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(REVIEW ARTICLE)

BRONCHOPLEURAL FISTULA IN THE CONTEXT OF INFECTIOUS AND NON-INFECTIOUS LUNG DISEASE: A LITERATURE REVIEW

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ABSTRACT

Introduction: Bronchopleural fistula (BPF) is an abnormal communication between the bronchial tree and the pleural space that is associated with considerable morbidity and mortality, particularly in settings with a high burden of pulmonary infection.

Objective: This review synthesizes current literature on the definition, etiology, pathophysiology, diagnosis, and management of BPF, with particular attention to its association with infectious and non-infectious lung disease.

Methodology: A literature review was conducted using peer-reviewed articles, case reports, and clinical guidelines retrieved from PubMed and other academic sources published between 2001 and 2025, with a focus on BPF etiology, classification, diagnostic modalities, and treatment approaches.

Findings: BPF is most commonly caused by pulmonary resection (lobectomy or pneumonectomy), with the right lung disproportionately affected due to its anatomical configuration. Infectious causes, particularly tuberculosis-related pyothorax and necrotizing pneumonia, remain leading contributors in tuberculosis-endemic regions such as Indonesia, while non-infectious causes include lung malignancy, chronic obstructive pulmonary disease, trauma, and iatrogenic injury. Diagnosis relies on a combination of clinical suspicion, radiographic findings, computed tomography, and bronchoscopy. Management follows a staged approach, beginning with non-invasive supportive measures such as chest tube drainage and progressing to invasive surgical repair, including thoracotomy, video-assisted thoracoscopic surgery, decortication, and, in resistant cases, open window thoracostomy.

Conclusion: BPF remains a diagnostically and therapeutically challenging condition whose management must be individualised according to onset, fistula size, and underlying etiology. Early recognition and a multidisciplinary approach are essential to reducing its associated mortality, particularly in areas affected by tuberculosis and limited healthcare resources.

Keywords: Bronchopleural fistula, Tuberculosis, Pneumonia, Lung resection, Thoracic surgery, Pleural disease

1 INTRODUCTION

Bronchopleural fistula (BPF) is defined as an abnormal communication between the bronchial tree, arising from the main stem, lobar, or segmental bronchus and the pleural space [1]. It is one of the most concerning complications in thoracic surgical practice, most frequently arising after pulmonary resection, and is closely linked to the development of pneumothorax and empyema. Despite advances in surgical technique and perioperative care, BPF continues to carry a comparatively high mortality rate, often requiring secondary surgical intervention depending on the clinical course.

Epidemiological data illustrate the scale of the problem. A multi-center study from Ethiopia reported a BPF incidence of 4% to 20% following lobectomy, with an associated mortality of 25% to 71% [2]. In that cohort, approximately 2% of patients admitted to a thoracic surgery unit were diagnosed with BPF, and nearly 70% of these had underlying tuberculosis with most fistulas developing spontaneously within one month after right-sided lobectomy performed for infectious indications such as bronchiectasis, aspergilloma, hydatid cyst, or post-tuberculous fibrotic lung disease [2].

Non-infectious pulmonary disease is an equally important contributor. Evidence from patients undergoing lobectomy or pneumonectomy for non-small cell lung cancer suggests that adjuvant chemotherapy and radiotherapy and subsequent fibrosis independently increase the risk of BPF [3]. Case reports support this association, with a patient with lung cancer developing clinical and radiographic evidence of BPF on postoperative day 24 after adjuvant chemotherapy following lobectomy, accompanied by pneumothorax and localized pleural effusion in the operated hemithorax [4]. Such observations indicate that malignancy-related tissue injury, independent of infection, can also induce fistula formation.

The burden of the underlying infectious and non-infectious lung diseases that predispose to BPF is considerable, particularly in tuberculosis-endemic regions. Tuberculosis continues to affect a substantial proportion of the world's population, and a meaningful fraction of cases are missed by routine screening programs [5]. In Indonesia, specifically, several hundred thousand tuberculosis cases are confirmed annually, and has one of the highest tuberculosis burdens globally [6]. Pneumonia similarly remains a leading cause of lower respiratory infection mortality worldwide, and lung cancer contributes several million new diagnoses globally each year and ranks among the leading causes of morbidity and mortality in Indonesia. Since both infectious and non-infectious pulmonary diseases may require salvage surgery and are associated with an elevated risk of BPF, regional thoracic surgery referral centres such as Dr. Soetomo General Academic Hospital in Surabaya encounter a broad spectrum of BPF presentations [7].

