

Chapter 310: Interventional Pulmonary Medicine

Part 7: Disorders of the Respiratory System | Part 7 – Respiratory Disorders | DETAILED EDITION

KEY CLINICAL POINTS

1. Convex endobronchial ultrasound (cEBUS) is the gold standard for lung cancer staging with sensitivity of 90% and specificity of 100%.
2. Central airway obstruction (CAO) management: Rigid bronchoscopy is the preferred tool for management in conjunction with ablative therapies, balloon bronchoplasty, and airway stenting.
3. Bronchial thermoplasty (BT) for severe asthma improves quality of life and reduces exacerbation rates but does not change FEV1 or airway hyperresponsiveness.
4. Bronchoscopic lung volume reduction (BLVR) via valve placement demonstrates improvements in lung function and quality of life with a lower rate of perioperative morbidity and mortality compared to surgical lung volume reduction (SLVR).
5. Persistent air leak is defined as a nonresolving pneumothorax with an air leak lasting more than 5–7 days.
6. Airway stent complications are not uncommon and include migration, mucostasis, infection, and the development of granulation tissue.
7. The Multicenter Intrapleural Sepsis Trial (MIST2) demonstrated that intrapleural sequential administration of recombinant tissue plasminogen activator (rtPA) and DNase resulted in significant radiographic and clinical improvements and allowed >90% of patients to avoid surgery.
8. Indwelling pleural catheters (IPCs) effectively relieve dyspnea, decrease the duration of hospital stay, and lessen the need for future procedures compared to pleurodesis via talc slurry.
9. Acute cellular rejection in lung transplant recipients is most common in the first posttransplant year, with approximately 50% experiencing at least one episode in the first year.
10. Donor-derived cell-free DNA is increasingly being explored as a noninvasive method of detection of allograft dysfunction, most importantly in the setting of acute and chronic rejection.

FIGURES IN THIS CHAPTER

1. Endobronchial ultrasound transbronchial needle aspiration image...
2. Types of central airway obstruction

1. DEFINITION & OVERVIEW

Interventional pulmonary medicine is a subspecialty of pulmonary and critical care medicine focusing on the evaluation and management of patients with thoracic malignancy, central airway obstruction, pleural disease, and advanced obstructive lung disease such as chronic obstructive pulmonary disease (COPD)/emphysema and asthma. Novel minimally invasive interventions have drastically changed the way we care for patients. In this chapter, we will summarize recent developments and evolving technologies in interventional pulmonology (IP).

2. DIAGNOSTIC BRONCHOSCOPY

With the introduction of the rigid bronchoscope by Gustav Killian in 1897, the mortality associated with foreign-body aspiration dropped from over 90% to less than 5%, as patients no longer had to suffer from airway obstruction and postobstructive pneumonia. Shigeto Ikeda developed the flexible bronchoscope in 1967, allowing access to the peripheral airways and lung parenchyma. In 2018, the first robotic-assisted bronchoscopy platforms were introduced, providing a novel approach with the ability to reach further into the peripheral lung reliably with precise control. Bronchoscopy has remained an important diagnostic and therapeutic procedure, and recent technology has significantly increased its utility.

2.1 Endobronchial Ultrasound

The diagnosis and staging of lung cancer remain one of the most important roles of advanced diagnostic bronchoscopy and IP. Convex endobronchial ultrasound (cEBUS) is a flexible bronchoscope combined with ultrasound technology that allows for real-time visualization during transbronchial needle aspiration (TBNA) of mediastinal and hilar lymph nodes and masses adjacent to the airways. With a sensitivity of 90% and a specificity of 100%, cEBUS is the gold standard for lung cancer staging and can also provide sufficient tissue to perform molecular profiling to guide targeted therapies in lung cancer with adequacy rates for testing that exceed 95%. cEBUS is also extremely helpful in diagnosing mediastinal and hilar adenopathy due to sarcoidosis. The use of endobronchial ultrasound to diagnose lymphomas has historically been of limited utility owing to lack of tissue architecture in needle aspirates. However, advances in cEBUS using a cryobiopsy technique in lieu of needle aspirate have shown promise but in providing adequate tissue and histopathologic architecture from intranodal cryobiopsy.

