Chapter 1

Oncological Airway Emergencies in the Critical Care Unit

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Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/65082

Abstract

Malignancies involving the upper and lower airways can be presented as acute and/or acute-on-chronic life-threatening emergencies. Most of them require intensive care unit (ICU) admission and acute intervention. Such emergencies include but are not exhaustive to epistaxis, massive hemoptysis, central airways obstruction, postobstructive pneumonia, tracheoesophageal fistula, and pleural disease. These are frequent consequences of disease, iatrogenicity, and various pleural diseases causing respiratory failure. The incidence, physiology, symptoms, and sequelae of each disease will be outlined in addition to potential surgical, pharmacologic, and conservative interventions. An anatomical approach from the upper airway, lower airway, mediastinum, and pleura will be taken. Here, we discuss interventions such as emergent cautery, nasal packing, emergent airways, and tracheostomy in addition to a brief glance at other surgical modalities. We will also detail central airway complications such as obstructing endobronchial tumors, massive hemoptysis, bronchoscopy, rigid bronchoscopy, stent placement, and other interventions (cautery, cryotherapy, one-way valves). Finally, pleural disorders such as tension pneumothorax, bronchopleural fistulas, massive pleural effusion, and hemothorax will be reviewed.

Keywords: respiratory failure, central airway obstruction (CAO), upper airway obstruction, epistaxis, massive hemoptysis, stridor, endoluminal disease, malignant pleural effusion, massive pleural effusion, tension pneumothorax, hemothorax, bronchopleural fistula, ENT, interventional pulmonology, cardiothoracic surgery, thoracotomy, thoracostomy, intrapleural fibrinolysis

1. Introduction

As the armamentarium of oncologists continues to improve, so do the outcomes of their patients. However, morbidity persists and many patients require intensive care unit (ICU) as a consequence of end-stage disease, multiorgan dysfunction, infection, and airway compromise. This chapter focuses on airway emergencies that are typically experienced in the ICU. Classification and designation of tumors will not be reviewed. Rather yet, the airway and mediastinal burden of tumor will be detailed. We have organized the discussion in an anatomical approach, sequenced as such: upper airway (nasal cavity, pharynx, and larynx), lower airway (trachea, primary bronchi, and parenchyma), and pleura.

1.1. Upper airway obstruction

We consider upper airway obstruction attributable to cancer a medical emergency. The clinical manifestations of airway obstruction will depend on the underlying disease, the anatomic location, acuity, and severity of airway compromise. Primary head and neck tumors causing upper airway obstruction are perilaryngeal tumors including supraglottic, pharyngeal, pyriform fossa, periglottic, vocal cord, and subglottic lesions. Almost all (95%) of head and neck cancers are squamous cell carcinomas [2], and most occur in patients with an extensive smoking history. Obstruction can occur via mass effect, edema, or hemorrhage. Metastatic breast, colon, melanoma, sarcoma, lymphoma, and esophageal cancers are also associated with upper airway obstruction [2]. Certain obstructions can be asymptomatic and can develop insidiously, making propensity to clinical deterioration unpredictable. Airway salvage and maintenance of oxygenation is the main interventional objective. In this chapter, we also emphasize early airway protection and limiting use of paralytics.

1.2. Etiology and pathogenesis

Upper airway obstruction can be classified as functional, anatomic (e.g., squamous cell carcinoma of larynx), acute, or subacute. Based on the site of obstruction, patients can be divided into different subclasses including obstructive lesions in and around the larynx, mid-tracheal obstruction due to retrosternal goiters, and thyroid carcinomas. We highlight a key respiratory physiologic determinant of airway resistance, Poiseuille's Law. Simply put, airway resistance is dependent on airway diameter and turbulence. Thusly, small changes in airway diameter lead to large changes in resistance of the airflow as the airway resistance is directly proportional to the length and inversely proportional to the fourth power of the airway radius [15].

1.3. Diagnosis

If suspected, we suggest an anatomic survey to rule out airway obstruction. Many modalities are available to the intensivist, such as direct laryngoscopy, bronchoscopy, and flouroscopic guidance. Our practice is to evaluate the patient starting cephalad and progressing caudad, both through direct visualization and for establishing a differential diagnosis. Coupling

http://dx.doi.org/10.5772/65082

underlying medical history and physical exam with appropriate imaging, the treatment plan should be formulated promptly. With CT imaging of the neck and mediastinal structures, we are able to identify the extension of disease and its positioning relative to nearby anatomy. Routine chest radiography in this sense is limited to its two-dimensional depictions and helps identify tracheal and skeletal abnormalities but mainly helps indicate what next imaging modality is needed.

1.4. Signs and symptoms

We commonly observe symptoms of upper airway obstruction as respiratory distress, hoarseness, stridor, facial swelling, or failure to oxygenate with a bag-valve mask. Supraglottic, subglottic, or cancers of the hypopharynx do not usually cause voice changes and are therefore diagnosed in late stages. The most common cause of hoarseness is edema of the true vocal cords. Six weeks of hoarseness in an adult is highly suspicious for a precancerous or cancerous laryngeal lesion. Although not considered a true emergency, hoarseness warrants thorough evaluation.

Stridor is defined as a high-pitched wheezing heard during the respiratory cycle, and is usually more intense during the inspiratory phase. It is appreciated when the airway is at least 5 mm or 50% of its previous diameter [13, 23]. The most common cancers associated with stridor from airway obstruction are squamous cell carcinoma of the larynx, trachea, and esophagus. Pancoast tumors can secondarily cause interstitial edema of the head and neck leading to airway compromise from superior vena cava (SVC) obstruction.

1.5. Management of upper airway obstruction

The primary objective for an intensivist is to establish and safely provide an airway. Malignancies of the base of the tongue, nasopharynx, pyriform fossa, epiglottis, and vocal cords will usually require a surgical airway such as tracheotomy or cricothyrotomy. These tumors have a high propensity for bleeding and special precautions must be taken and emergent surgical consultation must be considered. If the airway is amenable to intubation, smaller-sized endotracheal tubes should be amenable. Long-acting sedatives and muscle relaxants should be avoided as they predispose airway obstructions to airway collapse and respiratory failure. Long-term definitive management involved treating the underlying cause, which is usually treated surgically. However, the majority of patients with malignant airway obstructions will be unresectable due to locally advanced disease, metastatic disease, or poor surgical candidacy.

2. Epistaxis and Post Operative Hematoma

Epistaxis, or nosebleed, occurs in up to 10% of patients with advanced cancer. Common causes of epistaxis in the cancer population are intranasal neoplasms, polyps, leukemia, and coagulopathic disorders including thrombocytopenia secondary to malignancy, medication, or

anticoagulation. It is frequently associated with squamous cell carcinoma, melanoma, and papillomatous lesions [1]. Although rare, nasal cavities can also be a source of metastasis [2].