Given this burden and the heterogeneity of underlying causes, this review synthesizes the current literature on the definition and classification of BPF, its etiology and pathophysiology, its particular association with infectious lung disease, and the diagnostic and therapeutic strategies available for its management.

2 METHODOLOGY

This literature review drew on sources from PubMed, StatPearls, and other peer-reviewed academic databases, supplemented by institution-specific studies conducted at Dr. Soetomo General Academic Hospital Surabaya. Search terms included combinations of "bronchopleural fistula," "tuberculosis," "pneumonia," "lobectomy," "pneumonectomy," "empyema," and "pleural disease." Case reports, cohort studies, systematic reviews, and clinical guidelines published largely between 2001 and 2025 were included where they addressed the definition, etiology, pathophysiology, diagnosis, or management of BPF. Articles were selected based on their relevance and synthesised thematically.

3 DEFINITION AND CLASSIFICATION OF BRONCHOPLEURAL FISTULA

BPF is an abnormal channel connecting the bronchial tree such as the main stem, lobar, or segmental bronchus with the pleural space [1]. Based on the anatomical level at which the communication occurs, BPF is classified into two principal types, central and peripheral [8].

Central BPF refers to a direct communication between the trachea or a major bronchus and the pleural cavity. Its incidence varies from approximately 4% to 20%, depending on the underlying pulmonary condition [2]. Central BPF typically manifests within one to three months postoperatively and occurs more frequently on the right side. This right-sided predominance is attributed to the anatomical configuration of the lungs, as the right main-stem bronchus has a wider diameter and is covered by less mediastinal tissue than the left, leaving it at greater risk of mechanical and infectious injury.

In contrast, Peripheral BPF arises through indirect communication and is more commonly secondary to surgical or radiological intervention, malignancy, necrotizing infection, or other iatrogenic causes such as pulmonary puncture,

drainage-tube insertion, or prolonged positive-pressure ventilation. Peripheral BPF is typically localized to airways distal to the segmental bronchi or within the lung parenchyma itself, distinguishing it from the more proximal central form.

4 ETIOLOGY OF BRONCHOPLEURAL FISTULA

4.1 Lung Resection

Pulmonary resection, particularly lobectomy and pneumonectomy, is the most common cause of BPF [9]. Studies examining surgical technique suggest that the method of bronchial closure and use of tissue buttressing have little influence on BPF formation [10]. Instead, laterality of resection appears more influential, with right-sided pneumonectomy carrying a higher risk of BPF than left-sided resection, potentially due to the more vertically oriented anatomy of the left bronchus that provides greater protection [11]. In addition, preoperative factors also contribute meaningfully to risk. Preoperative corticosteroid or chemotherapy use, along with recent smoking and shorter smoking cessation periods have been associated with an increased likelihood of pulmonary complications, prolonged mechanical ventilation, and reintubation, which may predispose patients to BPF development [12].

4.2 Infection

Infection is the second major cause of BPF. Untreated tuberculosis, as an example, could progress to empyema and secondary spontaneous pneumothorax preceding fistula formation. Once tuberculous infection reaches the pleural cavity, BPF becomes an important complication to be aware of due to the need for prompt recognition and treatment. Additionally, pneumonia can similarly progress to pulmonary necrosis and subsequent BPF formation [13]. In both processes, the resulting tissue necrosis can be compounded by pleural fibrosis, giving rise to a chronic form of BPF [1]. Other than tuberculosis and pneumonia, other respiratory conditions including aspergilloma and bronchiectasis have been associated with BPF development, while non-infectious inflammatory airway diseases such as chronic obstructive pulmonary disease (COPD) and asthma have also been linked to a rising likelihood of BPF in patients undergoing lung surgery [14].

4.3 Trauma and Iatrogenic Injury

BPF can also result from iatrogenic injury sustained during thoracic procedures, including chest tube insertion, lung biopsy, nasogastric tube malposition, or lung resection itself. Because BPF represents a direct communication between the bronchial tree and the pleural cavity, its formation frequently induces the entry of air into the pleural space, known as spontaneous pneumothorax.

