranging from 1 point (2% mortality) to 7 points (91% mortality). Additionally, baseline medical conditions including reserve pulmonary function and presence of underlying organ failure have a substantial impact on mortality from life-threatening hemoptysis.²⁰ Conditions such as aspergilloma, bronchiectasis, and cancer also carry a higher hemoptysis-related mortality because of increased risks of recurrent hemoptysis.²¹

Procedural Preparedness and Prevention

Life-threatening hemoptysis may occur either as a new presentation or as an iatrogenic complication during an invasive procedure. Procedural risks of hemoptysis can be decreased by carefully selecting patients for invasive

Q20 **TABLE 1**] Etiologies of Life-Threatening Hemoptysis

221	Cardiac
222	Congenital heart disease
223	Congestive heart failure
224	Mitral stenosis
225	
226	Iatrogenic
227	Aortobronchial fistula from erosion of an aortic graft or
228	aneurysm
229	Endobronchial brachytherapy
230	Erosion of airway stent
231	Lung transplantation
232	Mediastinal or lung radiation therapy
233	Pulmonary artery rupture from right-sided heart
234	catheterization
235	Pulmonary laceration from chest tube placement or
236	thoracentesis
237	Pulmonary vein stenosis after radiofrequency ablation
238	Thrombolytic therapy
239	Tracheoinnominate artery fistula after tracheostomy
240	Transbronchial lung biopsy or cryobiopsy
241	Transthoracic needle aspiration
242	
243	Infectious
244	Aspergillosis and other mycetomas
245	Bacterial and viral bronchitis and pneumonia
246	Lung flukes and parasites
247	Necrotizing pneumonia and lung abscess
248	TB
249	
250	Medications
251	Anticoagulants (ie, heparin, warfarin, dabigatran,
252	enoxaparin, apixaban)
253	Antiplatelets (ie, clopidogrel, ticagrelor, prasugrel)
254	Bevacizumab
255	
256	Miscellaneous
257	Blast injury
258	Cocaine abuse
259	Foreign body aspiration
260	Idiopathic/cryptogenic
261	Trauma
262	
263	Pulmonary
264	Bronchiectasis
265	Broncholithiasis
266	Lymphangioleiomyomatosis
267	Malignancy
268	Pulmonary embolism and infarction
269	
270	Rheumatologic
271	Diffuse alveolar hemorrhage from vasculitis:
272	granulomatous polyangiitis, Goodpasture syndrome,
273	Behçet disease, systemic lupus erythematosus, and
274	cryoglobulinemia
275	
276	Vascular
277	Arteriovenous malformations, including hereditary
278	hemorrhagic telangiectasia
279	Pulmonary artery aneurysm
280	Ruptured thoracic aneurysm

procedures such as bronchoscopic lung biopsies and by performing lung biopsies in dependent lung regions when feasible to facilitate hemostasis without spillage of

blood into adjacent lung segments. Continuation of low-dose aspirin prior to most bronchoscopic procedures is acceptable and safe. However, we recommend against the use of clopidogrel and warfarin, alone or in combination, prior to transbronchial lung biopsy. In a comparative prospective study of 1,217 patients, Herth et al²² demonstrated that low-dose aspirin did not increase risk of bleeding during transbronchial lung biopsy. A prospective study by Ernst et al²³ showed significantly higher risk of bleeding in 18 patients on clopidogrel undergoing transbronchial lung biopsies—89% compared with only 3.4% in control subjects. A combination of aspirin with clopidogrel was associated with either moderate or severe hemorrhage in every instance. The study was stopped early because of serious bleeding complications.