Epistaxis is anatomically classified as being located in the anterior or posterior nasopharynx. Occasionally, patients might present with severe, life-threatening epistaxis that arises from the larger vessels in the posterior and superior nasal cavity. This bleeding can compromise the airway and results in respiratory failure. Although a thorough medical history and physical exam is necessary, rapid epistaxis can become a life-threatening event. If time allows for quantification of bleeding, the duration and/or a history of a bleeding disorder should be taken into account. Despite the profound incidence of all-cause epistaxis, a societal guideline on management does not exist. Our approach, as in all institutions, is evidence-based nevertheless [3]. A stepwise approach is pertinent and consists of hemostasis conservative measures, localized tamponade, and surgical specialist intervention [4].

2.1. Anterior epistaxis

Patients with active or frequent nosebleeds should be evaluated for an anterior source of bleeding. Approximately 90% of anterior nosebleeds occur at Kiesselbach's plexus or Little's area. As a consequence, most of the blood exits anteriorly. This is supplied from the external carotid artery, the superior labial branch of the facial artery, and the terminal branch of the sphenopalantine artery. The internal carotid also supplies the anterior and posterior ethmoidal arteries.

Visualizing the bleeding with nasal speculum/thudicum with a light source is the initial approach but is inferior to direct rhinoscopy/nasendoscopy [4–6]. If blood obfuscates visualization, irrigation or suctioning techniques should be pursued. Applying direct mechanical pressure may control bleeding, by manually occluding the anterior aspect of the nose in a pincer fashion while leaning forward or applying pressure with an ice pack for 15 min. This serves to tamponade the lesion and allows for platelet aggregation and clot activation. Patients should be kept upright [7].

Nasal packing is a skill that the intensivist should be comfortable in administering while awaiting otolaryngology evaluation. Risk of nasal packing includes but is not limited to tissue necrosis, obstruction, and infection. The anterior nares should be packed with Merocel® tampon or gauze soaked with 4% lidocaine and oxymetazoline to promote vasoconstriction. There is little data, however, showing oxymetazoline's role in hastening hemostasis. Friable lesions causing epistaxis can bleed even more with treatment intervention. If a bleeding vessel is visualized, electrical or chemical cautery (silver nitrate) for hemostasis should be pursued only on lateral nares and not the septum to prevent perforation. Anterior nasal packing should be applied for refractory bleeding. Packing failure can be explained by inadequate placement or anatomic deformity such as a deviated septum or nasal airway obstruction by tumor or polyp. In these patients, a careful endoscopic examination under general anesthesia should be considered. We do not recommend blood pressure reduction for the sole purpose of controlling bleeding. Nevertheless, one must assess signs of hemodynamic instability and necessity of volume resuscitation.

2.2. Posterior epistaxis

Posterior nosebleeds carry the highest risk of significant hemorrhage. Patients with persistent bleeding in spite of conventional treatment should be evaluated for a posterior bleeding source. Approximately 10% of bleeds occur posteriorly, along the nasal septum or lateral nasal wall. The blood supply includes the external carotids through the sphenopalantine branch of the internal maxillary artery. Bleeding enters the nasopharynx and oral cavity, placing the patient at a high risk of respiratory compromise [8, 9]. Concordantly, the management of a posterior bleed is more complicated. Posterior nasal packing is prone to impairing oxygenation. With heavy bleeding, electrocautery and then silver nitrate can aid hemostasis [10]. Both interventions carry a risk of septal perforation; however, electrocautery is easier to apply than silver nitrate during heavy bleeding [11]. It is recommended that an ear, nose, and throat specialist (ENT) be consulted for placement of an inflatable balloon or a 12–14 French Foley catheter for posterior packing.

At times, posterior gauze packs can be introduced through the mouth and retracted back into the nasopharynx, thus providing tamponade in the area of choanae and the sphenopalantine foramen. When conservative measures fail, embolization or surgical ligation of the offending vessel may be necessary. If surgical ligation by an otolaryngologist fails, patients can be referred to an interventional radiologist for angiography and embolization.

2.3. Postoperative neck hematoma

The diagnosis of a postoperative hematoma is based on clinical exam, CT head and neck imaging, and subsequently confirmed with needle aspiration. Hematomas of clinical significance could be presented acutely or in a subacute timeline post procedurally. Obstructions of the airways occur as a consequence of edema and/or direct compression of the airway. An acute presentation requires a focus on airway management, whereas chronic hematomas may be a nidus to infection. If the airway is obstructed, the method of intubation is dictated by the degree of airway edema and extent of previous surgery. Hematomas can also be decompressed by either aspiration or releasing surgical staples. If the hematoma is due to an arterial bleed, it can only be stopped by direct digital pressure or clamping. These patients should be evaluated surgically.

3. Approach to Lower Airway Emergencies

Tumors of the tracheobronchial tree and mediastinum can cause respiratory failure and ICU admission. Although primary tumors of the trachea are rare [12], mediastinal, primary lung, and metastatic lesions can cause a multitude of clinical symptoms. If not addressed promptly, morbidity and mortality can be significant. Diagnostic and therapeutic modalities are now available offering bronchoscopic and, if needed, surgical approaches to expedite and minimize patient complications. Approximately 20–30% of primary lung cancers can be presented with central airway disease and its sequelae [13] such as atelectasis, hemoptysis, central airway obstruction (CAO), and postobstructive pneumonias.

3.1. Hemoptysis

Although some of the most common causes of hemoptysis include bronchitis, bronchiectasis, and airway trauma, we will be focusing on neoplastic causes. The underlying cause is either due to endoluminal disease (primary or metastatic), distal invasive disease (including those of infectious etiology), and coagulopathy or as consequences of systemic disease (i.e., thrombocytopenia and drug induced injury). Approximately 20% of lung cancer patients will experience hemoptysis throughout their disease progression [14] with case series reports of up to 3% having massive hemoptysis [15].

Aside from neoplastic hemoptysis, other causes, such as heart failure, pulmonary tuberculosis, lung abscess, coagulopathic, and iatrogenic (airway interventions) should be in the list of initial differential diagnosis. Hemoptysis is frequently attributable to bronchogenic carcinoma; however, massive hemoptysis is usually due to squamous cell carcinoma (e.g., centrally located tumors) [16].

3.2. Diagnosis and management

Hemoptysis can be presented with clinically insignificant streaks or can be catastrophic. It can include severity that is so burdened by fulminant bleeding that it impairs ventilatory capacity. It is often in these scenarios that require ICU care, if escalation had not already been established.

The initial approach includes quantification of the amount of blood loss as to help assess the risk of respiratory failure and asphyxiation. There is no universally defined volume of hemoptysis to define as massive. However, volumes exceeding 200 cc/h or 600 cc in 24 h [15] are volumes large enough for expeditious diagnostic and therapeutic intervention. In large volume hemoptysis, airway protection becomes paramount and intubation is usually necessary. Regardless of the volume, hemoptysis is clinically considered massive when patients become difficult to ventilate (regardless of underlying morbidity) or if they demonstrate hemodynamic instability [17].

The initial precautions and interventions to massive life-threatening hemoptysis are universal. This includes maintaining head of the bead (HOB)>30 degrees, monitoring for hemodynamic instability, airway protection, and ensuring oxygenation. Patients should be positioned in the dependent position to preserve the nonbleeding lung from pooling or blood spillage. The objective is to identify the source of bleeding. Frequently life-threatening hemoptysis warrants bronchoscopic evaluation with balloon tamponade/endoluminal ablation.