4.4 Lung Neoplasm

Lung neoplasms, most notably lung cancer, represent an important, though less frequent, cause of BPF. Although the overall incidence of BPF is relatively low, it remains one of the most serious postoperative complications [15]. In a European case series, most lung cancer patients developed BPF after right-sided lobectomy compared with left-sided resection cases [16]. A representative case from China illustrates the clinical course in a patient who underwent right lower lobectomy for well-differentiated pulmonary adenocarcinoma with visceral pleural invasion. The patient was discharged on postoperative day 5 with satisfactory lung re-expansion but readmitted on postoperative day 37 with fatigue, productive cough, and fever. Chest computed tomography (CT) revealed pneumothorax and pleural effusion, consistent with late-onset postoperative BPF [4]. In addition, glucocorticoid use during chemotherapy has been proposed as a possible contributor to late-onset presentations, though the precise risk factors remain incompletely defined [4].

5 PATHOPHYSIOLOGY AND CLINICAL COURSE

BPF may arise at any point after lobectomy, whether with early or late onset, though it most commonly manifests within 8 to 12 days postoperatively. BPF can also follow suppurative pneumonia or massive pulmonary infarction, whether occurring spontaneously or as a postoperative event.

Clinically, BPF may present without an obviously associated disease process. Early signs can include mediastinal shift toward the contralateral side, reflecting air displacement on the operative side, and clearance of fluid or blood from the airway on coughing. A spontaneous reappearance of air within a previously drained pleural space is similarly suggestive, though this finding can also indicate a gas-forming infectious process rather than a true fistula.

Based on the timing and character of presentation, BPF is classified into acute, subacute, and chronic forms [1].

5.1 Acute BPF

Early recognition is critical in the acute form since the fistula can be immediately life-threatening due to tension pneumothorax or asphyxiation. Patients typically present with sudden dyspnea, hypotension, subcutaneous emphysema, and a productive cough with purulent sputum. Chest radiography in acute form typically demonstrates tracheal or mediastinal shift, a reduction or disappearance of a previously present pleural effusion, and a persistent air leak, which is considered particularly characteristic of BPF [1].

5.2 Subacute BPF

The subacute form is primarily associated with infection and tends to occur in immunocompromised patients or those with multiple comorbidities. Although it shares features with the chronic form, its course is more gradual and is associated with wasting, malaise, and fever [1].

5.3 Chronic BPF

The chronic form closely resembles the subacute presentation but is specifically associated with an ongoing infectious process and pleural fibrosis [1].

6 BRONCHOPLEURAL FISTULA ASSOCIATED WITH INFECTIOUS LUNG DISEASE

6.1 Tuberculosis

Tuberculosis (TB) is caused by Mycobacterium tuberculosis, an organism that predominantly affects the lungs but can also involve the gastrointestinal, musculoskeletal, lymphoreticular, dermatologic, central nervous, reproductive, and hepatic systems [17]. Globally, TB continues to place a substantial disease burden, particularly in developing countries. Around 10 million people were diagnosed with TB in 2020, with an estimated 1.5 million deaths. Indonesia remains among the countries with the highest TB burden worldwide, ranking third after India and China, with hundreds of thousands of confirmed cases annually and a prevalence that has remained largely stable over recent years [5-6]. Institutional data from Dr. Soetomo General Academic Hospital are also consistent with this burden among patients presenting for pulmonary evaluation and treatment [18].

TB and BPF are closely linked, with fistula formation most often occurring after lobectomy performed for TB treatment, predominantly on the right side. TB-related BPF is characterized by pleural fluid and typical yellow-greenish sputum findings with fever, productive cough, and a rising air–fluid level within the pleural cavity. A case report from Indonesia and elsewhere in Southeast Asia illustrates this association, including reports of giant BPF and empyema complicating TB in patients with comorbid diabetes mellitus and localized case reports of BPF with pyopneumothorax as a direct complication of pulmonary TB, highlighting both the regional relevance and the surgical challenge posed by TB-related BPF [19-21]. Outcomes in this setting depend heavily on the timeliness of diagnosis, prompt initiation of anti-tuberculous therapy, and precise management of intercostal drainage.

