Treatment of Bronchopleural Fistula

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KEYWORDS

• Bronchopleural fistula • Pneumonectomy • Bronchoscopy • Stent • Pneumothorax

KEY POINTS

- Bronchopleural fistula (BPF) is a pathological connection between the bronchial tree and pleural space, caused by surgery, infection, trauma, or malignancy.
- Clinical presentation is typically pneumothorax with acute dyspnea and chest pain. Pleural space infection is sometimes present with associated symptoms.
- Diagnosis: chest imaging demonstrates air in the pleural space; persistent air leak after chest tube thoracostomy; bronchoscopy may help localize.
- Management: chest tube thoracostomy followed by early surgical repair for post-operative BPF; bronchoscopic interventions are options in poor surgical candidates.
- Complications include persistent air leak, empyema, sepsis, respiratory failure, and prolonged hospitalization.

Video content accompanies this article at http://www.chestmed.theclinics.com.

INTRODUCTION

A bronchopleural fistula (BPF) represents a serious and often life-threatening complication in pulmonary medicine. It is defined by the presence of an abnormal communication between the bronchial tree (including main stem, lobar, segmental, or subsegmental bronchi) and the pleural cavity. The condition can arise from various etiologies, including surgical interventions, infections, malignancies, and trauma. Understanding the underlying causes and mechanisms is crucial for effective management and treatment.

This article aims to provide a comprehensive review of BPF, focusing on its etiologies, diagnosis, and treatment options. We will also explore the latest advancements in diagnostic and therapeutic techniques, highlighting their clinical implications.

ETIOLOGY AND EPIDEMIOLOGY

The incidence of BPF varies widely, with higher rates observed in patients undergoing lung resection surgeries, particularly pneumonectomy.[1] Following pneumonectomy, BPF occurs in 1.5% to 4.5% of patients as opposed to lobectomy and sublobar resection in which it occurs 0.5% to 1%.[1] The incidence of BPF has been reported up to 20% after pneumonectomy.[2]

Patient-identified preoperative risk factors for BPF include history of chemotherapy and/or radiation, diabetes mellitus, heavy smoking, and chronic obstructive pulmonary disease. Diabetic microangiopathy causing small vessel ischemia can lead to particularly poor stump healing after pulmonary resection with a meta-analysis showing a pooled increased odds of BPF of 1.97 (95% CI, 1.39–2.80) when compared with patients without

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Abbreviations

APF	alveolopleural fistula
BEPS	benign emptying of the postpneumonectomy space
BPF	bronchopleural fistula
CT	computed tomography

diabetes.[3] Limited functional status (with poor wound healing and/or nutrition), male sex, and age greater than 60 year old also have an increased risk of BPF.[4–6] Prolonged postoperative mechanical ventilation also appears to increase risk for BPF.[7]

Surgical risk factors for postoperative BPF, in addition to pneumonectomy, include right-sided surgery, positive bronchial margins for malignancy (although, in general, pneumonectomy for benign disease caries a high risk for BPF), a large remaining bronchial stump of greater than 25 mm, extensive lymph node dissection, and history of an ipsilateral thoracotomy.[8] It has been suggested that the bronchial closure technique of manual closure versus stapled closure could impact the subsequent development of BPF, although this remains controversial.[9–11] A risk calculator for the development of BPFs in nonsmall cell lung cancer after pneumonectomy has been published with the potential to be used to select patients for intervention.[12]

Additional etiologies of BPF include complications related to cancer treatment, infections, and trauma. A meta-analysis showed that neoadjuvant radiotherapy alone or chemoradiotherapy significantly increased the risk of BPF while neoadjuvant chemotherapy alone did not.[13]

Bacterial, tuberculous, and fungal infections that extend to the pleural space and create fistulous tracts have been reported in the literature.[14,15] In cases of malignant-related or infectious-related BPF, involvement of the bronchus decreases the likelihood that these patients will be appropriate surgical candidates.[5,15,16] Finally, blunt or penetrating chest trauma can result in BPF. The severity of the injury and the extent of bronchial and pleural damage influence the likelihood of fistula formation.

CLINICAL PRESENTATION

Development of tension pneumothorax in the early postoperative period following lung resection, especially pneumonectomy, is almost pathognomonic of BPF. However, it is important to recognize that these symptoms can be due to fluid accumulation (such as postoperative chylothorax or hemorrhage) or nonfunctional chest tube drainage (ie, displaced or blocked chest tube) and, therefore, nonspecific. Patients with BPFs often present with the symptoms of pneumothorax with acute onset dyspnea and chest pain; hemodynamic instability can indicate underlying tension physiology.

