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Bronchopleural fistula: An update for intensivists

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Abstract Bronchopleural fistula is a potentially fatal condition that may result after a variety of clinical conditions, most commonly after pulmonary resection. Either surgical or bronchoscopic repair is required to definitively correct these lesions, though a small number may resolve spontaneously with optimal ventilatory care and other options available to an intensivist in the management of this complex condition. The successful management of a bronchopleural fistula depends on formulating a treatment strategy tailored to individual patient needs.

1. Definition

The term bronchopleural fistula (BPF) refers to a leakage of inspired air from the airways into the pleural space for more than 24 hours. Although it is not uncommon to observe minor air leaks beyond 24 hours in the postpneumonectomy setting, most of them resolve spontaneously. The leak can be from either a clearly identifiable airway or parenchymal tissue; the latter is sometimes referred to as alveolar-pleural fistula [1]. Bronchopleural fistula can be classified as peripheral or central depending on the site of the leak. Apart from the obvious anatomical difference, the 2 differ significantly with reference to etiology, diagnostic techniques, and management options.

2. Etiology

Pulmonary surgical procedures remain the leading cause of a BPF, although refinements in surgical techniques have substantially reduced the incidence [2]. The incidence after pulmonary resection for lung cancer is reported between 4.5% and 20% after pneumonectomy and 0.5% after lobectomy [3,4]. The incidence is highest after right pneumonectomy and right lower lobectomy [5]. Some of the perioperative factors associated with increased incidence of BPF include incomplete tumor resection, steroid use, *Haemophilus influenza* in sputum at time of operation, anemia, elevated erythrocyte sedimentation rate, leukocytosis, tracheostomy, and use of bronchoscopy for airway toilet

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Table 1 Causes of a BPF [5-11]

Pulmonary resection
Persistent spontaneous pneumothorax including ruptured bulla(e)
Necrotizing pulmonary infection
Inflammatory lung diseases
Malignancy
Postchemotherapy or radiotherapy for lung cancer
Thoracic trauma
Post–lung transplant
ARDS
Iatrogenic (eg, chest tube insertion and central venous line placements)
Broncholithiasis
Idiopathic

[5,6]. Postoperative mechanical ventilation is also a significant independent risk factor [5]. Causes of BPF are presented in Table 1.

3. Clinical presentation

The clinical presentation of a BPF can be acute, subacute, or chronic. The acute presentation classically is that of tension pneumothorax [12]. The communication between a pleural cavity and the airways may also manifest as the sudden expectoration of purulent sputum, dyspnea, subcutaneous emphysema, mediastinal and tracheal shifts, and decrease in the level of an established pleural effusion [5]. This may be the only sign and is often diagnostic. The subacute and chronic presentations are usually associated with an infected pleural space and present in a more insidious form with less productive cough, fever, and malaise with varying levels of respiratory compromise.

4. Adverse sequelae

A number of adverse consequences of BPF account for the morbidity and mortality associated with this condition (Table 2). Mortality rates of 18% to 50% have been reported [9,13,14]. A particularly poor prognosis exists for BPF developing late in the course of a nontraumatic illness requiring mechanical ventilation, where there are leaks in excess of 500 mL per breath [10]. Right pneumonectomy complicated by BPF similarly has a high mortality [15].

5. Diagnostic techniques

The presence of a BPF is usually obvious in the intensive care setting and seldom requires special diagnostic techniques. Conversely, the diagnosis of a BPF may be difficult, especially when the leak is small or very early in the natural course of a fistula. Chest x-ray demonstrating a drop in the level of an established pleural effusion invariably suggests a BPF. Detection of methylene blue in the chest drain after an intratracheal instillation may also be diagnostic [16]. Nuclear medicine techniques such as inhalation of xenon-133 or technicium-99m diethylenetriamine pentaacetic acid scintigraphy [17] have been developed. Measuring the O_2 and N_2O concentrations in a pneumonectomy cavity after inhalation of a mixture of O_2 and N_2O has also been described [18]. Computed tomography is a more commonly used and simpler technique that may detect peripheral BPFs and facilitate planning of definitive therapy [19,20]. Bronchoscopy is a useful therapeutic and diagnostic adjunct, allowing simultaneous evaluation of the stump, localization of a fistula, and potentially definitive management if an amenable lesion is found [5].