In malignant hemoptysis, chest radiography helps illustrate lunch parenchyma. Aside from identifying masses and cavitations, radiographs are superseded by multidetector CT (MDCT). The CT helps visualize abnormal arteries, information which is critical for possible embolization. While a diagnostic evaluation as to the source includes these investigational modalities, emergent bleeding in the ICU deems a patient too unstable for transport. Should the history and or radiographic imaging not be available, emergent intubation preferably via bronchoscopy should be completed to isolate the nonbleeding bronchus [18]. Nevertheless, identifying the cause of hemoptysis in an emergency should overlap the therapeutic interventions and

must not be a cause of delay. Priority should be taken to identify which lung, or if both, the bleeding is originating from. Admittedly, a medical history and physical exam is not extensively helpful in identifying the location of bleeding. History should thus be succinct and oriented at cardiopulmonary, infectious, coagulopathic, and infectious etiologies.

Attention should be paid to any role in coagulopathy reversal, necessity of blood product transfusion, and assessing oxygenation with blood gas analysis. Moreover, large-volume hemoptysis is a state of volume depletion, and aggressive intravenous fluid replenishment should be considered if clinically feasible. Also, there is no optimal ventilator setting for massive hemoptysis.

3.3. Bronchoscopy

In an emergent setting, patients should be intubated (with a large bore endotracheal tube), especially if patients will inevitably need bronchoscopy. Bronchoscopic evaluation for hemoptysis is often laden with blood and/or clots forming debris that requires the intensivist to retract, clean, and reinsert the bronchoscope. Also, for clearer visualization, large-volume lavage can risk oxygenation, highlighting the importance of keeping a patient intubated. Both flexible and rigid bronchoscopies have a role in massive hemoptysis; however, with a rigid bronchoscope, suctioning capabilities are greater, as are the therapeutic interventions.

Arteriography for persistent hemoptysis is very useful, as embolization of a bleeding artery is often therapeutic [19, 20]. This is completed by an interventional radiologist in a procedure suite. If hemoptysis has temporarily ceased, we remind the reader that CT chest imaging is frequently useful in localizing the source of bleeding. However, patient transfer requires moderate patient stability and can be time consuming. Tagged red blood cell scanning is not useful in the emergent setting. Thoracic surgery consultation should be pursued if bleeding persists despite therapeutic intervention.

Diagnostic bronchoscopy will also aid in identifying any endoluminal/lobar source, thus dictating the necessary intervention. Should a central bleeding lesion be found during the initial survey, isolation of the nonbleeding side (as highlighted earlier) is recommended as to prevent aspiration of blood into normal parenchyma. Insertion of an endoluminal bronchial blocker (Arndt® Blocker) for initial airway tamponade has utility for prevention of such an event [21]. Once the endobronchial blocker is inserted, the balloon should be kept inflated for at least 24 h before assessing rebleeding. In addition to balloon tamponade, other interventions include cold lavage, cryotherapy, and ablative therapy. Topical vasoconstrictors, such as epinephrine, can also be applied to help slow bleeding.

Compared to flexible bronchoscopy, the larger lumen of the rigid bronchoscope facilitates a greater ability to control bleeding while facilitating ablative therapies, and is discussed in a later section in this chapter (see "Central Airway Obstruction: Immediate Bronchoscopic Ablative Therapy"). If an endobronchial blocker is not available, direct bronchoscopic-guided single-lung intubation may be required until further intervention is amenable. This is done by inserting an endotracheal tube in the main stem bronchus of the nonbleeding lung to wall off any blood overflow. Double-lumen intubation allows breaths to be ventilated to both lungs

but is tenuous in the rapidly bleeding airway in which insertion and position maintenance are difficult to maintain. Interventional pulmonology consultation is recommended for the aforementioned potential ablative and/or cryotherapy. Transport to the operating room for rigid bronchoscopy is recommended [21]. As a summation, massive hemoptysis is a life-threatening clinical presentation that warrants immediate action and a multidisciplinary approach. Outlook on treatments options would include endoluminal ablation (argon plasma coagulation or Nd:YAG laser), emergent radiation for distal masses, bronchial or pulmonary artery embolization, and/or a combination of all.

4. Approach to Central Airway Obstruction

A central airway obstruction is an airflow obstruction either at the trachea, carina, or main-stem bronchi. For the intensivist, we outline the malignant etiologies, however, there are benign, traumatic, and iatrogenic (e.g., tracheomalacia) causes as well. Admission into the ICU due to CAO is frequently due to an acute-on-chronic decompensation of a compromised airway. Primary lung tumors are the most common causes of central airway obstruction, most commonly with squamous cell carcinoma followed by adenocarcinoma [22]. Malignant causes can also be due to endoluminal, metastatic, lymph node, mediastinal, or, less commonly, nasopharyngeal disease. Further, we will only concentrate on life-threatening acute CAO. Malignant CAO is primarily palliative in the setting of advanced disease.

The CAO occurs through three basic mechanisms. Simply put, the airway is obstructed either by direct invasion, compression, or endoluminal disease. A mixed picture is possible as well. CAO can develop over months to years; however, those that develop acutely can cause catastrophic outcomes. Patient presentation varies on the degree of obstruction. Significant obstruction causing enough luminal narrowing to disrupt airflow is the primary reason for the sensation of dyspnea. Additional signs and symptoms include cough, localized wheezing, respiratory failure, stridor, and postobstructive pneumonia [23]. Consideration must be made about tracheal luminal narrowing at the time of symptoms, such that exertional dyspnea occurs at about 8 mm of narrowing and symptoms at rest occur at 5 mm [22]. Obstruction can occur in primarily three anatomical variations, defined by the location of mass effect.

One should be prompted to consider CAO in difficult to oxygenate patients with an acute onset of wheezing, stridor, or tachypnea. Oxygenation and ventilation should be prioritized and patients must be assessed for the necessity of ventilator support. We recommend pursuit of the establishment of a secure airway before imaging. If airway obstruction is causing almost definite respiratory failure, cricothyrotomy, tracheostomy, or retrograde intubation may be necessary [24, 25]. Often times in the acutely decompensating patient, rigid bronchoscopic intubation although ideal may not be immediately available. Naturally, larger-diameter endotracheal tubes are preferred. Fiberoptic intubation may be of role, although availability is institution dependent [26]. Intervention should thus be focused on airway patency. There is no role of spirometry in the diagnosis of acute CAO. Also, choice of induction anesthesia is an important consideration, as a moderate amount of sedation is usually required for rigid

bronchoscopic intubation. When paralytics or heavy sedatives are used, the already compromised airway can further occlude. Preoxygenation in these instances is of prime importance, and at times the addition of a mixture of helium and oxygen (known as heliox) as a bridge to intubation or definitive treatment is useful in providing laminar flow [27]. Overall, we recommend paralytics be used as a last resort as intubation can be irreversibly compromised if the airway is lost.

Decompensation could also occur with acute bleeding, swelling and/or additional secretions occluding an already narrowed lumen. Clinical parameters such as hypoxia and hypercapnia may not be of much guidance and may misdirect clinicians' initial index of suspicion.