2.2 Peripheral Bronchoscopy

Evaluations of pulmonary nodules and lung masses are frequent indications for bronchoscopy as a way to achieve a minimally invasive diagnosis. Historically, the diagnostic yield of bronchoscopy to target peripheral pulmonary lesions was <60%. Multiple guidance platforms now allow for improved access in the periphery of the lung. Smaller or ultrathin bronchoscopes <4 mm in diameter can be combined with available imaging tools to improve target localization. Radial-probe endobronchial ultrasound utilizes a radial scanning ultrasound probe that is inserted through the bronchoscope and into the lung, producing a real-time image of the target lesion. Electromagnetic navigation bronchoscopy (ENB) involves image-guidance systems that manipulate thin-slice computed tomography (CT) images to create virtual airway reconstructions used as guided maps during bronchoscopy. Robotic-assisted bronchoscopic platforms offer the enhanced articulation and stability of a robotic arm, replacing the traditional flexible bronchoscope. Recent innovation has allowed for advances in intraprocedural imaging. Mobile cone beam CT scanners in combination with advanced peripheral bronchoscopy allow for image confirmation of a biopsy within the lesion of interest. Studies are currently underway to explore further the utility of these systems for peripheral lesion biopsy and the impact of advanced imaging techniques.

3. THERAPEUTIC BRONCHOSCOPY

Therapeutic bronchoscopy is indicated for the relief of malignant and nonmalignant central airway obstruction, asthma, and emphysema. Active research is also focusing on the utility of bronchoscopy for the ablation of early-stage lung cancer, as well as the treatment of chronic bronchitis.

3.1 Central Airway Obstruction

Central airway obstruction (CAO) describes obstruction of the trachea, main stem bronchi, bronchus intermedius, and/or lobar bronchi, and can present as intrinsic (endoluminal), extrinsic (extraluminal), or mixed (extraluminal tumor resulting in mass effect and endoluminal involvement). Patients often initially present with cough and exertional dyspnea, and then progress with increasing severity of obstruction to dyspnea at rest, stridor, and respiratory failure. Patients may also have wheezing, hemoptysis, or symptoms of postobstructive infection. Rigid bronchoscopy is the preferred tool to manage CAO in conjunction with ablative therapies, balloon bronchoplasty, and airway stenting to offer rapid symptomatic relief with immediate reductions in the level of required oxygenation. Therapeutic bronchoscopy for CAO has been shown to significantly improve both quality of life and survival.

3.2 Ablative Therapies for CAO

Ablative therapy in the airway consists of both heat (laser, electrocautery, and argon plasma coagulation) and cold (cryotherapy) modalities. These techniques are most commonly used to destroy tumor and provide hemostasis. The cryoprobe can also be used for foreign-body removal. Other modalities, such as brachytherapy (BRT) and photodynamic therapy (PDT), have a delayed therapeutic effect and are often not suitable for situations where immediate relief of airway obstruction is desired. Under bronchoscopic guidance, high-dose therapeutics can be safely injected directly into tumor to enhance response and limit systemic side effects. Multiple studies are ongoing to assess the efficacy of endobronchial intratumoral chemotherapy (EITC).

3.3 Bronchoplasty

Bronchoplasty (or bronchial dilation) can be achieved with the barrel of the rigid bronchoscope or with balloons that can be passed via the rigid or flexible bronchoscope. Bronchoplasty is most commonly used for dilation of stenotic airways or disruption of webs related to nonmalignant causes of airway diseases. Although dilation generally leads to immediate relief of the stenosis, results can be short-lived, and hence, this technique is often combined with airway stenting. Complications are rare but can include airway tears if proper techniques are not followed.

3.4 Airway Stenting

After airway patency is achieved, airway stents can be utilized to prevent recurrence of CAO. Reports of endoscopically implantable stents for the airways date back to 1914. Airway stents are commonly used to treat patients with CAO due to extrinsic compression from a variety of malignant and nonmalignant disorders. Stents are effective and lead to symptomatic relief in >90% of patients. A variety of airway stents are available, each with its own benefits and detriments; it is important to choose the right stent for the specific indication. Stent complications are not uncommon and include migration, mucostasis, infection, and the development of granulation tissue. First-generation biodegradable stents, custom three-dimensional printed stents, and drug-coated stents are currently being evaluated, working toward a personalized airway stenting and its associated complications.