In postoperative BPF, most patients develop symptoms within 2 weeks of lung resection. If a drainage catheter remains in the chest at the time of BPF development, symptoms are often less pronounced; therefore, a high index of suspicion is needed to identify BPF early in such scenarios. A persistent or new larger air leak through the chest tube drainage system may be the only sign present.[17] Decreased air entry and occasional subcutaneous emphysema are seen on physical examination with additional nonspecific findings.

Patients commonly present with concomitant infectious symptoms when BPF recognition is delayed following surgery. Symptoms of infection of the pleural space or empyema include fever, malaise, muscle wasting, and cough with purulent sputum (often high in volume due to drainage directly from the pleural space), as well as reduced air entry and dullness to percussion on the affected side.

In rare cases, when the BPF is associated with an empyema that is not adequately drained, the infection can erode through the chest wall and a pleurocutaneous opening with the drainage of mucopurulent material may be seen (empyema necessitans).

DIAGNOSIS

Imaging

Imaging, either a chest radiograph or computed tomography (CT), will show air outside the lung in the pleural space with tracheal deviation/contralateral mediastinal shift if tension physiology is present (**Fig. 1**). Additional radiographic features may include pneumomediastinum and/or subcutaneous emphysema. The presence of air bubbles around the surgical site or bronchial stump and visualization of the fistula may also be seen on CT imaging. One study reported that BPF could be localized using CT in 55% of patients, especially if enhanced by 3-dimensional reconstruction.[18]

Bronchoscopy

Direct airway inspection through bronchoscopy is critical for proper evaluation of the surgical site (if applicable), assessment of fistula size, and exclusion of other etiologies (**Fig. 2**). Additional

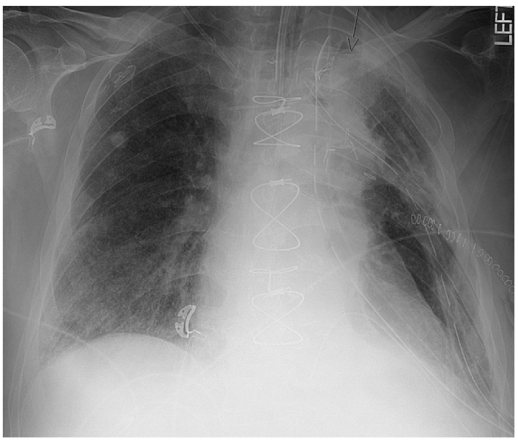

Fig. 1. Chest X ray of a patient with a BPF following surgery.

diagnostic methodologies, such as bronchoalveolar lavage and endobronchial ultrasound biopsy of lymph nodes, can be performed at the time of evaluation.

Commonly encountered bronchoscopic findings of BPF include bubbling at the surgical site when saline is instilled or the presence of an overt mucosal defect. Instillation of methylene blue into the pleural space through the chest tube with simultaneous bronchoscopic visualization of dye in the tracheobronchial tree can enhance detection and localization. Unfortunately, not all defects are readily apparent endoscopically, especially in the presence of tissue edema or significant secretions.

Sequential balloon occlusion of the bronchi is sometimes used, particularly for the localization of a smaller or segmental (ie, more distal) BPF, with evaluation of the air leak seen through chest drainage (Video 1).

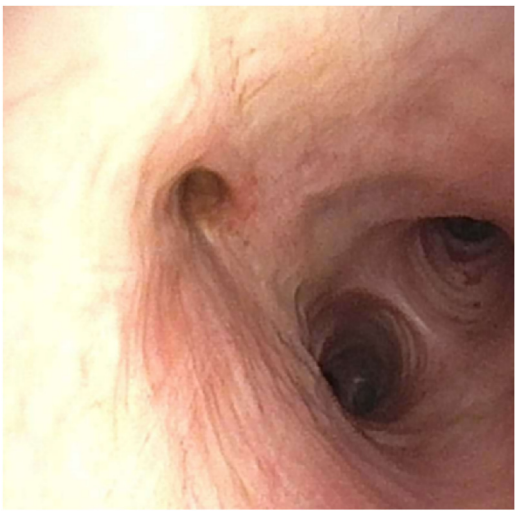

Fig. 2. BPF seen during bronchoscopy.