Although initial evaluation of a patient's clinical presentation with medical history and physical exam is pertinent, obtaining relevant imaging in addition to bronchoscopic consideration is central to the management of CAO. Chest radiographs are often the first illustrations attained but they provide little information to the depth and complexity of obstruction. Chest CT imaging is the modality of choice for providing detailed anatomical information that plays a relevant role in formulating a management plan.

4.1. Interventional bronchoscopy

The institutional availability of interventional bronchoscopy is expanding, as is the role in acute CAO management. Direct bronchoscopic visualization can preclude CT imaging, as direct visualization may provide an accurate diagnosis and anatomic obstructive characteristics faster. Not only is bronchoscopy diagnostic, it is primarily considered therapeutic for foreign object retrieval and suctioning of secretions or blood [28]. Ost et al. demonstrated that interventional procedures have been shown to have 93% technical success, where 48% of subjects experiencing improved dyspnea, and a 3.9% complication rate (**Table 1**) [29].

Malignant	Nonmalignant
Primary endoluminal carcinoma	Lymphadenopathy
Bronchogenic	Sarcoidosis
Adenoid Cystic	Relapsing polychondritis
Mucoepidermoid	Granulation tissue
Carcinoid	Hamartomas
Metastatic carcinoma	Papillomatosis
Bronchogenic	Airway stents
Renal Cell	Artificial airways
Thyroid	Mucus pluging
Sarcoma	Blood clot
Melanoma	Granulomatos disease
Laryngeal carcinoma	Goiter
Esophageal carcinoma	Webs
Tumors of the mediastinum	
Lymphadenopathy	

Table 1. Diseases causing central airway obstruction.

4.2. Rigid bronchoscopy

A rigid bronchoscope (**Figure 1**) is pivotal for acute intraluminal CAO for stenting, dilation, and coring. There are a plurality of techniques and devices available; however, the objective is universally oriented at airway patency. In addition, interventional procedures for CAO also provide improvement in palliative symptoms such as exercise tolerance and dyspnea [30]. The interventional modalities vary depending on institution, available resources, operator preferences, and location of CAO. Dilation, via balloon or mechanical coring, can be used for both extraluminal and endoluminal tumor burden. Dilation with a rigid bronchoscope can be advantageous as it can also be simultaneously utilized for patient intubation. CAO with high risk of perforation or bleeding may be sequentially dilated.

Figure 1. Rigid Bronchoscope (picture courtesy, Emil Abramian MD).

4.3. Immediate bronchoscopic ablative therapy

Immediate ablation is highly effective at clearing CAO. However, ablation usually requires coupling with a second intervention, such as stenting. Ablation primarily consists of argon plasma coagulation (APC) and electrocautery. Extraluminal obstructions are managed with dilation and stenting. These procedures have been found to have similar outcomes, and modality is dependent on the proceduralist's preference [31]. Eventual maintenance of airway patency is usually obtained by multiple interventional approaches (e.g., tumor coring and subsequent stenting) [28]. Reopening of the airway (>50%) was achieved in the majority of cases in a recent multicenter study [29].

Laser therapy (Nd:YAG, argon, excimer) is a promptly effective therapy for intraluminal CAO; however, it is not suitable for long lesions (>4 cm). Laser ablation essentially results in destruction of the obstructing vascularizing vessels and ends with subsequent obstruction extraction. Electrocautery is an alternative to laser therapy but the direct thermal administration causes a risk for airway fire, and is only suitable for endoluminal disease.

Argon plasma coagulation (APC), another noncontact thermal ablative, is highly effective for vascular lesions with a high tendency to bleed, or those that are nestled in airway bifurcations. In contrast to laser therapy, argon gas is electrically coupled to create electrical current that creates target tissue destruction through a grounding principle. As such, flat lesions and lesions at airway bifurcations that are difficult to visualize are effectively managed with APC. The naturally coagulant effects of argon are also advantageous for achieving hemostatis. Moreover, obliteration of granulation tissue surrounding metallic stents is safely approached with APC. Exercising caution with APC in a patient with high-FiO2 requirements (risk of airway fire) is recommended.

Risk for airway fire is elevated in patients with FiO2 requirements greater than 40%, and thus cryotherapy is an advantageous technique for endoluminal obstructions. Cooling agents such as nitrous oxide and liquid nitrogen are used to repeatedly freeze and thaw tissue, ultimately rendering tissue nonviable. Also, the resistance of cartilage and fibrous tissue to thermal conductive effects of cryotherapy accounts for its safety. Efficacy has been shown for reduction in bleeding and hemoptysis [32]. Effects of cryotherapy, however, are temporary and delayed, and should not be used in an emergent CAO. Moreover, cryotherapy should not be utilized for extrinsic compression.

There is no role of photodynamic therapy in emergent CAO management.

4.4. Airway stenting

There are various materials and manufacturers of airway stents. Silicone stenting after an initial ablative procedure has been shown to safely maintain airway patency [33]. It is preferred over traditional metal stents that are commonly associated with airway perforation, granulation tissue formation, and bleeding. Popularly used and commonly known as the Dumon™ stent (Novatech), named after Jean Francois Dumon, it is a studded silicone stent that comes in a straight and Y-shaped mold (for saddling on carinal placement). The length and caliber of the stent is determined periprocedurally and is sized by the operant. Although stents are relatively thermoresistant and inexpensive, they do have the potential to migrate. Combined silicone and metal stents, known as hybrid stents, are frequently used but are more expensive. They combine the benefits of silicone and metal to give optimal compressive resistance while minimizing granulation tissue and perforation.

Another variant, the radioopaque Polyflex silicone stent (Boston Scientific) has synthetic threads that allow for stent flexibility and optimal thinness. These stents, however, have a greater risk of stent migration than the studded Dumon stent [34]. Finally, Dynamic Y stents are more anatomically forgiving, as they have anterior rings that mimic the tracheal lumen but the long length can impair mucous clearance. Overall, safety is high for these therapeutic

interventions and complications such as pneumothorax, airway trauma, infection, stent migration, respiratory compromise, and death are low [35].

5. Postobstructive Pneumonia

Despite the paucity of literature outlining the management of postobstructive pneumonia, it is quite frequent in those with bronchogenic carcinoma. Most typically seen with small cell and squamous cell carcinomas, it can be caused by endobronchial involvement by a tumor or through extrinsic compression and parenchymal involvement. Other malignant causes include metastatic colon, breast, and renal cancers. Diagnosis is crucial as one must consider that the mortality of pneumonia is worse in those with underlying malignancy. Prolonged postobstructive pneumonia may lead to cavitation and necrosis. The intensivist should have a high degree of suspicion for postobstructive pneumonia in patients with radiographic evidence of atelectasis or mucous plugging. Diagnosis should be established and luminal patency should be estimated via CT imaging or endobronchial ultrasound (EBUS).

Patients with postobstructive pneumonia tend to have a longer duration of pulmonary symptoms, compared to those with uncomplicated community-acquired pneumonia. Also, rises in serum biomarkers such as the white blood cell count and procalcitonin are frequently not be observed. Those presenting with fever, however, have shown to provide greater bacteriologic yield [36–38]. Mortality, however, is higher [39].