Uremia from renal failure is also recognized as a risk factor for coagulopathy because of uremic platelet dysfunction.²⁴ However, there are limited data on the risks uremia poses specifically for procedural hemoptysis. Some recommend desmopressin as an adjunct to mitigate this risk because it has been proven to decrease bleeding time in patients with uremia in small studies.^{25,26} Limited data exist on the safe minimum threshold for platelet count when performing endobronchial or transbronchial lung biopsies.²⁷ Papin et al²⁸ reported a series of 24 patients with thrombocytopenia (mean platelet count, 30,000/mm³ ± 16,500/mm³) undergoing transbronchial lung biopsies wherein 20.8% had bleeding complications. Pulmonary hypertension is also regarded as a relative contraindication for transbronchial biopsies. However, in a retrospective study of 107 patients with pulmonary hypertension suggested by elevated right ventricular systolic pressure on echocardiography, no increased risk of bleeding with transbronchial biopsy or endobronchial ultrasound-guided transbronchial needle aspiration was noted, compared with 83 patients in a control group with nonelevated right ventricular systolic pressure.²⁹

Transbronchial cryobiopsy has emerged as an alternative to surgical lung biopsy in the diagnosis of diffuse parenchymal lung disease.^{30,31} However, because of the elevated risk of major hemorrhage, expert consensus suggests routine use of a bronchial blocker or Fogarty balloon to isolate procedural bleeding in patients who are intubated.³⁰ In addition, some protocols recommend performing this procedure with rigid bronchoscopy to allow for immediate control of any significant hemorrhage.³¹

TABLE 2] Massive Hemoptysis Toolkit and Management Plan Checklist

Intubation tray with range of endotracheal tubes including sizes \geq 8.5 mm
Therapeutic flexible bronchoscope with large working channel, diagnostic and pediatric flexible bronchoscope to aid with bronchial blocker placement, rigid bronchoscope when skills and expertise are available
Bronchial blocker and ice-cold saline
Prompt transfer to ICU
Large-volume IV to allow rapid volume resuscitation and radiocontrast injection
Patient coagulation parameters including type and screen
Prompt page to pulmonology/interventional pulmonology for airways stabilization and management, interventional radiology for bronchial artery embolization, and thoracic surgery for potential surgical evaluation
Prompt availability of CT scan
Cryotherapy probe for blood clot extraction
Electrocautery or argon plasma coagulation for ablation of endobronchial lesions

A standardized algorithm for response to hemoptysis includes readily available iced saline for local control of hemorrhage, a bronchial blocker for prevention of blood spillage to contralateral airways, balloon tamponade, and intubation supplies with larger-sized endotracheal tubes (ETTs) immediately accessible and confirmed. **Table 2** shows a checklist of tools required and important actions necessary to improve emergency preparedness and rapid response to bleeding emergencies.

Many of the advanced techniques to control hemoptysis require expertise and specialized equipment.³² Management of massive hemoptysis should be approached in a multidisciplinary fashion. A group of respiratory therapists, interventional radiologists, intensivists, pulmonologists, and surgeons should comprise a hemoptysis response team. Because massive hemoptysis is uncommon and often encountered unexpectedly, we suggest that life-threatening hemoptysis management algorithm simulations and drills be implemented in every institution that cares for patients with massive hemoptysis, and in any procedural unit, where risk of hemoptysis exists.

Pathophysiology

To understand the management of massive hemoptysis, an in-depth knowledge of the pulmonary vascular

anatomy is required. The lungs are perfused with twin blood supplies: deoxygenated blood in the pulmonary arteries at lower pulmonary pressures (mean pulmonary artery pressure, 12-16 mm Hg) and oxygenated blood flowing within the bronchial arteries at systemic pressures (mean arterial pressure, 100 mm Hg).³³ Over time, inflammation, hypoxia, and neoplasia can incite proliferation of bronchial vasculature via secretion of proangiogenic factors such as vascular endothelial growth factor and angiopoietin-1.³⁴ New vessels are usually thin-walled and fragile, are exposed to increased systemic arterial pressures, and are prone to rupture into the airways resulting in hemoptysis. It is estimated that 90% of cases of massive hemoptysis emanate from the bronchial vasculature.³⁵ Therefore, BAE has emerged as an exceedingly useful minimally invasive tool in the management of hemoptysis. Additional recruitment of nonbronchial collateral vessels can occur from ectopic sites such as adjacent intercostal arteries, inferior phrenic arteries, the thyrocervical trunk, internal mammary arteries, and subclavian arteries among other sites.³⁶ Multidetector CT scan has been proven to be highly effective in localizing bleeding from normal or ectopic bronchial arteries.³⁵⁻³⁷

Initial Evaluation

When a complete history and physical examination is permitted, the clinical time line and coexistent symptoms may provide valuable clues for the origin of hemoptysis. The diagnostic workup should follow immediately after airway and hemodynamic stabilization. The presence of infectious symptoms, recent surgical procedures, administration of anticoagulant or antiplatelet medications, and history of malignancy, TB, or underlying pulmonary disease could be very revealing as to suspect causes. Additionally, epistaxis and hematemesis should be considered and ruled out as other potential sources of blood.