DIFFERENTIAL DIAGNOSIS

Classically, decreasing air-fluid level over time (less than or equal to 2 cm) indicating displacement of postoperative fluid by air was considered a sign of BPF requiring surgical intervention. However, a condition known as benign emptying of the postpneumonectomy space (BEPS) may also cause these postoperative signs. The diagnosis of BEPS is confirmed when there is absence of symptoms (no fever, white cell count elevation, or fluid expectoration), negative culture results if fluid sampled (while patient is not receiving antibiotic therapy), absence of BPF during bronchoscopy or ventilation scintigraphy scan (or both), and recovery without drainage catheter placement or other intervention.[19]

If BPF is suspected due to air in the pleural space, an additional etiologic consideration is empyema due to gas-producing bacteria. Culture of the fluid with a gas-producing anaerobic organism, especially if there is absence of an active air leak following chest tube placement, suggests empyema from gas forming organism rather than BPF.

Finally, appropriate management of BPF requires differentiation from an alveolopleural fistula (APF), which is a communication of the lung parenchymal distal to the level of the subsegmental bronchus and the pleural space. While these commonly both occur following surgical intervention and have similar presenting symptoms, the treatment of each entity is unique. APF is the most common postoperative complication after elective lung resection.[20] The incidence of air leak from APF after lung resection is 25% to 50% on postoperative day 1 and up to 20% on day 2.[21–23] Unlike BPF, the air leak associated with APF tends to be less vigorous and is typically not associated with pleural space infection. The largest and most uncommon continuous air leak is present throughout the respiratory cycle and seen in the patients who are receiving mechanical ventilation or have BPF.[24]

Management for APF often requires chest tube insertion for the drainage of air. Prolonged air leak from the site of defect should be suspected if the chest tube has been required for 5 days or more. APF-associated prolonged air leaks are not fatal but are associated with prolonged hospital stays, higher rates of intensive care unit admission, and high morbidity.[25] While most patients respond to conservative therapy, there is no

consensus or guidelines on how to manage patients suffering from this complication for an extended period. Interventional treatments can include ambulatory one-way valve devices, bronchoscopic methods, pleural procedures (autologous blood patches, chemical pleurodesis, etc), or surgery. While specifics on these treatments are not the focus of this article, we will mention that endobronchial valves placed during bronchoscopy for prolonged air leaks in the setting of APF have gained popularity in the last decade. In patients who exhibit decreased or cessation of the air leak using a sequential balloon occlusion through flexible bronchoscopy, the bronchial segmental or subsegmental airway feeding the APF can be blocked using endobronchial valves. The largest report of patients receiving valves for APF, showed that out of the 75 patients included, 70% experienced resolution of the air leak with a median time of 16 days to resolution.[22]

MANAGEMENT

Current Evidence

Currently, there is limited methodologically robust data on the best management of BPF with no consensus statement or guidelines available. Management is driven by expert opinion with significant practice variation among physicians.

General Approach

The natural history of BPF almost always necessitates treatment in the form of surgical closure or bronchoscopic intervention. Spontaneous closure is rare.

Once BPF is detected, chest tube thoracostomy drainage should be prioritized for patient stabilization or prevention of tension physiology from developing. Ultrasound guidance for drainage catheter(s) is usually helpful to optimize placement in the supradiaphragmatic/midaxillary line. The consensus is that water seal alone or low continuous suction should be used.

Sampling of any fluid is important to rule out infection. Pleural studies including pH, cell count, total protein, lactate dehydrogenase, glucose, cytology, triglycerides, Gram stain, and culture (aerobic and anaerobic bottles) should be sent for analysis.

While awaiting laboratory evidence of infection, broad-spectrum antibiotics should be initiated. Most experts recommend empiric treatment of anaerobic microorganisms. In patients with complex pleural spaces with significant septations and/or loculations, intrapleural enzyme therapy may be appropriate for complete chest drainage.

Postural drainage has been reported to help with fluid drainage by placing patients in either a head-up (reverse Trendelenburg) or head-down (Trendelenburg) position. Prior to consideration of postural drainage, patients should be able to expectorate, have limited chest tube drainage of less than 30 mL per day of output, and be eligible for pleural irrigation.[15] In a retrospective case series of 13 patients with BPF, all patients' BPFs closed with conservative management with chest tube placement, postural drainage $\pm$ debridement, and irrigation.[15] This approach should be reserved for patients without interventional options due to the unpredictable nature of healing that could require months of chest tube placement until spontaneous closure.