3.5 Endobronchial Intratumoral Chemotherapy

Endobronchial intratumoral chemotherapy (EITC) is an intervention aimed at improving and/or maintaining airway patency in patients with malignant CAO, with the potential to eliminate the need for radiotherapy. There is limited experience with bronchoscopic radiofrequency ablation (B-RFA) and microwave ablation (MWA) as a potential means to treat early-stage lung cancer. Ultimately, the efficacy of bronchoscopic ablation of early-stage nonoperable lung cancer must be proven in longitudinal studies demonstrating noninferiority in survival as compared to the current gold standard of stereotactic body radiation therapy (SBRT). To date, there are extremely limited safety and efficacy data for bronchoscopic ablation with multiple studies currently ongoing. Until there are adequate data to support the safe and effective use of this approach, bronchoscopic ablation is not recommended for clinical use.

3.6 Bronchoscopic Therapies for Asthma

Bronchial thermoplasty (BT) is a treatment for patients with severe persistent asthma who remain symptomatic despite maximal medical treatment that delivers radiofrequency energy to the airways to reduce their smooth muscle mass. A pivotal randomized clinical trial did not show a change in forced expiratory volume in 1 s (FEV1) or airway hyperresponsiveness but was able to demonstrate an improvement in quality of life and reduction in exacerbation rates, visits to the emergency department, and days lost from school or work. At this time, the ideal asthma phenotypes and ideal candidates for this treatment modality remain to be determined, and thus, the utility of this approach remains limited.

3.7 Bronchoscopic Therapies for Chronic Obstructive Pulmonary Disease

The National Emphysema Treatment Trial (NETT), published in 2003, demonstrated that lung volume reduction (LVR) surgery for severe emphysema confers improved survival and exercise capacity in patients with severe emphysema to mimic the physiologic effects of surgical lung volume reduction (SLVR) in a less invasive fashion. The landmark Multicenter Intrapleural Sepsis Trial (MIST2) demonstrated that intrapleural sequential administration of recombinant tissue plasminogen activator (rtPA) and DNase resulted in significant radiographic and clinical improvements and allowed >90% of patients to avoid surgery. Randomized controlled trials are currently underway to compare intrapleural administration of rtPA and DNase to surgical decortication. Several bronchoscopic therapeutic modalities have been tested, including valves, coils, steam, stents, and foam, in patients with severe emphysema.

4. PLEURAL INTERVENTIONS

Thoracic ultrasound has become invaluable in the evaluation of patients with pleural effusion and pneumothorax. Medical thoracoscopy (also called pleuroscopy) is a minimally invasive technique most commonly used to evaluate recurrent exudative pleural effusions and is associated with a diagnostic yield of >95%. Indwelling pleural catheters (IPCs) have gained tremendous popularity and have been declared by evidence-based guidelines to be as acceptable as chemical pleurodesis for the management of symptomatic malignant pleural effusions. When comparing IPC and pleurodesis via talc slurry, two multicentered, open-label, randomized controlled trials demonstrated IPC effectively relieved dyspnea, decreased the duration of hospital stay, and lessened the need for future procedures. A recent study in patients without significant lung entrapment has shown that the outpatient administration of talc through an indwelling pleural catheter for the treatment of malignant pleural effusion resulted in a significantly higher chance of pleurodesis at 35 days than an indwelling catheter alone, with no deleterious effects. Pleural infection (empyema or complex parapneumonic effusion) is commonly encountered in clinical practice. The mainstay of therapy typically consisted of antibiotics, drainage of the infected pleural space with tube thoracostomy, and possible need for surgical decortication.

4.1 Persistent Air Leak

Persistent air leak is defined as a nonresolving pneumothorax with an air leak lasting more than 5–7 days. For over a decade, the U.S. Food and Drug Administration has maintained a humanitarian device exemption for compassionate use of the Spiration Valve System for management of persistent air leak following lobectomy, segmentectomy, or LVR surgery, although the device has also been used "off label" for the treatment of persistent air leak due to primary and secondary spontaneous pneumothoraces.