Distinguishing the side of culprit bleed is vital in life-threatening hemoptysis because the decision to lateralize, placing the bleeding side into a dependent position, is one of the most important first steps in stabilization. To determine the side of bleeding, chest radiograph is known to have limited sensitivity.³⁷⁻³⁹ In a study of 80 patients with large or massive hemoptysis, chest radiograph was able to discern the location of hemorrhage in only 46% of cases and suggested the specific cause of bleeding in only 35%.³⁷ In a separate study of 722 patients with minor and massive hemoptysis, a new diagnosis of malignancy was made in

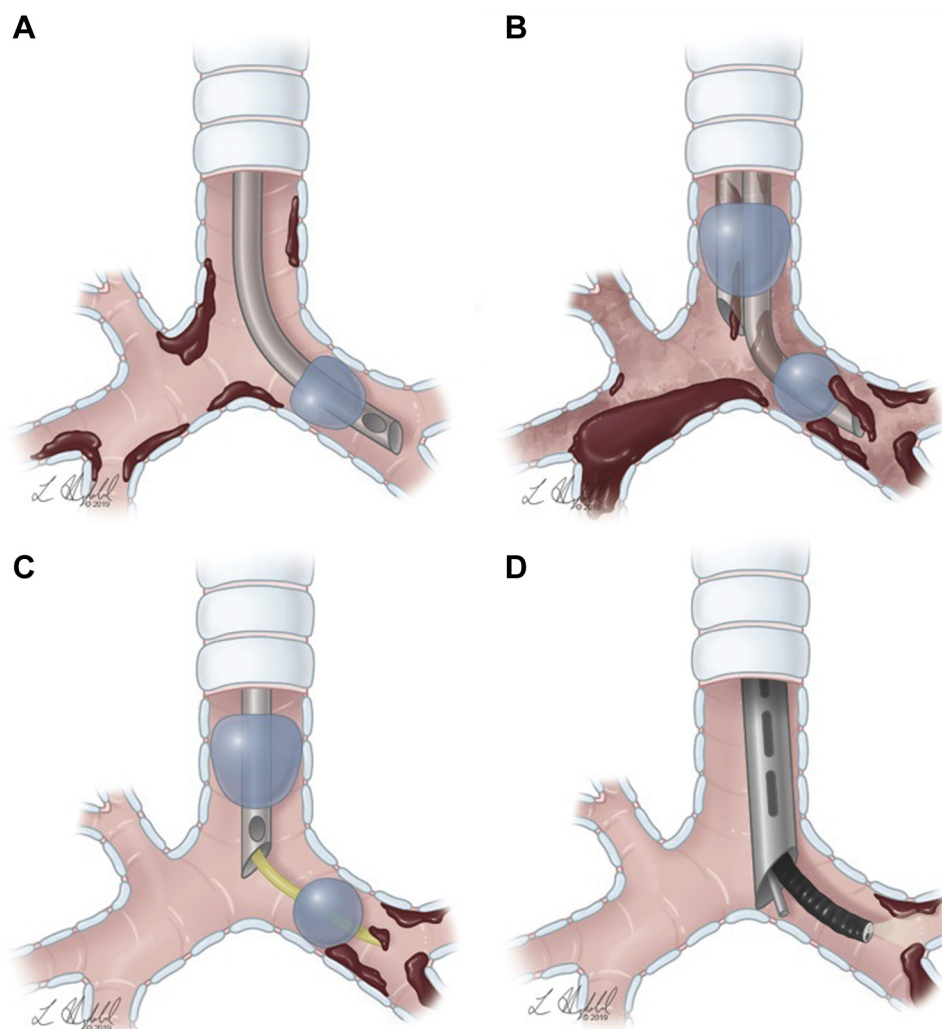


Figure 1 – A-D, Airway control in massive hemoptysis. A, A large (> 8.5 mm inner diameter) endotracheal tube (ETT) used to secure the left-sided mainstem. The diameter of the ETT accommodates a therapeutic flexible bronchoscope with a large working channel that can effectively suction any spilled blood on the left side, as depicted in the image. B, A double lumen tube (DLT) is the least optimal choice for massive hemoptysis. As illustrated in the image, the small lumens of the tube afford only passage of a smaller pediatric bronchoscope that is inefficient in clot extraction. As a result, in this image of right-sided hemorrhage with spillage of blood to the contralateral lung, the lumens of the DLT are occluded with clot and clot evacuation from either side as suboptimal. C, A bronchial blocker can be positioned to prevent spillage of blood to the contralateral side. As illustrated, the patient can be intubated with a large (≥ 8.5 mm inner diameter) ETT and bronchial blocker can secure the right-sided mainstem bronchus. This option is of particular value in the setting of left-sided hemorrhage because right-sided mainstem intubation with an ETT often leads to obstruction of the RUL origin by the ETT's inflated cuff, minimizing ventilation and oxygenation only to the right side of the middle and lower lung. D, Left-sided mainstem is intubated with rigid bronchoscope in the case of left-sided hemorrhage. The bevel of the rigid bronchoscope safeguards the right-sided airways, whereas blood can be suctioned efficiently with the use of a rigid suction catheter and therapeutic flexible