Optimizing other patient factors such as concomitant medical issues, nutrition, and mechanical ventilation to avoid barotrauma continue to be a standard of care. Patients requiring mechanical ventilation for significant hypoxia or hemodynamic instability tend to undergo corrective intervention following extubation as positive pressure ventilation might interfere with stump healing. Immediate or early extubation should be the goal following surgery as prolonged positive pressure ventilations is an independent risk factor for early BPF and has been reported to occur in as high as 19% of mechanically ventilated patients in the postoperative period.[10,26,27]

Surgical Intervention

BPFs detected early in the postoperative period (less than 2 weeks from surgery) are typically successfully repaired by surgical means, especially in the absence of infection of the bronchial stump. Early dehiscence tends to be more amenable to immediate repair or stump revision as the tissue integrity is relatively preserved, scarring is minimal, and a lack of a matured fistula tract and pleural contamination.[21,28]

Surgical repair usually involves revision of the stump with debridement of necrotic tissue and suture reclosure of the bronchial stump with vascularized flap tissue such as omentum or muscle through video-assisted thoracoscopic surgery approach.[29]

In patients who are unable to tolerate stump revision or if early surgical or bronchoscopic repair fails, an open-window procedure, such as the Eloesser flap or Clagett window, should be employed as adequate drainage, antibiotic therapy, and tissue healing allow the majority of BPFs to close over time. An Eloesser flap is a U-shaped incision and the resection of several subjacent posterolateral ribs; the U-shaped flap

is then folded into the pleural space, creating a permanent communication.[21] A Clagett window is the resection of a posterolateral lower rib and the formation of an open window in the lateral aspect of the chest to allow continuous drainage and irrigation of the cavity.[21] The duration of the open window thoracostomy usually depends on the patient's response to treatment.[30]

For patients who are not immediate surgical candidates, conservative management and bronchoscopic intervention can be considered as bridges if patient characteristics (like nutrition or functional status) can be optimized or reversed with additional time.

Bronchoscopic Intervention

In patients who are poor surgical candidates, bronchoscopic interventions for the treatment of BPF have been successful. Bronchoscopic approach may be the best strategy for patients with septic shock, severe hypoxemia, requiring mechanical ventilation, and those who require a bridge to surgery as described earlier. Success rate for fistula closure via bronchoscopy ranges from 30% to 80%.[31–33]

When the bronchial stump is impacted by disease, such as in infection or in malignancy (with positive margins seen on pathologic resected specimens), bronchoscopic management is largely focused on temporary fistula closure. While there is no single method of treatment that is recommended, the choice of treatment should consider patient factors and fistula size and location.

For fistulas larger than 8 mm, closure with airway stents, coils, or Amplatzer devices have been reported. These devices have advantages in that they can be removed if fistula closure is achieved. Airway stents are often the first method of closure and have been reported to be successful in numerous case reports in the central airways (**Fig. 3**). Stents appropriate for BPF jailing include silicone and covered metallic stents.[34–38] Airway stenting has been reported successful in 97% first attempt and 100% second-attempt stent placements in a series of 148 patients from China.[39]

Occasionally, an Amplatzer device, a vascular plug closure device with 2 discs that sit on either side of the defect, used primarily in occlusion of atrial septal defects, can be used. This is an off-label use of this device which should be communicated to the patient appropriately.[40,41] A case series of 31 patients with BPF treated with Amplatzer devices (Amplatzer devices and Amplatzer vascular plugs) reported a 96% immediate rate of success.[40] Twenty-four patients had BPF due to surgery with 21 patients having a history of lung cancer. While this series had a significant rate of mortality (n = 17/31 patients), the cause of death was mainly due to disease recurrence or postoperative complications such as infection. No patient died due to BPF recurrence.[40] These devices offer hope as a therapeutic option for those who are not surgical candidates, though experience and data remain limited.[42] Finally, for fistulas greater than 8 mm, the use of angiography coils either alone or in combination with other occlusive materials to successfully treat BPF have been case-reported.[38,43–45]

While stents, Amplatzer devices, and coils can also be used to seal smaller fistulas, fistulas less than 8 mm have been closed with occlusive materials. These materials have been reported in case series only with no comparative studies between effectiveness. Methyl-2-cyanoacrylate, N-butyl-cyanoacrylate, albumin-glutaraldehyde tissue adhesive, silver nitrate, polyvinyl alcohol sponge, and fibrin glue (alone or with other adjuncts such as spongy calf bone fragments) all of which have been injected through catheters in the working channel of a bronchoscope to seal BPF with higher success rates in smaller fistulas.[31,46–54] Occasionally, sclerosants such as ethanol, polidocanol, and tetracycline have been injected endoluminally either as solo agents or in combination with other therapies such as autologous blood.[55–57] Ablative therapies (heat and cold) have been used but risk damaging the remaining tissue and enlarging the defect.[58] Investigational methods have been focused on tissue generation including transplanted bone marrow-derived mesenchymal stem cells and dehydrated amniotic membrane allograft.[59–61]