6. Management

The management of BPF is conveniently considered under supportive and definitive strategies.

7. Supportive

7.1. Intercostal catheters

Intercostal catheters (ICCs) are required for the management of air accumulating in the pleural space and to drain coexisting pleural effusions or empyema to allow reexpansion of the lung. Length of the ICC (l) and the radius (r) are the important determinants of flow as governed by the Fanning equation, which describes turbulent flows of moist gases through a tube (Table 3). A short wide-bore ICC can achieve the best results when a large air leak is present [13].

Air leaks may vary from less than a liter to in excess of 16 L/min [21-23]. The smallest internal diameter of an ICC

Table 2 Complications of a BPF

Incomplete expansion of affected lung
Derecruitment of unaffected lung
Volutrauma or barotrauma of unaffected lung (complicating mechanical ventilation)
Inability to maintain PEEP
Systemic hypoxemia with pulmonary O_2 toxicity
Respiratory acidosis
Ventilator auto triggering
Empyema
Inaccurate calorimetry
Death

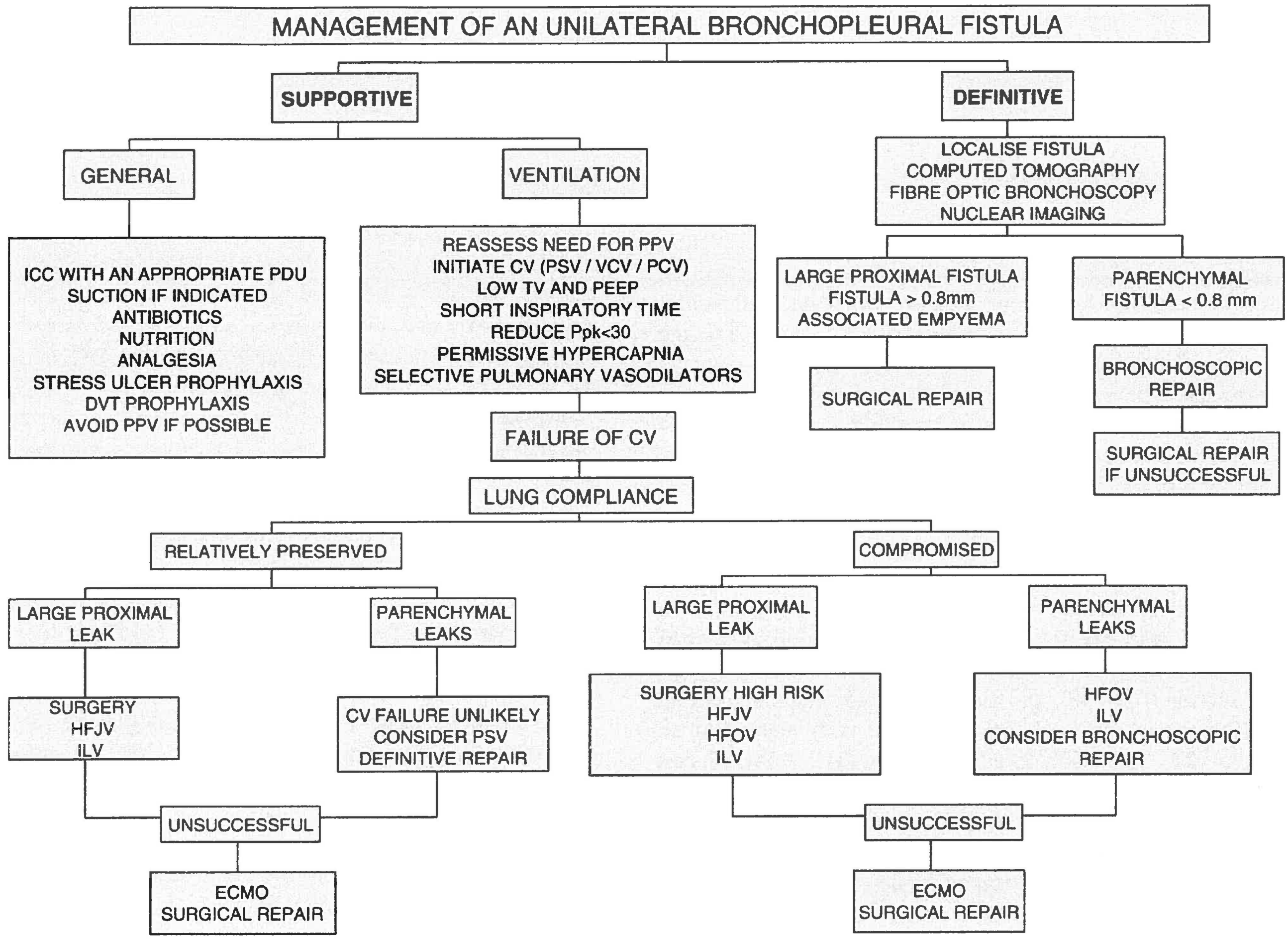

Fig. 1 Summary of treatment options for an unilateral bronchopleural fistula. CV indicates conventional ventilation; PSV, pressure support ventilation; VCV, volume-controlled ventilation; PCV, pressure-controlled ventilation; TV, tidal volume; Ppk, peak pressure; ECMO, extracorporeal membrane oxygenation.

that would allow a maximal flow of 15 L/min at −10 cm H_2O suction is 6 mm [22,23]. A pneumotachograph or a water-filled spirometer can measure the air leak [24]. This is generally not practical in the clinical setting. For mechanically ventilated patients receiving volume-controlled ventilation, the volume of the leak can be estimated as the difference between exhaled and set minute volume assuming an intact circuit.

Various manipulations of ICC have been reported to minimize air leak and improve gas exchange. However, these manipulations are problematic, not particularly practical and increase the risk of a tension pneumothorax [25-28]. The negative pressures applied to a chest tube to assist drainage of the pleural space may increase flow through the fistula by increasing transpulmonary pressures and induce autotriggering of ventilator [29,30]. If not considered, autotriggering may also lead to inappropriate use of sedatives