bronchoscope simultaneously. As illustrated, this technique is superior in control of hemorrhage in the bleeding side, while securing the unaffected lung. Ventilation of the right side of the lung is maintained through the rigid tube's side ports, whereas ventilation also continues in the left-sided airways that are free of clots. The lumen of the rigid bronchoscope accommodates tools for therapeutic interventions such as tumor debulking, thermal ablation, and flexible bronchoscopy.

144 patients; of these, 35 patients (24%) had normal chest radiograph findings.⁴⁰

Multidetector CT scan is superior to chest radiograph in ability to identify both the anatomic origin and underlying cause of hemorrhage and to define the course of both bronchial and nonbronchial collateral arteries.^{37,38,41,42} In a retrospective study, CT scan identified the location and cause of bleeding in 70% and 77% of cases, respectively.³⁷ In a comparative

retrospective study of 400 patients with hemoptysis, Khalil et al⁴³ observed that patients who underwent multiple detector CT angiography prior to BAE were more likely to have successful resolution of hemorrhage from embolization and were also less likely to need emergent surgery.

A prospective study of 606 patients with any degree of hemoptysis found CT scan more likely to diagnose the underlying cause of hemorrhage (77.3% of cases) in

551 comparison with bronchoscopy (48.7% of cases).¹⁴ The
 552 combination of both CT scan and bronchoscopy was
 553 diagnostic of the etiology of hemorrhage in 83.9% of
 554 cases. However, the study population was of a
 555 combination of both minor and massive hemoptysis,
 556 thereby underestimating the true diagnostic ability for
 557 bronchoscopy to lateralize the side of culprit bleeding in
 558 cases of massive hemoptysis. The choice of
 559 bronchoscopy vs CT scan depends on the equipment
 560 availability, institutional practice, and patient
 561 population. Although bronchoscopy is invaluable in
 562 diagnosis and stabilization, it is not readily available in
 563 all institutions and should not delay care to a patient
 564 who is clinically stable for transfer to CT scan for
 565 efficient hemorrhage localization and a speedy transition
 566 to definitive therapies such as BAE.
 567
 568