Alternative approaches have been proposed in case reports such as endoscopic autologous fat implantation but do not represent the most common approach to treatment of BPF.[62]

PROGNOSIS

Historically, the mortality associated with BPF ranged from 20% to 50%.[21] More recent data suggest that mortality of BPF within 30 days of surgery is 11% to 18% and 0% to 7% for BPF that develops beyond 30 days of surgery.[2,12,63] The increased risk of mortality in the early postoperative period is the high likelihood of infection that can lead to pneumonia of the contralateral lung. Additionally, an increased risk of cardiac and pulmonary complications can occur in patients with BPF-associated empyema.[27] Survival differences for patients postpneumonectomy at 1 year is

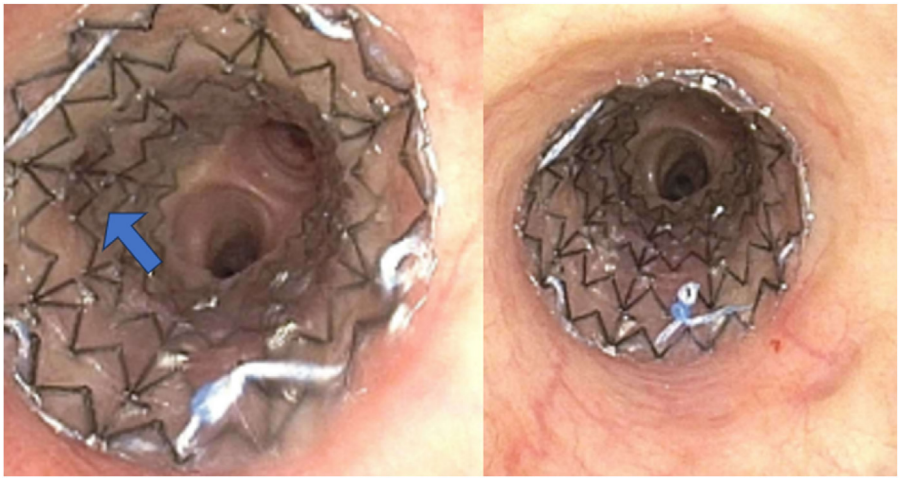

Fig. 3. Stent covering left main fistula tract.

80% for late presentation as compared with 47% for early empyema[64]

FUTURE CONSIDERATIONS/EMERGING THERAPIES/EMERGING TREATMENT

There are several recently closed or pending clinical trials investigating different treatment strategies for BPFs. Occluder devices, stem cells, and engineered tissue are potential directions in the future for treatment.

SUMMARY

BPF remains a challenging clinical entity with significant morbidity and mortality. A comprehensive understanding of its etiologies, clinical presentation, diagnosis, and treatment options is essential for effective management. Advances in surgical, endoscopic, and novel therapeutic approaches offer hope for improved outcomes in BPF patients. Continued research and clinical trials are crucial for developing and refining these treatment strategies.

CLINICS CARE POINTS

- Bronchopleural fistula (BPF) is a pathologic connection between the bronchial tree and the pleural space and is a serious and often life-threatening condition. It can result from surgical interventions, infections, malignancies, and trauma.
- While the incidence of BPF varies, it is higher in patients who have undergone lung resection surgery, particularly pneumonectomy. Preoperative risk factors include a history of chemotherapy and/or radiation, diabetes mellitus, heavy smoking, and more.
- Clinical Presentation: Patients with BPF often present with symptoms of pneumothorax, such as acute dyspnea and chest pain. Additional symptoms may be present if the BPF is related to an underlying infection.
- Diagnosis: Imaging, either a chest radiograph or computed tomography, will show air outside the lung in the pleural space. Direct airway inspection through bronchoscopy is critical for proper evaluation of the surgical site and assessment of fistula size.
- Management: Current evidence on the best management of BPF is limited. Once BPF is detected, chest tube thoracostomy drainage should be prioritized for patient stabilization. Surgical intervention is typically successful for BPFs detected early in the postoperative period. In patients who are poor surgical candidates, bronchoscopic interventions have been successful.
- Future Considerations: Emerging therapies, including regenerative medicine approaches and advanced biomaterials, hold promise for improving BPF treatment outcomes. Continued research and clinical trials are crucial for developing and refining these treatment strategies.

DISCLOSURE

The authors have nothing to disclose.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at https://doi.org/10.1016/j.ccm.2025.02.015.

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