and paralytic agents to suppress hyperventilation. This may be avoided by decreasing sensitivity and minimizing airway pressure [31]. Determining ideal ICC suction pressures requires frequent reassessment of fistula flow rate. Intercostal catheters can be used as a portal for delivery of sclerosing agents for pleurodesis if pneumothorax is present: for local anesthetics if analgesia is an issue or antibiotics into the pleural cavity, which, when combined with drainage of an empyema, may assist in disinfection of pleural cavity before a BPF is repaired [32,33]. Video assisted thoracoscopy (VAT) and pleurodesis, however, may be a superior option enabling the operator to visualize the fistula site and the pleural cavity.

Table 3 Fanning equation

$V = \Pi^2 r^5 P/fl$
V = flow
P = pressure
F = friction factor
L = length of the tube
R = radius of the tube

Conversely, chest tubes represent a potential portal for introduction of infection into the pleural space and may delay BPF healing and repair if not removed in a timely fashion.

7.2. Drainage systems

Once an adequate sized chest tube is in place, a pleural drainage unit (PDU) needs to be attached to provide suction and a water seal to prevent backflow of air into the pleural cavity. Understanding the limitations of various drainage systems is essential when selecting from the wide range of commercially available PDUs. It is important that the drainage system is capable of handling large volumes of air drained by the chest tube. Resistance of the ICC and PDU are important determinants of this airflow. Addition of suction is indicated when gravity-assisted water seal drainage is inadequate in draining air and other pleural contents. Three compartment drainage systems are gaining popularity, and a number of commercially available units can handle flows from 10.8 to 42.1 L/min at a suction pressure of −20 cm H_2O. A review of 4 common units at different levels of suction (0 to −40) and air leaks demonstrated significant difference in maximal flows achieved with increasing air leaks [21]. A suction level of −20 cm H_2O achieved best results, and increasing the suction pressure to −40 cm H_2O failed to improve maximal flows. Baumann et al [34] compared various commercially available PDUs and observed significant difference in flows, with mean flows averaging from 10.8 to 42.2 L/min.