570 Airway Stabilization and Isolation of 571 Hemorrhage

572 Immediate airway control and isolation of the bleeding
 573 airway is very important. There are several strategies for
 574 isolation of hemorrhage. If the side of bleeding is known,
 575 immediate lateralization by moving the patient into the
 576 decubitus position with bleeding side down is the first
 577 step to prevent hemorrhage from flooding into other
 578 regions of lung.⁴⁴ For massive hemoptysis, intubation
 579 with larger diameter ETTs of ≥ 8.5 mm inner diameter
 580 is recommended when possible to enable passage of
 581 therapeutic flexible bronchoscopes with large working
 582 channels that allow extraction of obstructing blood clots
 583 and placement of bronchial blockers.⁴⁵ Several strategies
 584 for placement of inflatable bronchial blockers or Fogarty
 585 balloons either coaxially through an ETT or in parallel to
 586 the tube have been described (Fig 1C).^{32,46} In the
 587 absence of balloon occlusion, selective intubation into
 588 the left- or right-sided mainstem with an ETT can
 589 isolate the lung from hemorrhage on the contralateral
 590 side. The left-sided mainstem bronchus, given its longer
 591 anatomy, is better suited to accommodate an ETT
 592 balloon cuff than the shorter right-sided mainstem
 593 bronchus, where the right side upper lobe aperture is at
 594 high risk of occlusion (Fig 1A). Nasotracheal intubation
 595 is discouraged given the inability to perform selective
 596 bronchial intubation with the foreshortened length of
 597 the ETT and limitations on the ETT size permitted via
 598 this method. Flexible bronchoscopy should be used to
 599 direct and confirm placement of bronchial blockers
 600 while performing selective intubation.⁴⁶
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Dual lumen ETTs are designed to isolate each lung and
 are commonly used in thoracic surgery; however, their

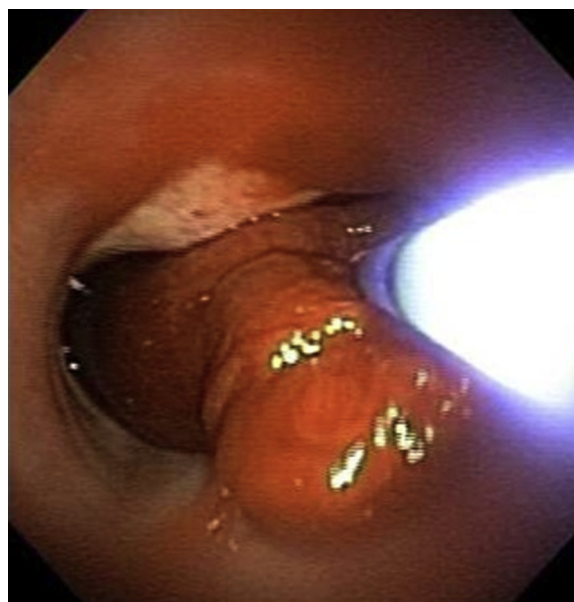


Figure 2 – Cryoprobe used to freeze and extract a large clot occluding the right- and left-sided mainstem bronchi and the trachea.

role in massive hemoptysis is obsolete because their
 narrow individual lumens do not permit efficient
 evacuation of clots or use of standard-sized flexible
 bronchoscopes with working channels large enough to
 evacuate hemorrhage and blood clots from airways (Fig
 1B).^{46,47} Immediate transfer to an ICU should be
 arranged for ongoing monitoring and treatment.

Flexible Bronchoscopy

Flexible bronchoscopy has multiple different roles in the
 setting of massive hemoptysis. Whether it is used for
 lateralization, selective intubation, bronchial blocker
 placement, clot extraction, or therapeutic purposes, its
 versatility and mobility make flexible bronchoscopy a
 valuable tool. Although the timing of flexible
 bronchoscopy in the management of patients who are
 stable with minor hemoptysis remains controversial,
 among patients who are unstable, early bronchoscopy is
 preferred to localize hemorrhage, isolate bleeding with a
 bronchial blocker, or for selective intubation and
 evacuating blood from the airways.^{11,44,48} Both CT scan
 and bronchoscopy are complementary in localization
 and diagnosis of hemoptysis.³⁸ In patients who are
 unstable where transfer is unsafe and intubation and
 lung isolation is of the utmost importance, flexible
 bronchoscopy is the procedure of choice and can be
 performed at the bedside, if available. When removal of
 large obstructing blood clots cannot be efficiently
 performed through the channel of the flexible