Patients may present with signs and symptoms of septic shock (e.g., hypotension and tachycardia) or can be as uncomplicated as cough or dyspnea. Prior to any intervention, early antibiotic coverage must be initiated with appropriate coverage for Gram negative bacilli (*Enterobacter cloacae, Aacinetobacter sp*, and *Pseudomonas aeruginosa*), respiratory anaerobes, *Staphylococcus aureus* [40]. Patients can also be iatrogenically inoculated through interventional procedures, such as airway stent placement. The virulence of the inoculum is unclear; however, they may contribute to impaired innate airway mucous clearance.

The microbiota of postobstructive pneumonia appears to be polymicrobial and isolating an organism can be difficult. If microbiologic speciation is critical or if infection must be differentiated from alternative pathologic process, bronchoscopic sampling has greater yield than sputum culture [41]. Tumor debulking and airway reestablishment through interventional bronchoscopic techniques (argon plasma anticoagulation) help reduce mass effect and facilitate antibiotic penetration. Although it was studied as a palliative form of tumor burden, de Aquino Gorayeb et al. were able to demonstrate an improvement in performance status and postobstructive pneumonia (80% response) to high-dose brachytherapy [42].

If radiographic imaging is unavailable, intraprocedural empiric treatment should be considered, prior to therapeutic aspiration. Additionally, decanting pus from one airway still may provide a very brisk systemic response that must be treated aggressively with clinically appropriate volume resuscitation, in addition to aforementioned antibiotics. Antibiotic timeline must be tailored to the appropriate organism. The trachea, bronchus, and pulmonary

parenchyma provide a wide array of complications during the care of an oncologically critically ill patient. A judicious, yet timely systematic approach will ensure that the above aforementioned complications can be quickly dealt with.

6. Approach to Pneumothorax

Pneumothorax is defined as air in the pleural space. A common condition observed in the patients with malignancy and is more attributable to primary lesions than metastatic disease [43]. Pneumothorax can complicate an already deteriorating patient that may have subtle findings or can potentially require emergent intervention.

Traumatic
Blunt force
Iatrogenic
Thoracic surgery
Central venous catheter insertion
Transthoracic biopsy
Mechanical ventilation
Spontaneous
Primary
Secondary
Neoplastic (primary or metastatic)
Infectious
Interstitial lung disease (idiopathic, medication induced, radiation induced)
Chronic obstructive pulmonary disease
Cystic fibrosis [45]

Table 2. Classification of pneumothorax.

Here, we classify pneumothorax into primary spontaneous pneumothorax (PSP), secondary spontaneous pneumothorax (SSP), and traumatic pneumothorax. PSP occurs in patients without underlying lung disease. Secondary spontaneous pneumothorax is attributable to an underlying pulmonary disorder. Traumatic pneumothorax can be due to blunt physical trauma or from iatrogenic causes, such as invasive procedures and radiation therapy. Secondary

spontaneous pneumothorax has shown an association with higher morbidity and mortality than primary spontaneous pneumothorax [44] (**Table 2**).

Iatrogenic pneumothorax is most common in hospitalized patients. Increasing incidence has correlated with the incidence of invasive diagnostic and therapeutic procedures, such as transthoracic lung biopsy and central venous catheter (CVC) insertion. Transthoracic needle aspiration is responsible for 45.7% and CVC in 24.8% [46]. Image guidance with CT for transthoracic biopsy reduced rates to 20% [47], although rates can vary significantly by institution. Currently, there is conflicting data whether smaller lesions or those with longer anatomic depth are associated with higher rates of pneumothorax [48]. As a complication of mechanical ventilation, pneumothorax carries an increase in morbidity and mortality, and has the highest risk of pneumothorax in the intensive care unit (ICU), particularly with the use of positive-end expiratory pressure [49, 50]. Rates of barotrauma have been noted to be as high as 15% [51].

Secondary spontaneous pneumothorax (SSP) is seen in both primary and metastatic diseases, regardless of pleural invasion. Tumor pleural involvement can cause cavitation, necrosis, and subsequent pleural damage. There have been many reports of pneumothorax secondary to chemotherapy administration [52–54] likely as a consequence of lysis of chemosensitive lesions.

Tension pneumothorax, as seen with mechanical ventilation or cardiopulmonary resuscitation, is a medical emergency. The incidence has not been definitively established, and statistical analysis is in its infancy [55]. Reports in adult ICUs have been as high as 3% [56]. Suspicion for such should be high when there is patient decompensation after known pneumothorax. It is suggested that delaying intervention until radiography has contributed to mortality [57]. This is a medical emergency and requires immediate mechanical decompression even before confirmation with imaging [58].

Bronchopleural fistula (BPF) is the presence of a significant, persistent air leakage after tube thoracostomy. Incidence has been reported up to 4.5% [59]. Occurrence of BPF has been reduced in recent years due to management of patients at risk (e.g., acute respiratory distress syndrome) with low tidal volume ventilation protocols [60, 61]. Despite this, knowledge of BPF is necessary for patients with a persistent pneumothorax and/or status post lung resection.

The mechanism involves airway disruption or alveolar rupture and can be due to mechanical volume overdistension [62, 63], elevated transpulmonary pressures [64], pleural trauma from an invasive procedure, or spontaneous rupture. Additional causes include inappropriate right main bronchus intubation and severe sepsis. Animal studies have demonstrated that excessive volume, rather than elevated airway pressures have been linked to alveolar rupture. Hence the term *volutrauma*, as opposed to *barotrauma*, more appropriately describes alveolar rupture [63]. Nevertheless, elevated transpulmonary pressures can play a major role in alveolar rupture [64]. Current recommendations, further outlined under *Management*, involve low-volume ventilation (≤6 mL/kg of predicted body weight), close monitoring for auto-PEEP, and avoidance of excessive hyperventilation [61].

6.1. Pathophysiology

In a normal lung, negative intrapleural pressure throughout the entire breathing cycle is maintained in the pleural space relative to the atmosphere, allowing for physiologic lung expansion, known as elastic recoil [65]. Transpulmonary pressure between lung alveoli and the pleura is disrupted due to alveolar permeability. This results in permeation of alveolar gas into low-resistance anatomic surfaces, such as the mediastinum, peritoneum, and pleural space. On inspiration, air that has translocated from alveoli enters directly to pleural cavity [66].

In tension physiology, once the nidus has occurred, the pleural cavity pressure equalizes with the chest wall environment causing a reduction of transpulmonary pressure, reducing vital capacity [67]. In the healthy awake adult, compensatory intrapleural pressures rise in attempt to compensate for tension pneumothorax. There is significant impairment of this with patients on mechanical ventilation, who usually are sedated. With positive pressure ventilation, inspiratory pressures are significantly elevated, creating an exaggerated pressure gradient. This is worsened from environmental air compressing lung parenchyma and distorting intrapleural pressure, risking mediastinal shift to the opposite lung and diaphragmatic depression. Alveoli may leak air into the pleura during inspiration only, creating a one-way valve effect, causing accumulation of pleural air. Rising pleural pressure can progress to affect nearby structures, resulting in ipsilateral lung deflation, mediastinal shift, and a rapid reduction in cardiac output [67].