The traditional PDUs regulate suction pressures by the height of the water column in the suction control chamber. Excessive suction at the source results in loud bubbling and exaggerates the evaporation of water in the suction control chamber, decreasing the suction applied to the patient over time as the water level decreases. Newer-generation 'dry' suction units may be advantageous because they permit higher suction pressures, are easy to set up, and operate quietly with an absence of bubbling. The suction levels are controlled by a self-compensating regulator as opposed to the fluid column. Suction pressures can be controlled by adjustments on the dial on the suction control unit allowing increased flows through the system by increasing the source suction without imposing significant negative intrapleural pressures. Effectively, this translates to higher flows through the unit without the disadvantageous increases in transpulmonary pressures, which is ideal in the setting of a BPF. The newer PDUs also include various safety features including bidirectional pressure relief valves.

7.3. Mechanical ventilation

7.3.1. Conventional ventilation

Positive pressure ventilation (PPV) in patients with BPF can be challenging especially in those with large air leaks and underlying severe parenchymal lung disease. Spontaneous ventilation should be maintained whenever feasible. The primary aim of PPV in these circumstances is to keep the airway pressure below the critical opening pressure of the fistula as well as optimizing pleural suction pressures and preventing further lung injury. To reduce the flow across a BPF, minimal levels of positive end expiratory pressure (PEEP), a short inspiratory time, low tidal volumes, and a low respiratory rate are useful. [25,26,30]. The volume of the air leak through the BPF is proportional to the mean airway pressure [35], and the aforesaid strategies are aimed at reducing this. Peak airway pressures greater than 30 cm H_2O are associated with increased air leak [36].

Conventional mechanical ventilation will most often suffice, and intractable respiratory acidosis is rare unless underlying severe lung disease is present. Permissive hypercapnia, if not contraindicated, may be a useful strategy. Conventional volume or pressure control modes with previously mentioned strategies to minimize air leak can be tried. Early tracheotomy may be useful in assisting a more prompt respiratory wean and progress toward spontaneous breathing.

There are no controlled studies comparing various modes of conventional mechanical ventilation in the setting of a BPF. One of the larger reports including 39 patients with BPF maintained on conventional ventilation showed significant mortality in patients with air leak greater than 500 mL/breath and also in those developing BPF late in the course of their illness. Only 2 of the patients in this series developed significant respiratory acidosis unresponsive to conventional ventilation despite them having major air leaks [10]. There are several case reports regarding the successful use of pressure control ventilation especially in patients with coexisting acute respiratory distress syndrome (ARDS) [37]. Synchronized intermittent mandatory ventilation and other modes such as pressure support ventilation, which support spontaneous breathing, may reduce mean airway pressures and the air leak.

7.3.2. Independent lung ventilation

Independent lung ventilation (ILV), a commonly used technique in anesthesia for thoracic surgery, may be used in intensive care patients as an alternative to conventional ventilation in special situations. When a lung injury is predominantly unilateral, ventilating both lungs as a single unit may potentiate volutrauma and barotrauma to the normal lung and worsen the intrapulmonary shunting in the diseased lung because there is heterogeneous distribution of ventilation and PEEP [38]. In the setting of a BPF, ILV facilitates optimal ventilation of the normal or less diseased lung, while allowing the maintenance of lower airway pressures on the affected side reducing the air leak.

Independent lung ventilation necessitates functional lung separation, and various techniques have been described for obtaining this [38]. When the compliance characteristics of the 2 lungs are different as in a BPF, physiological and anatomical separation may be required to improve gas exchange and lung protection. Some of the techniques that may be used for lung separation include deliberate endobronchial intubation with or without bronchoscopic assistance, endobronchial blockade (eg, bronchial blockers) [38,39], Univent tubes (Fuji Systems Corp., Tokyo, Japan [38,40], coaxial tubes, and double-lumen endotracheal tubes (DLTs). Most of these techniques permit ventilation of 1 lung only and are often limited by hypoxemia and intrapulmonary shunt necessitating lateral positioning of the patient with the "good lung" in a dependent position. These techniques may facilitate definitive management, but their use is generally limited by practicalities that dictate short-term use.