TABLE 3] Bronchoscopic Interventions in Management of Hemoptysis^a

Intervention	Study/Year	Location	Hemoptysis	Study Design	Result
TXA	Wand et al ⁶² /2018	Israel	Submassive hemoptysis	47 patients, prospective RCT	Patients randomized to nebulized TXA vs placebo after 24 h of hemoptysis. TXA group was more likely to have decrease in volume of expectorated blood and less likely to need interventional bronchoscopy or BAE than placebo group. Patients with MH defined as hemorrhage of > 200 mL/24 h were excluded.
TXA	Bellam et al ⁶¹ /2016	India	Submassive hemoptysis	66 patients, single blinded randomized prospective trial	Patients with submassive hemoptysis randomized to IV TXA or placebo. TXA group had decrease in hemoptysis by day 2, based on visual analog score. Patients with MH were excluded.
Gel and thrombin slurry	Peralta et al ⁵⁶ /2018	United States	Mild, moderate, or severe	13 patients, retrospective	Hemostasis attained in 10 of cases (77%).
Temporary silicone spigot	Bylicki et al ⁵⁷ /2012	France	Moderate hemoptysis	9 patients, retrospective	Spigots were definitive in only a single case but temporized bleeding and afforded time for BAE or surgery in each other case.
Temporary airway stenting	Lee et al ⁶⁰ /2012	Korea	Not stated	3 patients, retrospective	Report of 3 cases with obstructive lung cancer and hemoptysis successfully treated with airways stents.
Nd:YAG laser	Han et al ⁵⁴ /2007	Australia	Not stated	52 patients, retrospective	Nd:YAG laser was able to stop bleeding in 77% of cases and reduce bleeding in an additional 17%.
rFVIIa	Heslet et al ⁶³ /2006	Denmark	Diffuse alveolar hemorrhage	6 patients, retrospective	Hemostasis and PaO ₂ /Fio ₂ ratio improved in all 6 patients after treatment with rFVIIa given bronchoscopically as a lavage into bilateral mainstem bronchi.
Oxidized regenerated cellulose	Valipour et al ⁵³ /2005	Austria	Massive hemoptysis	57 patients, retrospective	56 of 57 patients (98%) had resolution of hemoptysis at 48 h; 9% developed postobstructive pneumonia.

(Continued)

TABLE 3] (Continued)

Intervention	Study/Year	Location	Hemoptysis	Study Design	Result
N-butyl cyanoacrylate glue	Bhattacharyya et al ⁵⁸ /2002	India	Any hemoptysis lasting > 7 d	6 patients, retrospective	Endoscopic glue stopped hemoptysis in all 6 cases, 1 with recurrent hemoptysis within 24 h.
APC	Morice et al ⁵⁵ /2001	United States	Moderate and severe or mild hemoptysis lasting > 7 d.	31 patients, retrospective	APC was effective in controlling hemoptysis in all cases; 6 patients had hemoptysis > 200 mL/24 h.
Thrombin or thrombin-fibrinogen glue	Tsukamoto et al ⁵⁹ /1989	Japan	All hemoptysis	19 of 33 patients treated with each modality, retrospective	Endobronchial thrombin application was effective in stopping hemoptysis in 6 cases (60%) and thrombin-fibrinogen was effective in 9 cases (64%).

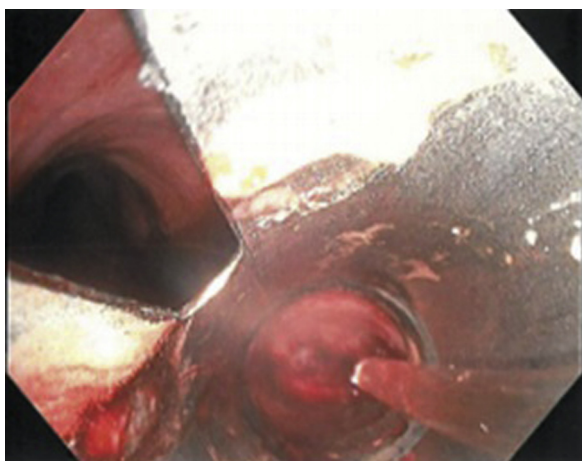
APC = argon plasma coagulation; BAE = bronchial artery embolization; MH = massive hemoptysis; RCT = randomized controlled trial; rFVIIa = recombinant activated factor VII; TXA = tranexamic acid.
^aChronological listing of literature with MH in the studied population. Case reports are excluded.

bronchoscope, clot extraction using a cryoprobe is highly effective by embedding the probe within the clot to extract the frozen adherent clot with the bronchoscope in one unit (Fig 2).⁴⁹