6.2 Pneumonia

Pneumonia is defined as inflammation of the alveoli and surrounding lung tissue presenting with acute fever, malaise, cough, and dyspnea [22]. Pneumonia can be classified according to its setting of acquisition, host immune status, and causative pathogen, with community-acquired and hospital-acquired pneumonia (CAP and HAP) representing common categories [23]. Common bacterial causes of CAP include Streptococcus pneumoniae, Staphylococcus aureus, Mycoplasma pneumoniae, and gram-negative enteric bacilli, with host immune status strongly influencing both clinical severity and treatment approach.

Pathophysiologically, the respiratory tract is normally exposed to microorganisms. However, host defence mechanisms could limit their proliferation as a protective mechanism. When these defences are impaired, pathogens can multiply and cause infection. The resulting acute inflammatory response leads to alveolar consolidation, which can be detected on chest radiography and CT. In pneumonia, the progression of inflammation and accumulation of exudate within the lung parenchyma are the key pathological features [22]. Pneumonia can progress to BPF through a necrotizing process. Similarly, right-sided predominance is again attributable to the anatomical exposure of the right main bronchus as in TB-related BPF cases. This suggests that necrotizing pneumonia represents a particularly severe manifestation, capable of causing extensive destruction of lung parenchyma [13,24]. Comparable presentations have also been documented even in pediatric populations with necrotizing pneumococcal pneumonia complicated by BPF [25].

6.3 Other Non-Tuberculous Infections

Beyond TB and pneumonia, other respiratory infections can also give rise to BPF. Institutional data from Dr. Soetomo General Academic Hospital indicate that non-TB infectious BPF, while less common than TB-related BPF, still accounts for a clinically significant proportion of cases, at approximately 18.2% [7]. Aspergilloma and bronchiectasis have both been implicated as causes, as has pleural aspergillosis, which typically arises in immunocompromised patients or in the context of chronic necrotizing pulmonary aspergillosis [26]. Furthermore, COPD is also a contributor to BPF formation. A reported case from Japan described an 80-year-old patient with an acute exacerbation of asthma and COPD who subsequently developed a fistula in the setting of respiratory infection [27], illustrating that a broad range of respiratory infections beyond TB and pneumonia can progress to BPF as part of their downstream pathogenesis.

7 DIAGNOSIS OF BRONCHOPLEURAL FISTULA

Timely diagnosis of BPF is essential, given the narrow therapeutic window that determines subsequent management [28]. Both computed tomography (CT) and bronchoscopy should be pursued in a timely manner whenever BPF is clinically suspected [29]. In this context, radiographic features that should raise suspicion include a persistent increase in intrapleural air, the appearance of a new air-fluid level, a shift in a previously stable air-fluid level, development of tension pneumothorax, and a drop in the air-fluid level exceeding 2 cm. Moreover, a history of chest tube insertion may also increase the pretest probability of BPF.

On CT, direct visualization of the fistulous tract is possible in a subset of patients, particularly with thin-section, non-contrast acquisition. Three-dimensional spiral reconstruction can further demonstrate the full extent of the communication. Bronchoscopy complements CT by allowing direct visualization of the fistula opening and localization of the affected bronchial segment. The suggestive finding in this modality would be the appearance of continuous bubbling during bronchial lavage [29].

When the fistula cannot be visualized bronchoscopically, bronchography using selective instillation of methylene blue into the segmental bronchi can help confirm its location. If instillation alone is insufficient, a balloon-tipped catheter can be advanced into the suspected airway and inflated. The appearance of the air leak upon occlusion confirms the diagnosis and localizes the fistula.

In difficult settings, CT and bronchoscopy can be combined. A water-soluble, non-ionic, low-osmolar iodinated contrast agent such as iohexol can be used, then instilled via catheter or through the bronchoscope's working channel directly at the suspected fistula site, followed by standard axial and sagittal CT acquisition. This combined technique offers faster and more accurate characterization of the fistula tract than bronchoscopy alone, permits multiplanar reconstruction for improved anatomical characterization, and provides high confidence in defining the relationship between the fistula and surrounding structures [29]. Ultimately, the diagnostic approach chosen depends on the index of clinical suspicion, and prompt diagnosis remains the key determinant of appropriate next steps in management.