A DLT is the preferred technique for lung separation for prolonged periods of time in intensive care. Originally designed by Carlen, the DLT has seen a great deal of design modifications over the years, and tubes from various manufacturers are currently available. Double-lumen endotracheal tubes enable ventilation and suctioning of each lung separately [41]. They may be placed using direct laryngoscopy, fiber-optic bronchoscopy or through a tracheostomy. It should be emphasized that insertion of a DLT can be challenging especially in hypoxic patient with or without difficult airways. Left-sided DLTs are preferred because there is less risk of right upper-lobe collapse and malpositioning [42]. The technical aspects of ILV, DLT design, and insertion have been reviewed elsewhere [38].

Although fiber-optic bronchoscopy is not routinely required for the placement of a DLT [43], when available, it confirms position immediately because auscultatory techniques for confirmation of position may be unreliable [44]. It is also useful for surveillance of tube position and bronchial toilet and should be readily available because malpositioning and loss of functional separation may occur with minimal tube movements [42]. Sedation and paralysis are required to tolerate abnormal pulmonary mechanics. Suctioning and bronchoscopy through the narrow lumens of the DLT may be difficult [44], necessitating long suction catheters and a pediatric bronchoscope. The potential complications with DLTs include laryngobronchial mucosal trauma, tube blockage, airway edema, and inflammation. Bronchial rupture is a dreaded complication of an over-inflated bronchial cuff.

Once the DLT is in place and functional lung separation achieved, ILV may be instituted synchronously (which in real life equates to identical respiratory rate on both ventilators) or asynchronously using different conventional and nonconventional modes of ventilation (depending on lung compliance and the air leak) using 1 (requires specially designed valves) or 2 ventilators. The superiority of one mode over another has not been established [38,45]. It remains unclear if ventilator synchrony plays a significant role in the setting of a BPF. Asynchronous ILV is easier to establish, less complicated, and usually well tolerated [45], whereas true synchronization most commonly requires 2 ventilators with special software and an external cable connecting them. There are several case reports of successful use of synchronous and asynchronous ILV in both animal and human studies using different modes of ventilation on either lungs or also different synchronization techniques [46-50]. Further studies are required in various subgroups of patients depending on fistula location and underlying lung mechanics.

Independent lung ventilation is technically demanding and increases resource utilization in terms of equipment, monitoring, and skilled nursing care. With careful patient selection, it can be a useful alternative when conventional methods have failed. Conventional mechanical ventilation should be resumed at the earliest opportunity. For patients with disparities in lung compliance, improvement to the point of a 20% or less difference in compliance between sides may be a prudent indication for changing to a single ventilator and subsequently a standard endotracheal tube [51].

7.3.3. High-frequency ventilation

High-frequency ventilation (HFV) has been shown to provide adequate gas exchange at lower airway pressures. The details of mechanisms of gas exchange during HFV are described elsewhere [52,53]. In high-frequency jet ventilation (HFJV), gas under high pressure is delivered through a small bore cannula inserted into the endotracheal tube. Tidal volume is determined by the jet pressure and inspiratory time. Tidal volumes of 2 to 5 mL/kg are delivered at frequencies of 100 to 200 breaths/min [53]. There is little control over tidal volume, temperature, and humidification. Significant hyperinflation and hemodynamic instability due to passive expiration may occur.

In the largest reported series of patients with BPF as a sequela of ARDS, HFJV was no better than conventional ventilation, and no significant change in air loss from the ICC was observed [54]. High-frequency jet ventilation and nitric oxide have been used simultaneously in 1 patient with ARDS with coexisting large bilateral BPFs [55]. With conflicting case reports pertaining to the clinical efficacy of HFV, further controlled studies are required [29,56]. Ultrahigh-frequency jet ventilation at 450 breaths/min has been described in a controlled animal study to yield better results than those of HFJV or conventional PPV [57].