Bronchoscopy also allows direct instillation of medications into bleeding segments. Historically, both ice cold saline and dilutions of epinephrine have been used. Both therapies are thought to cause local vasoconstriction and have been used widely without rigorous evidence. Conlan and Hurwitz⁵⁰ described a series of 12 patients with massive hemoptysis treated with 50 mL aliquots of 4°C iced saline (300-750 mL per patient) with resolution of hemorrhage. Although Conlan and Hurwitz⁵⁰ noted transient sinus bradycardia in a single patient, there was control of hemorrhage in all patients undergoing treatment. No rigorous controlled trial has been performed to evaluate the efficacy of iced saline for control of hemorrhage. Use of iced saline has become common practice; however, instilled volumes of iced saline are typically smaller.

Endobronchial epinephrine and norepinephrine are also commonly used; however, safe dosage and concentration vary quite widely in the literature.⁵¹ In contrast to iced saline, the safety of endobronchial epinephrine has been questioned given reports of coronary vasospasm and arrhythmia.^{51,52} If used, lower concentrations of epinephrine 1:100,000 in 2 mL aliquots, not exceeding 0.6 mg, are suggested.⁵¹ Close cardiac monitoring and avoidance in patients with coronary artery disease or arrhythmia is recommended. Additionally, instilled epinephrine is quickly diluted and washed immediately away from bleeding segments by active hemorrhage. For this reason, the utility of endobronchial epinephrine in cases of life-threatening hemoptysis is questionable at best. Despite adhering to fundamental airway management principles and use of conservative measures such as iced saline lavage, most cases require additional therapy for hemostasis. Valipour et al⁵³ studied 76 patients with massive hemoptysis and found that only 13 cases (17%) had resolution of hemoptysis with such conservative measures alone.

In addition to the steps previously mentioned, flexible bronchoscopy offers other benefits whether hemorrhage is emanating from larger central airways or smaller inaccessible peripheral airways. In distal airway hemorrhage, the bronchoscope can identify the segmental bleeding airway and then be wedged into the bleeding segment to provide local tamponade until a blood clot is formed. This technique is often used in the



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Figure 3 – Left-sided airways is secured, ventilation is maintained through the side ports of the rigid bronchoscope, and right-sided hemorrhage is controlled.

setting of procedure-related hemorrhage, such as transbronchial lung biopsies, when the exact site of bleeding is known.

In instances where hemorrhage originates from the proximal airways, commonly because of malignant central airway disease, local thermoablative therapies such as electrocautery, argon plasma coagulation, or Nd:YAG laser all have demonstrated utility to provide hemostasis.^{54,55} It is noteworthy however that most causes of massive hemoptysis do not occur in the immediately accessible central airways.

Other techniques of local hemoptysis control using substrates to promote hemostasis or tamponade including oxidized regenerated cellulose, gelatin-thrombin, silicone spigots, airway stents, and polymer surgical sealants have been described.^{53,56-60} Tranexamic acid (TXA), an antifibrinolytic medication that competitively inhibits plasminogen activation, has been prospectively studied in groups of submassive hemoptysis in both IV and nebulized form. Although patients with massive hemoptysis were not included, TXA was associated with a decrease in hemoptysis and need for interventional procedures.^{61,62} Additionally, recombinant activated factor VII has also been used in cases of hemoptysis because of diffuse alveolar hemorrhage.⁶³ Table 3 lists various endobronchial techniques used in the management of massive hemoptysis. However, most available literature on massive hemoptysis is limited for several reasons including the following: small sample sizes, lack of control groups for comparison, inclusion of heterogeneous populations, and simultaneous utilization of several different therapeutic measures.

Rigid Bronchoscopy

Rigid bronchoscopy is a highly effective tool offering several benefits over flexible bronchoscopy in the management of massive hemoptysis.⁶⁴ The rigid bronchoscope provides superior airway stabilization by permitting immediate selective isolation of either mainstem bronchus while also providing ventilation.⁵⁰ Large obstructing blood clots can be quickly evacuated from the airways. Additionally, the larger channel can accommodate specialized instruments for concurrent use, such as a flexible bronchoscope, bronchial blockers, thermal ablation fibers, cautery instruments, or tools for debulking and tamponade (Figs 1D, 3). Flexible bronchoscopy is used in tandem with rigid bronchoscopy to better evaluate the upper lobes and more distal airways. Rigid bronchoscopy may not be available universally given the need for specialized equipment and training.