8 MANAGEMENT OF BRONCHOPLEURAL FISTULA

Management of BPF begins with the mitigation of immediate life-threatening complications, which can include endobronchial contamination, pulmonary flooding, and pneumothorax. The appropriate approach depends on the timing of onset, fistula size, anatomic location, and the patient's overall clinical status. No single, universally adopted management algorithm exists, and treatment decisions are frequently guided by surgeon experience rather than a standardized protocol. However, structured algorithms have been proposed, including one developed by the European Institute of Oncology in Italy based on their institutional experience with post-lobectomy BPF [30]. The algorithm itself emphasizes early diagnosis followed by emergency supportive measures such as chest tube placement to evacuate air-fluid collections and antibiotic therapy to control infection followed by observation to characterize onset and fistula size before further intervention.

The British Thoracic Society (BTS) has similarly issued guidance applicable to BPF within the broader context of spontaneous pneumothorax management [31]. This guidance recommends conservative management as the initial step to minimize symptoms. As an example, if patients are unsuitable for conservative management, the surgeon could proceed to chest tube insertion or needle aspiration, with subsequent observation for recurrence since recurrent pneumothorax warrants escalation to salvage surgery.

8.1 Non-Invasive Management

Non-invasive management, comprising chest tube drainage, supportive care, and bronchoscopic techniques, is generally appropriate for early-onset BPF with a fistula diameter below 5 mm. Based on the previously mentioned algorithm,

following initiation of non-invasive treatment, patients are observed for evidence of fistula closure and resolution of infection. If both improve, the patient can continue with outpatient follow-up. Late-onset BPF can be managed similarly, with chest tube insertion and supportive care followed by monitoring for closure. When these measures fail to achieve improvement, surgical management may be necessary [31].

8.2 Invasive Management

Invasive management is indicated when the fistula is too large for bronchoscopic closure, or when non-invasive measures fail to produce improvement. Surgical options include chest drainage with re-intervention, re-suture of the bronchial stump, completion resection, open window thoracostomy, and major pulmonary resection, with the choice guided by the specific clinical scenario [32].

Fistulas larger than 5 mm frequently involve necrotic tissue requiring debridement to liberate the remaining lung, followed by direct surgical repair. The same approach applies when smaller fistulas fail to respond to initial non-invasive treatment. On the other hand, successful closure after surgical repair may be followed by completion procedures such as pneumonectomy or extended lobectomy where indicated [33]. When closure remains unsuccessful, open window thoracostomy may be required as a salvage procedure.

In late-onset BPF, failure of initial closure has been associated with several factors, including an ineligible surgical candidate, small fistula and air-fluid collection sizes, and a history of lower lobectomy or right upper lobectomy. When these factors are present, open window thoracostomy is often favored. In their absence, alternative surgical strategies such as completion pneumonectomy may be pursued, with open window thoracostomy reserved for cases with recurrent fistula formation. The surgical approach, whether via thoracotomy or video-assisted thoracoscopic surgery (VATS), is chosen based on the complexity of the case and the likelihood of conversion from a minimally invasive to an open approach [34-36].

8.3 Post-Repair Maintenance

Following surgical repair, meticulous management of pleural space drainage is essential to prevent infection and to create beneficial conditions for healing. Antibiotic therapy is commonly used to sterilize the pleural space and rigorous local sterilization is required to accelerate wound healing in patients managed with open window thoracostomy. Additionally, maintaining a sterile postoperative environment is therefore fundamental to prevent secondary infection and optimize long-term outcomes [31].

9 CONCLUSION

Bronchopleural fistula (BPF) is a serious complication of both surgical and non-surgical pulmonary disease, with a comparatively higher burden on the right lung due to its anatomical configuration. Its causes vary, including lung resection, infectious diseases such as tuberculosis and pneumonia, trauma, iatrogenic injury, and malignancy, with TB-related BPF being particularly relevant in endemic, resource-limited settings such as Indonesia. BPF diagnosis relies on clinical suspicion, radiographic findings, CT, and bronchoscopy, while management ranges from conservative drainage to surgical repair and, in unresponsive cases, open window thoracostomy. As no universal management algorithm exists, treatment should be individualised according to fistula size, timing of onset, and underlying cause. Further research from TB-endemic referral centres is needed to improve risk stratification and standardise management of this high-mortality condition.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The author declares no financial or non-financial conflict of interest related to this work.

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