5. LUNG TRANSPLANTATION MANAGEMENT

While survival after lung transplantation continues to improve by era, the survival rates in this group are lower than in other solid-organ cohorts. Approximately 50% of lung transplant recipients will experience at least one episode of acute rejection in the first posttransplant year, and by 5 years posttransplant, approximately half will have developed chronic rejection. As a result, posttransplant immune suppression regimens may be more aggressive than in other solid-organ recipients, as described above. The immunosuppressive regimen must be balanced against the potential toxicities that accrue with these medications over time. Acute cellular rejection in lung transplant recipients is most common in the first posttransplant year, with a decreased but not absent frequency thereafter. Infections can stimulate cellular rejection, most clearly demonstrated in the setting of CMV infection, but also noted after other infections. Most programs incorporate a schedule of routine surveillance bronchoscopy to assess for acute cellular rejection posttransplant. Donor-derived cell-free DNA, which is produced in the setting of cell turnover and parenchymal injury, is increasingly being explored as a noninvasive method of detection of allograft dysfunction, most importantly in the setting of acute and chronic rejection. Acute cellular rejection manifests as a lymphocytic infiltrate involving the distal small vessels and capillaries and/or a lymphocytic bronchiolitis involving the distal airways of the lung. Acute cellular rejection, a risk factor for the development of CLAD, is treated with augmented oxygenation and immune suppression. Antibody-mediated rejection in its classic form is a neutrophilic vasculitis associated with the small vessels and capillaries of the lung, with associated deposition of by-products of the complement cascade, in the setting of allograft dysfunction and circulating donor-specific HLA antibodies in the blood. The manifestations of antibody-mediated rejection in the lung allograft are less specific than in other organs. Further research is ongoing into the diagnostic and treatment considerations of this entity in lung transplantation. CLAD is an overarching description of the syndrome of long-term allograft rejection. The classic manifestation of CLAD is obliterative bronchiolitis, the development of fibrinous material within the distal airways that leads to small-airways obstruction. As transbronchial biopsies are insensitive for diagnosing obliterative bronchiolitis, a clinical diagnostic designation of bronchiolitis obliterans syndrome can be made when specific PFT criteria are met and other causes of PFT decline are excluded. CLAD can also present as a restrictive phenotype, with imaging demonstrating upper lobe–predominant pleural thickening, small lung volumes, and interstitial changes on high-resolution computed tomography (CT). Numerous therapies for CLAD have been utilized, including azithromycin, montelukast, extracorporeal photopheresis, alemtuzumab, and others, with varying degrees of success. Infection is a significant complication of lung transplantation, with persistent risk over the lifetime of the transplant recipient. As time progresses, the chance of opportunistic infection increases. The risk of bacterial infection and fungal infection remains, and can affect the lung parenchyma, airways and anastomotic sites, and other organs. Viral infections, such as CMV reactivation and infection, EBV-associated posttransplant lymphoproliferative disease, and other rarer infections, can also develop in the later posttransplant setting as well. Numerous longer-term medical complications can be seen in lung transplant recipients. Essential hypertension, diabetes mellitus, chronic renal insufficiency, and bone loss are some examples of chronic medical conditions observed following transplantation. A multidisciplinary approach to care that involves the patient's primary care physician, local pulmonologist, and appropriate subspecialists, along with transplant pharmacy, as well as social work and care coordination, is beneficial in addressing the

complex needs of lung transplant recipients over time.

6. DIFFERENTIAL DIAGNOSIS

The differential diagnosis of central airway obstruction (CAO) is shown in Table 310-1. CAO describes obstruction of the trachea, main stem bronchi, bronchus intermedius, and/or lobar bronchi, and can present as intrinsic (endoluminal), extrinsic (extraluminal), or mixed (extraluminal tumor resulting in mass effect and endoluminal involvement).