BAE

After successful stabilization of the airway and initial hemostasis, most patients with massive hemoptysis require definitive therapy, often in the form of percutaneous BAE. First introduced in 1972, BAE is both minimally invasive and highly effective in controlling hemoptysis.⁶⁵ Using a percutaneous approach, an arteriogram reveals the bronchial arteries that typically originate at the level of T5 and T6 from the thoracic aorta; however, collateral bronchial arteries may originate from ectopic sites. Active extravasation is found in only a minority of cases (10%-15%); however, other visible abnormalities such as tortuosity, arteriovenous malformations, aneurysms, dilation, and hypertrophy of bronchial arteries may also suggest a culprit source of bleeding. A variety of embolization agents can be used such as 300 to 600 μ polyvinyl alcohol particles, trisacryl gelatin microspheres, N-butyl cyanoacrylate glue, gelatin sponges, and metallic coils to occlude the bronchial vascular supply.^{5,65-67}

In a systematic review of BAE, Panda et al⁶⁷ examined 22 studies totaling 3,265 patients and defined the initial success rate of BAE from 70% to 99%. However, the recurrence rate for bleeding is high, estimated up to 58% within 30 days.⁶⁸ Interestingly, although the technologies to perform BAE have evolved, the rate of recurrent hemoptysis has remained unchanged.⁶⁷ Risk factors for recurrence post-BAE include bleeding from aspergillomas, TB, bronchiectasis, nonbronchial systemic collateral circulation, and bronchopulmonary shunting.^{4,67} BAE failure can be caused by recanalization

of embolized arteries, incomplete embolization of existing arteries, and development of new collateral blood supply.^{5,69} Although uncommon, the most feared complication of embolization is spinal cord ischemia because of embolism of anterior spinal arteries, estimated to occur in 1.4% to 6.5% of cases.³⁵ With improvements in imaging and highly selective embolization techniques, this complication has become less common.⁴ Other rare complications include esophageal ischemia or subintimal dissection of the aorta or bronchial arteries.

Surgical Management

Although surgery was once regarded as the only available therapy for life-threatening hemoptysis, with improvements in flexible bronchoscopy, CT scan, and interventional radiology, the indications for surgery have evolved. However, massive hemoptysis related to iatrogenic pulmonary artery rupture, complex arteriovenous malformations, or refractory hemoptysis secondary to aspergillomas, large lung abscesses, and chest trauma all remain circumstances where surgery should be considered promptly as the first line of therapy.^{44,70,71} In other circumstances, surgery remains an emergent contingency if other methods fail. Andrejak et al⁷² reviewed outcomes of 111 cases of severe hemoptysis treated with surgery and reported higher hospital mortality among cases performed emergently (34%) compared with scheduled cases after initial control of hemorrhage (4%) or planned after discharge (0%). Given the higher associated risk of surgery, initial intervention with BAE or local bronchoscopic control is preferred. Risk factors of poor outcome with surgery include older age, pneumonectomy, alcoholism, presurgical need for blood transfusion, or vasopressor medications.⁷²

Conclusions

Response to life-threatening hemoptysis should consist of an initial stabilization phase wherein the airway is secured and the origin of hemoptysis is localized and isolated from adjacent nonbleeding lung, followed by a multidisciplinary approach to guide therapy. Subsequently, treatment should involve BAE, therapeutic bronchoscopy, surgery, or a combination of methods. In selective circumstances, additional adjuncts to control bleeding may be advantageous. However, adherence to a systematic management algorithm focused on the fundamentals of airway management and preservation of lung regions from becoming

overwhelmed by hemorrhage take precedence. Although minor to moderate hemoptysis is a frequent clinical presentation, massive hemoptysis may occur with little warning and always constitutes an emergency. Therefore, successful management requires careful implementation of simulations, drills, and preparedness practices in a designated response team that includes respiratory therapists, pulmonologists, interventional radiologists, and thoracic surgeons.

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