6.2. Measurement

Assessing the size of a pneumothorax guides practitioners as to pursuing conservative versus invasive management. Light's index [68, 69] measures the percentile of pneumothorax:

Light's index = 100% − (diameter of collapsed lung^3/diameter of hemithorax^3) (100%). Light's index is helpful for quantifying reexpansion of lung after intervention [68, 69].

An alternative method involves measuring the average of the intrapleural distance at the level of the apical, mid-thorax, and basal levels. According to the British Medical Society, a "large" pneumothorax is defined as having >2 cm lung margin from the chest wall on roentgenogram [49]. Those classified as large warrants surgical decompression. It is important to note, however, that clinical symptoms outweigh measurement indices on interventional decision making.

6.3. Physical examination

Patients that develop secondary spontaneous pneumothorax present with varying degrees of severity dependent on the rate and volume of air accumulation, patient's age, status of mechanical ventilation, and baseline pulmonary function at the time of diagnosis. Because the pathophysiology involves a reduction in vital capacity, a predisposed lung can be presented with dramatic constellation of symptoms. Dyspnea, anxiety, and chest discomfort are common presenting symptoms [70]. Physical exam findings can include diminished breath sounds, increased manual percussion resonance on the ipsilateral affected lung, subcutaneous

emphysema (Hamman's sign) [71], and tracheal deviation. Clinical signs can include tachypnea, oxygen desaturation, and increased work of breathing.

For the mechanically ventilated, frequent signs of tension pneumothorax include an acute onset of elevated pulmonary pressures (both peak and plateau) and hypotension [72]. Diagnosis includes obtaining chest radiography, which is demonstrated with a pleural line that is absent in lung markings beyond the line. However, it may take over 24 h for evidence after insult. A deep sulcus sign may only be the only radiographic evidence of pneumothorax, when seen on a supine image. Air collects basally, as opposed to the lung apex, causing a deepening of the costophrenic angle [73]. Diaphragmatic inversion with tracheal deviation is suggestive, although not pathognomonic, of tension pneumothorax [72]. Even with anatomic deviation, appropriate diagnosis was missed approximately half the time [74].

6.4. Management

American College of Chest Physicians (ACCP) guidelines provide recommendations based on patient stability and size of pneumothorax. Supplemental O_2 should be considered universally [44, 75], with caution taken for patients with chronic obstructive pulmonary disease and a proclivity to retain carbon dioxide. Small, stable pneumothoraces may be conservatively observed with appropriate follow up. Large pneumothoraces require hospitalization and needle or tube decompression.

Supplemental oxygen improves the rate of pleural air resorption through reduction of arterial nitrogen content. Reduced arterial nitrogen content creates a larger pleural space gradient, thus accelerating resorption of pleural air [44, 76].

Drainage is usually indicated in most patients with secondary spontaneous pneumothorax [44]. To further extrapolate indications for drainage, those who have symptomatic "large" SSP (as outlined earlier), the risk of resolution is outweighed by progressive risk of pleural compromise, and thoracostomy is warranted [77]. Small SSP (<2 cm from chest wall) can be managed with small bore chest tube. Asymptomatic patients with <1 cm from chest wall pneumothoraces can be managed conservatively with supplemental oxygen and serial chest radiography. Tube thoracostomy, when compared to needle decompression, has shown greater rate of success [44]. If a needle aspiration yields greater than 2.5 L of air, chest tube is indicated due to suspected air leak. Intervention can be guided with sonographic or fluoroscopic imaging if necessary.

Chest tube should be connected to water seal device and may be connected to a one-way Heimlich valve or low suction to aid reexpansion of lung [44]. Chest tube thoracostomy was successful in 78.1% of cases, and was not dependent on tube size [46]. If air leak has resolved and the lung has re-expanded on radiograph at least 12 h after last documented leak, the chest tube can be clamped, and removed after approximately 24 h [75]. Long term stabilization and pneumothorax recurrence may warrant intervention for prevention (e.g., pleurodesis) [44].

Persistent air leakage after 4 days of bronchopleural fistula after tube thoracostomy favors intervention over expectant management for spontaneous closure [44, 75, 77]. If a patient is mechanically ventilated, it is recommended to reduce tidal volume and airway pressures as

tolerated, if not already done so [56]. Reducing overdistention of alveoli and development of intrinsic peep helps reduce transpulmonary gradients. This is achieved through the following maneuvers: Increasing inspiratory to expiratory ratio (I:E) through inspiratory flow control, decreasing tidal volume to ≤6 mL/kg predicted body weight, and adjusting the amount of ventilator driven patient breaths.

Bronchoscopic maneuvers such as deployment of endobronchial stenting, bronchoscopic valves [78], coiling [79, 80], injection of sclerosant, or laser coagulation has been utilized with efficacy [81–85].

Possible interventions include video-assisted thoracoscopic surgery (VATS) with mechanical or chemical pleurodesis, or VATS with resection of blebs. Additional chest tube placement or bronchoscopic intervention with the intent of sealing air leak is not recommended [75]. Chemical pleurodesis through tube thoracostomy is not recommended as well, although patients with poor surgical candidacy, current recommendations are talc slurry or doxycycline. Blood patch pleurodesis has shown outcomes with variable success [86, 87]. This is performed by instilling the patient's own venous blood (50-100 mL) into the pleural space through a chest tube.

Overall recurrence of secondary spontaneous pneumothorax is frequent [49]. We therefore recommend consideration for recurrence prevention through two options; surgical and chemical. Surgical options include VATS or open thoracotomy, depending on independent practitioner preference and patient candidacy. Open thoracotomy has shown lower recurrence rates but has higher blood loss and longer recovery times, and therefore, VATS with pleural obliteration is preferred [44, 75, 88]. Pleural obliteration can be achieved through pleurectomy, talc administration, and abrasion with gauze [89–91]. Chemical pleurodesis through tube thoracostomy has been shown to reduce recurrence of SSP, however success ranges 78–91% versus 95–100% with surgical intervention [44].

7. General Approach to Pleural Effusions

Approximately two-thirds of massive pleural effusions are associated with an underlying malignancy, [92] the majority of which present with 500–2000 mL of pleural fluid accumulation. Fluid collection can be serous, hematogenous, or serosanguinous. Of all exudative pleural effusions, pneumonia and malignancy are the two leading causes [93, 94]. In males, lung cancer is the most frequent metastatic pleural malignancy, breast cancer is most frequent in women [95, 96], and in up to 15% of cases, is unknown [97]. Often times recurrent, the responsible mechanism for pleural fluid accumulation is due to hilar and mediastinal lymphatic obstruction or seeding [92, 98]. Isolation of malignant cells in pleural fluid indicates a malignant pleural effusion (MPE). The development of hemothorax is due to the role of tumor angiogenesis, tumor invasion into blood vessels, or direct humoral capillary permeability [99]. Malignant pleural effusion (MPE) is a frequent complication of advanced malignancy, and carries a poor prognosis, affecting more than 150,000 people annually in the U.S. [100]. Median survival, depending on underlying malignancy, is less than 6 months once a diagnosis of MPE

is made [96, 100]. MPE is diagnosed with malignant cells found in pleural fluid, which is often difficult to obtain. Pleural fluid analysis, in conjunction with the clinical history, is also sufficient to substantiate a diagnosis. Although in the ongoing years, the Light's criteria has faced scrutiny for excluding additional biomarkers (e.g., amylase) and including the closely correlated serum and pleural fluid lactate dehydrogenase (LDH) [101], it remains the mainstay of differentiating a transudative versus an exudative pleural effusion.