7. INVESTIGATIONS & DIAGNOSIS

Convex endobronchial ultrasound (cEBUS) is a flexible bronchoscope combined with ultrasound technology that allows for real-time visualization during transbronchial needle aspiration (TBNA) of mediastinal and hilar lymph nodes and masses adjacent to the airways. With a sensitivity of 90% and a specificity of 100%, cEBUS is the gold standard for lung cancer staging and can also provide sufficient tissue to perform molecular profiling to guide targeted therapies in lung cancer with adequacy rates for testing that exceed 95%. cEBUS is also extremely helpful in diagnosing mediastinal and hilar adenopathy due to sarcoidosis. The use of endobronchial ultrasound to diagnose lymphomas has historically been of limited utility owing to lack of tissue architecture in needle aspirates. However, advances in cEBUS using a cryobiopsy technique in lieu of needle aspirate have shown promise but in providing adequate tissue and histopathologic architecture from intranodal cryobiopsy. Radial-probe endobronchial ultrasound utilizes a radial scanning ultrasound probe that is inserted through the bronchoscope and into the lung, producing a real-time image of the target lesion. Thoracic ultrasound has become invaluable in the evaluation of patients with pleural effusion and pneumothorax. Medical thoracoscopy (also called pleuroscopy) is a minimally invasive technique most commonly used to evaluate recurrent exudative pleural effusions and is associated with a diagnostic yield of >95%.

8. PROGNOSIS & COMPLICATIONS

Predictors of short- and long-term outcomes after lung transplantation are outlined in Table 309-3. While survival after lung transplantation continues to improve by era, the survival rates in this group are lower than in other solid-organ cohorts. Approximately 50% of lung transplant recipients will experience at least one episode of acute rejection in the first posttransplant year, and by 5 years posttransplant, approximately half will have developed chronic rejection. Stent complications are not uncommon and include migration, mucostasis, infection, and the development of granulation tissue. First-generation biodegradable stents, custom three-dimensional printed stents, and drug-coated stents are currently being evaluated, working toward a personalized airway stenting and its associated complications.