High-frequency oscillatory ventilation (HFOV) is emerging as a theoretical potential alternative for optimal protective ventilation. As yet, however, there is little data on the use of HFOV in adults. High-frequency oscillatory ventilation allows constant use of higher mean airway pressures, minimizing dead space and inducing reductions in the peak airway pressures [58]. High-frequency oscillatory ventilation creates pressure oscillations in the airways, thus generating small tidal volumes while maintaining a relatively constant mean airway pressure. A fresh flow of inspired gas is maintained to eliminate CO_2 from the system. The tidal volume is proportional to the amplitude of the airway oscillations. The active expiration decreases the risk of hyperinflation as opposed to HFJV [53].

Although there are several case reports describing successful use of HFOV in patients with ARDS, experience in patients with BPF is limited. One of the available studies reported on an improvement in oxygenation, reduction in mean airway pressure, and the air leak [53]. High-frequency oscillatory ventilation seems to be more lung protective in comparison to HFJV with expiration being active and with better control of tidal volumes.

There are several other reports of successful use of both HFJV and HFOV [29,55,59,60] in setting of BPF. High-frequency jet ventilation generally seems to be useful in patients with proximal BPF without significant underlying lung disease [13]. High-frequency oscillatory ventilation may be more suitable to patients with high-output BPF with poor lung compliance [53,60].

7.3.4. Extracorporeal support

There is little data available on the use of extracorporeal techniques like extracorporeal membrane oxygenation for oxygenation and carbon dioxide removal in the setting of a BPF. These techniques, however, may have a role to play in the future especially in the group of patients where other strategies fail to provide the desired results. A potential limiting factor is the use of systemic anticoagulation. Despite this case, reports of successful use of extracorporeal techniques in patients with traumatic lung injuries exist [61].

7.3.5. Adjuncts

It should not be forgotten that skilled medical and nursing care is important in managing patients with BPF as with any other critical illness. Bronchopleural fistula is frequently a manifestation of underlying severe lung disease. Because these patients are usually very catabolic, assessment of requirements and nutritional therapy is an essential part of their management. Indirect calorimetry used to estimate resting energy expenditure may be inaccurate in patients with BPF. There is a significant loss of respiratory gases, which would have participated in gas exchange through a BPF, and inability to collect the expired gases accurately renders indirect calorimetry unreliable and limits its use [62,63]. Carbohydrate intake should be carefully monitored in patients with intractable respiratory acidosis and overfeeding avoided. Meticulous supportive measures are equally important to supplement the specific management of BPF.

8. Definitive therapy

Definitive therapy in the form of surgery or bronchoscopic repair is often required, although some fistulae may resolve spontaneously or with appropriate management of the air leak and tailored ventilation.

8.1. Surgical options

Pulmonary resection surgery remains a leading risk factor for development of BPF, and refinement in surgical techniques has made postoperative BPF less prevalent. Success rates of up to 95% have been reported with BPF repair [10]. The condition of the patient and the pleural cavity usually determine the timing of surgical repair. Early postoperative stump leaks usually require urgent intervention. Patients with chronic BPF and empyema may require extensive nutritional rehabilitation before repair. Infection to the contralateral lung should be treated aggressively. Suture closure of BPF is commonly buttressed by a vascularized pedicle of omentum or muscle [64]. Pleural flaps alone are not recommended due to their inadequate vascularity. Muscle flaps are reserved for situations where omentum is not available or circumstances where the residual cavity is obliterated concomitantly. The success rates with omentum and muscle are 92% and 64% respectively, making omentum an ideal pedicle flap [64]. The residual pleural cavity can either be obliterated at the time of BPF repair by muscle transposition [65], omentoplasty, thoracoplasty [66], and a combination of these techniques, or by a delayed muscle transposition or Clagett procedure [67], a staged procedure consisting of open pleural drainage, serial operative debridements, and eventual chest closure after filling the pleural cavity with antibiotic solution. Satisfactory repair of the BPF and meticulous infection control are crucial to the success of pleural space obliteration. Completion pneumonectomy and thoracoplasty have also been performed successfully in specific circumstances [68].

There are reports pertaining to successful use of VAT in the repair of BPF. VAT may be more suitable in nonsurgical causes of BPF (eg, ruptured emphysematous bulla). Visualization of the fistula through a thoracoscope and subsequent application of Bioglue (CryoLife International Inc, Kennesaw, Ga) have been used successfully [69]. Thoracoscopy is less invasive and provides an alternative approach in draining postpneumonectomy empyemas provided that the BPF if present can be repaired concomitantly [70]. Trans-sternal and transpericardial approaches to repair the bronchial stumps after pneumonectomy have been attempted successfully, but hospital mortality remains unacceptably high [71,72].