Light's criteria deems a pleural fluid as exudative if at least one of the following criteria are met [102]:

Pleural fluid protein/serum protein ratio greater than 0.5,

Pleural fluid LDH/serum LDH ratio greater than 0.6, or

Pleural fluid LDH greater than two-thirds the upper limits of the laboratory's normal serum LDH.

Amylase-rich pleural fluid can be suggestive of acute pancreatitis, esophageal rupture, or malignancy [103]. Recent studies have suggested that elevated serum lactate dehydrogenase to pleural fluid adenosine deaminase has been predictive of malignancy [104].

It is important to note, however, alternative causes of large pleural effusions in the setting of malignancy, such as congestive heart failure, venous thromboembolism, toxic effects of chemotherapy administration [105], radiation [106], low protein states, and pneumonia. Cytologic analysis of pleural fluid helps differentiate the underlying cause. Obstruction of the thoracic duct may also cause chylothorax and is suggested by pleural fluid triglyceride levels above 110 mg/dL (**Table 3**) [107].

Straw – Transudative process
Pus – Empyema
Red – Hemothorax
Pulmonary infarction
Postcardiac arrest
Iatrogenic (post procedure)
White – Chylothorax
Black – Aspergillosis
Ammonia – Urinothorax

Table 3. Qualitative description of pleural fluid.

Complicated parapneumonic effusions are often culture negative, have poor response to systemic antimicrobials, and may be loculated. Diagnosis is through pleural fluid analysis and utilization of the following criteria: pleural fluid pH less than 7.20, glucose level less than 60 mg/dL, and LDH > 1000 IU/L [108]. Meeting the aforementioned criterion renders a poor

prognosis [109]. Complicated parapneumonic effusions warrant chest tube placement that otherwise runs the risk of progression to thoracic empyema [110]. The majority of organisms isolated through fluid culture or Gram stain consist of staphylococci and anaerobes such as *Fusobacterium*, *Peptostreptococcus*, *Bacteroides fragilis*, and *Prevotella* species [111, 112]. Long-term sequelae of unresolving empyema, hemothorax, and surgical manipulation may result in a trapped lung. Trapped lung occurs when reexpansion of atelectatic lung is impaired due to a fibrinous peel overlying visceral pleura, creating a chronic pleural effusion. Lung entrapment, in turn, is an unexpandable lung due to active malignancy or infection [113, 114]. For patients with significantly trapped lung, pleurodesis can be deferred.

Chemotherapy associated with large-volume effusions include methotrexate, procarbazine, cyclophosphamide, mitomycin, bleomycin, and IL-1 (**Table 4**) [106].

Malignancies associated with malignant pleural effusions [62]	**Indirect causes of pleural effusions (paramalignant)**
Lung 37.5%	Local tumor effect
Breast 16.8%	Trapped lung
Lymphoma 11.5%	
Genitourinary 9.4%	Chylothorax
GI tract 6.8%	Lymphatic obstruction
	SVC (superior vena cava) syndrome
	Pulmonary embolism
	Hypoalbuminemic state
	Chemotherapy/radiation therapy (incomplete)
	Tumor necrosis factor
	Interleukin-2
	Methotrexate
	Bleomycin
	Cyclophosphamide

Table 4. Malignant and indirect (paramalignant) causes of effusions.

Severity in symptoms is dependent on residual lung function, acuity in rate of fluid accumulation, and whether or not the patient is on mechanical ventilation. Large pleural effusions are often symptomatic and results in reduced chest wall compliance and lung volume [115]. These include orthopnea, cough, dyspnea, and fever. Examination of the affected lung may include diminished breath sounds, tactile fremitus, and crackles. Tracheal deviation may also be a presenting finding with larger-volume effusions. Diagnosis of pleural effusion is suspected with physical examination and confirmed radiographically. Treatment can be either palliative

or aimed at improving survival. Reaccumulation of MPE can worsen a patient's symptoms; however, in asymptomatic individuals, cost, preference, and functional status should be taken into account.

Diagnostic and therapeutic considerations with large volumes are first achieved with thoracentesis [116]. Pleural fluid analysis helps determine between transudative or exudative effusions and may indicate the primary cause [117]. The severity of symptoms and global prognosis of the patient dictates the necessity of further invasiveness [118]. Recurrence is high with therapeutic aspiration without pleurodesis incurs a high rate. Thoracentesis is not without complications, including pneumothorax, empyema, and adhesions [96]. Other procedures include pleural biopsy, bronchoscopy, pleuroscopy, and video-assisted thoracoscopic surgery (VATS) with biopsy.

In the setting of clinical acuity, such as hemodynamic compromise, tracheal deviation, diminishing hypoxemia, or a progressively unstable airway, emergent indication is indicated for lung reexpansion. Thoracentesis should be performed for relief of symptoms, and chest tube drainage is recommended for empyema and/or complicated parapneumonic effusions. If a patient has a very limited lifespan (i.e., <1 month), pleurodesis is less strongly recommended. Aspiration on each occasion should not exceed 1.5 L to avoid reexpansion of pulmonary edema [119].

Inadequate or improperly draining tubes may warrant decortication. Nearly all patients with malignant pleural effusion who undergo drainage face recurrence within 30 days [120, 121]. Such patients benefit from pleurodesis, when in consideration of life expectancy. Repeat thoracentesis is selectively recommended for patients with short life expectancy, as it can lead to formation of adhesions, mentioned earlier. Repeat aspiration helps palliate symptoms for the terminally ill, especially with the use of small-bore catheters [122].

Pleurodesis can be done surgically or chemically. Chemical pleurodesis may require a prolonged hospital stay and carries a small risk of pneumonitis [123]. Thoracoscopic pleurodesis is recommended over catheter based [124, 125].

Surgical outcomes are often difficult to achieve due to poor surgical candidacy. Chemical pleurodesis involves infusion of a sclerosing agent such as talc (poudrage or slurry), 5-FU, minocycline, bleomycin, and silver nitrate, with talc being the most successful agent for providing reaccumulation after 1 month [126–128].

Pleurodesis helps achieve lung expansion and reestablishes normal symphysis of visceral and parietal pleura. The primary mechanism involves inciting a broad spread inflammatory response, in turn promoting fibrin deposits [129]. Suspected antitumor effects of talc by induction of apoptosis of cancer cells may also help provide a role in blunting tumor progression intrapleurally. Bleomycin carries a well-established antineoplastic role [130]. With recent meta-analyses, both talc poudrage and slurry are equally efficacious with thoracoscopic technique considered ideal [96].

Alternatives include chronic indwelling catheter placement, which is an increasingly popular option due to its low risk of infection, displacement, and manageability as an outpatient [131].

Both talc pleurodesis and chronic indwelling catheters have been shown to be effective initial treatments for MPE [126]. Indwelling catheters also have a role once a patient develops trapped lung.