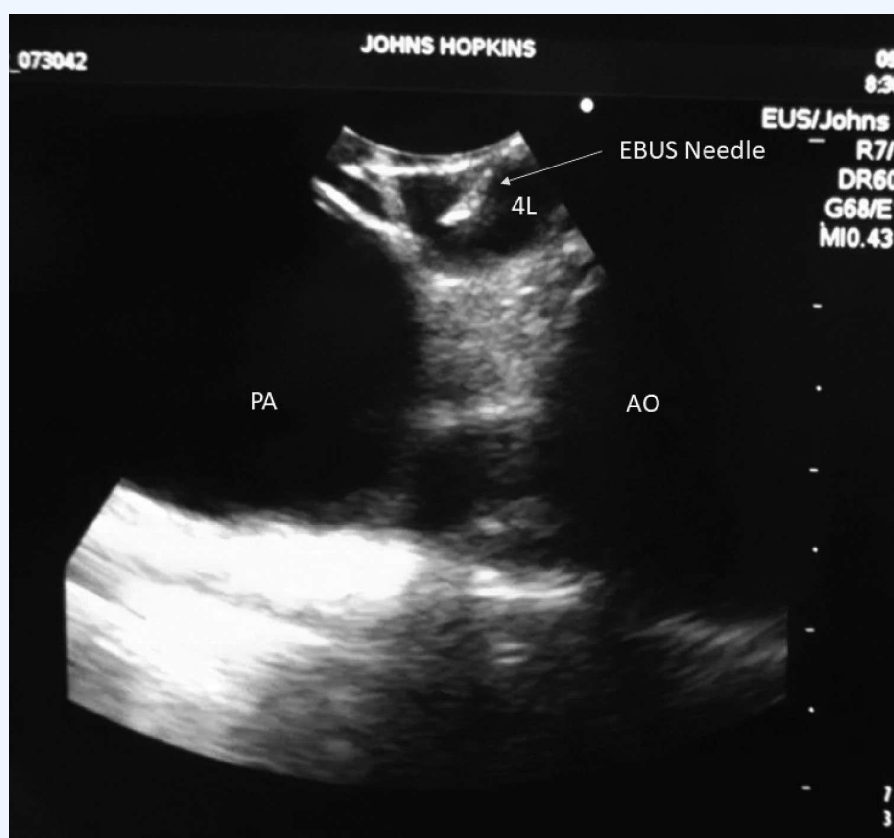
9. SPECIAL CONSIDERATIONS

A multidisciplinary approach to care that involves the patient's primary care physician, local pulmonologist, and appropriate subspecialists, along with transplant pharmacy, as well as social work and care coordination, is beneficial in addressing the complex needs of lung transplant recipients over time. Essential hypertension, diabetes mellitus, chronic renal insufficiency, and bone loss are some examples of chronic medical conditions observed following transplantation. Active research is also focusing on the utility of bronchoscopy for the ablation of early-stage lung cancer, as well as the treatment of chronic bronchitis.

10. KEY PEARLS & CLINICAL TRAPS

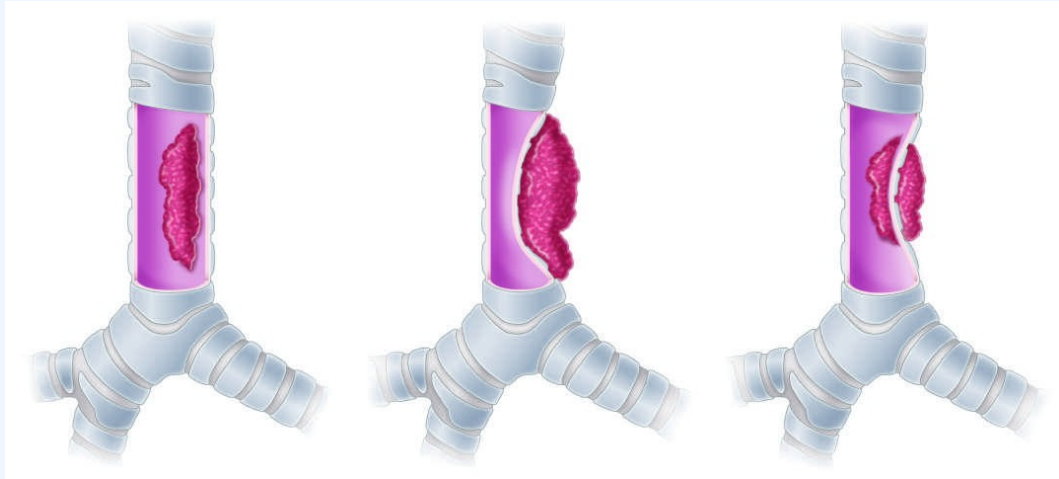
Bronchial thermoplasty (BT) for severe asthma improves quality of life and reduces exacerbation rates but does not change FEV1 or airway hyperresponsiveness. Bronchoscopic lung volume reduction (BLVR) via valve placement demonstrates improvements in lung function and quality of life with a lower rate of perioperative morbidity and mortality compared to surgical lung volume reduction (SLVR). Persistent air leak is defined as a nonresolving pneumothorax with an air leak lasting more than 5–7 days. The Multicenter Intrapleural Sepsis Trial (MIST2) demonstrated that intrapleural sequential administration of recombinant tissue plasminogen activator (rtPA) and DNase resulted in significant radiographic and clinical improvements and allowed >90% of patients to avoid surgery. Acute cellular rejection in lung transplant recipients is most common in the first posttransplant year, with a decreased but not absent frequency thereafter. Infections can stimulate cellular rejection, most clearly demonstrated in the setting of CMV infection, but also noted after other infections.

FIGURES & ILLUSTRATIONS — FROM HARRISON'S



Harrison's 22e · Figure 1

FIGURE 310-1 Endobronchial ultrasound transbronchial needle aspiration image of needle under ultrasound guidance sampling station 4L lymph node. AO, aorta; PA, pulmonary artery. — Endobronchial ultrasound transbronchial needle aspiration image of needle under ultrasound guidance sampling station 4L lymph node. AO, aorta; PA, pulmonary artery.



Harrison's 22e · Figure 2

FIGURE 310-2 Types of central airway obstruction. — Types of central airway obstruction: A) Intrinsic, B) Extrinsic, C) Mixed (extraluminal tumor resulting in mass effect and endoluminal involvement).