8.2. Bronchoscopic options

Flexible bronchoscopy is being increasingly used as a diagnostic and therapeutic modality in the management of BPF. A BPF greater than 8 mm and large central BPFs are usually unsuitable for bronchoscopic management. Bronchoscopic techniques are gaining popularity, however, for repair of small leaks as well as for bridging to surgical repair in debilitated patients with large leaks. The technique comprises initial evaluation to determine whether the condition is amenable to repair. This involves direct visualization and demonstration that occlusion of a bronchial segment with a balloon catheter decreases or stops the air leak [12]. Although the proximal fistulae are easy to visualize, a peripheral BPF presents a significant challenge to the bronchoscopist. Once the site is located and the fistula deemed amenable to repair, application of various sealants into the fistula or the bronchial segment leading up to the fistula has been tried. The potential success of this approach seems to be limited to smaller, low-flow peripheral fistulae [5].

Although Ratliff et al [73] described successful management of a BPF using an endobronchial lead shot, Hartmann and Rausch [74] reported closure of a BPF using endoscopic application of tissue glue. A wide range of synthetic and biologically derived substances have been used with variable success in the management of BPF [1,14,69,75-81]. The initial plug that occludes the leak subsequently induces an inflammatory reaction and mucosal proliferation leading to permanent closure [14]. Alternatively, direct mechanical obstruction of the bronchial segment may be achieved with balloon catheter occlusion [82], collagen screw plugs [83], endobronchial coils [84,85], and endobronchial valves [86]. One-way endobronchial valves may be placed in the segmental bronchus allowing unidirectional airflow from the parenchyma to the airway and redirecting the inflowing air away from the affected segment [86,87]. Unlike other modalities used for mechanical obstruction, these valves allow drainage of distal secretions reducing infectious complications and are easily removable once adequate healing of the fistula has been achieved.

Neodymium-doped yttrium aluminum garnet laser is another option for bronchoscopic closure of small proximal fistulae (<2 mm) in the absence of tumor or infection. The laser beam may be directed to the mucosa surrounding the fistula to induce tissue edema, protein denaturation, and inflammation eventually facilitating the closure of the fistula by fibrosis [88,89]. There are no controlled studies available to demonstrate the superiority of one modality over the other, and clear guidelines for patient selection for endoscopic management do not exist. Because most of the endoscopic techniques require sedation alone, they may be more suited for the critically ill patient than surgical procedures that require general anesthesia.

The options available for an intensivist in the management of a BPF are summarised in Fig. 1. It should be noted that, many of these options are not supported by quality evidence, which is unlikely to be soon available, given the rarity of the condition.The choice of the technique should therefore be based on the clinical situation, availability of resources and familiarity with diffferent techniques.

9. Conclusions

Intensivists encounter not only critically ill patients with BPF but also a significant number of patients in whom the potential for development of a BPF exists. With the widespread use of mechanical ventilation and other invasive procedures, due care should be taken to avoid lung injuries. When faced with a BPF, an intensivist should develop an individually tailored approach to patient management, with inputs from other specialties and with sound knowledge of available supportive and specific therapeutic options. Early recognition of the condition and placement of chest drains attached to an appropriate PDU may prevent fatal complications. Various chest tube manipulations may be exercised with caution to alter intrapleural pressures and thereby limiting air leak and promoting fistula healing. Supportive intensive care is essential while planning complex ventilation strategies. In most cases, conventional ventilation may be manipulated to meet ventilatory and oxygenation demands without increasing fistula flows. Techniques such as ILV, HFV, and extracorporeal membrane oxygenation may minimize air leak and are potential alternatives to be considered when conventional ventilation fails. The critically ill patient may not be a suitable surgical candidate, and bronchoscopy can be invaluable for assessment and repair or as a bridge to surgical repair. The present-day intensivist seems to be better equipped to deal with a BPF than ever before.

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