For clinically stable patients with poor response to initial thoracostomy drainage or with multiloculated effusions, and are poor candidates for surgical intervention, intrapleural tissue plasminogen activator (tPA) combined with DNase has been a growingly influential therapy, without additional excess of adverse events [132, 133]. Administration of fibrinolytics or DNase alone did not improve outcomes [133, 134]. Pleuroperitoneal shunting is an additional option to consider, especially in patients with trapped lung (**Table 5**) [100, 109].

Thoracentesis/ thoracostomy	Large pleural effusions. Thoracostomy for chest tube insertion, fibrinolysis, and pleurodesis.
Pleurodesis	Recurrent pleural effusion
Video-assisted thoracoscopic surgery (VATS)	Complicated/parapneumonic effusion, pleurodesis, and pleurectomy. Lysis of adhesions, blebectomy, decortication, lobectomy, and lung volume reduction. Contraindicated in hemodynamic instability. Less invasive and painful than thoracotomy.
Thoracotomy with decortication	Major surgery. Full mediastinal visualization. Better for large tumors, close to mediastinal/vascular structures. Higher risk of complications and estimated blood loss [101].
PleurX® catheter	Can be managed outpatient, role palliative care.
Pleuroperitoneal shunt	Exhaustion of alternative options, useful for chylothorax in managing nutritional and immunologic status.

Table 5. Interventional procedures in management of massive pleural effusion.

8. Approach to Hemothorax

Hemothorax is evident when frank blood is aspirated from pleural space during thoracentesis, tube thoracostomy, or VATS, and is confirmed when pleural fluid hematocrit exceeds more than >50% of serum hematocrit concentration. Pleural bleeding can be simplified as being due to mediastinal or pleural tissue insult. Diagnosis is mainly attributable to mechanical chest trauma, and its overall incidence has not been well quantified. Nontraumatic hemothorax is most commonly due to malignancy and is explained by the role of tumor angiogenesis, invasion into blood vessels, or direct humoral capillary permeability [99]. Not to be confused with a bloody tap, where the latter instance clears after centrifuge, hemothorax has a propensity to not clot due to continuing defibrination from mediastinal motion. Other causes may be a consequence of iatrogenic anticoagulation [136], pulmonary embolism causing pulmonary infarction, or catamenial hemothorax [137, 138]. Surgical manipulation, such as thoracentesis, bronchoscopic biopsy, mediastinoscopy [139], needle biopsy, and central venous catheter insertion may also be a cause [140]. Spontaneous hemothorax, i.e., hemothorax without identifiable cause, is infrequent [141]. Causes are outlined below (**Table 6**) [75].

Nontraumatic
Neoplastic
Metastatic diseases
Vascular malignancy
Bronchogenic carcinoma
Mesothelioma
Angiosarcoma
Coagulopathy
Anticoagulation
Thrombocytopenia
Congenital disorders
Pulmonary embolism
Pulmonary infarct
Vascular
Arteriovenous malformation
Aneurysm
Connective tissue disease
Aortic dissection
Traumatic
Central venous catheter
Thoracentesis
Transbronchial biopsy
Percutaneous needle aspirate
Pleural biopsy
Thoracic surgery

Table 6. Nontraumatic and traumatic causes of hemorrhagic pleural effusions.

8.1. Imaging

Hemothorax and pleural effusion is not distinguishable on routine chest radiography or ultrasonography. Presenting history aids index of suspicion helps distinguishing between hemothorax and pleural effusion. Chest CT imaging blood presents with higher attenuation than pleural effusion. Later stages of hemothorax can include pleural deposition, thickening, and loculation [142]. CT imaging is also well associated with determining the necessity of VATS [143]. Hemopneumothorax is characterized by a pneumothorax with ipsilateral air-fluid level. Suspicion for vascular etiologies may warrant CT angiography.

8.2. Management

Outlining the management of a patient with confirmed hemothorax in the intensive care unit depends on patient stability and prognosis, and spans from supportive care to emergent

thoracotomy [144]. Goals of care are for blood evacuation to avoid fibrin deposition and subsequent trapped lung, and the development of empyema [145].

Discontinuation of anticoagulant therapy and correction of any coagulopathy is recommended if hemothorax is attributable to systemic anticoagulation [145, 146]. Massive hemothorax may require blood transfusion resuscitation. Blood collection in the pleural space in minimal amounts may spontaneously reabsorb; however, chest tube drainage is necessary for rapidly developing hemothorax [27]. Drainage reestablishes parieto-pleural symphysis and creates a tamponade if the source of bleeding is from pleural rupture. With concomitant pneumothorax, i.e., hemopneumothorax, drainage is definitively indicated. In contrast to chest tube management of spontaneous pneumothorax, large-bore chest tubes should be placed due to the rapidity of clotting [75, 146, 147].

Thoracotomy is warranted for the hemodynamically unstable and those with massive hemothorax. This constitutes patients with severely rapid exsanguination with retained volume greater than 500 mL, accumulated output over 1500 mL, or if exsanguination is above 200 ml per h [139, 148]. Chest tubes can be maintained in the chest wall cavity until the amount of tube drainage in 24 h is less than 100 mL but removal should not be prolonged to reduce the risk of infectious inoculation [149]. Residual clotted blood after thoracostomy should be removed thoracoscopically to reduce the risk of empyema and fibrothorax [150]. Fibrothoraces that require VATS decortication should be delayed months after initial insult in order to allow coalescence and stabilization of a fibrin peel [145]. VATS permits safe decortication of adhesions and removal of clotted blood. The role of intrapleural fibrinolytics in the management of hemothorax is currently in its infancy. VATS has better proven efficacy and shorter Hospitalization stay [135]; however, fibrinolytics are a considerable option when patients are without underlying coagulopathy but are clinically unstable for VATS [148, 151–153]. Fibrinolytics can be applied for chemical lysis of intrapleural adhesions, commonly seen with fibrothorax [75]. There is no evidence indicating systemic side effects to intrapleural fibrinolysis. Antimicrobials early in the treatment of traumatic hemothorax reduce rates of empyema. There is evidence showing benefit in prophylactic administration spontaneous pneumothorax as well. Initial antibiotic coverage for empyema should include *Staphylococcus* and *Streptococcus* [154].

9. Conclusion

Substantial challenges present themselves in the ICU, with airway compromise being one of the high priorities. Either caused by primary cancers or secondary metastasis, the upper and lower airways have very little room for error. Hemorrhaging from or into the nasopharynx, trachea, and its tributaries can precipitate an inability to ventilate and oxygenate rapidly. Understanding the anatomical and physiological challenges are the first steps to managing such complex scenarios. Rapid stabilization with nasal packing and/or protection of ventilatory units, via intubation, is an essential task for the intensivist. Subsequently understanding or having a high index of suspicion as to the origin of respiratory failure helps prevent further decline in respiratory status. Central airway obstruction requires urgent/emergent advanced

bronchoscopic evaluation with potential therapeutic intervention. One must be also cognizant that large pleural effusions (of varying origin) and/or pneumothoraces contribute to the spectrum of emergencies faced in an oncological critical care unit.

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