Review Article

Bronchoscopic management in persistent air leak: a narrative review

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Background and Objective: Persistent air leak (PAL) represents a challenging medical condition characterized by prolonged air leak from the lung parenchyma into the pleural cavity, often associated with alveolar-pleural fistula or bronchopleural fistula (BPF). The objective of this narrative review is to explore the causes, clinical implications, and the evolving landscape of bronchoscopic treatment options for PAL.

Methods: The literature search for this review was conducted using databases such as PubMed/MEDLINE, and Scopus databases. Articles published from inception until 28th August, 2023, focusing on studies that discussed the causes, diagnosis, and management strategies for PAL were included. Keywords included bronchoscopic management, bronchopleural fistula, endobronchial valve, sealant, blood patch pleurodesis, spigot, air leak, PAL, management, comparative study.

Key Content and Findings: PAL commonly arises from secondary spontaneous pneumothorax, necrotizing pneumonia, barotrauma induced by mechanical ventilation, chest trauma, or postoperative complications. Understanding the underlying etiology is crucial for tailoring effective management strategies. While conventional intercostal drainage resolves the majority of pneumothorax cases, PAL is diagnosed when the air leak persists beyond 5 to 7 days. Prolonged PAL can lead to worsening pneumothorax, respiratory distress, and increased morbidity. Early identification and intervention are essential to prevent complications. Conservative approaches involve close monitoring and supplemental oxygen therapy. These strategies aim to promote natural healing and resolution of the air leak without invasive interventions. Bronchoscopic techniques, such as endobronchial valves (EBVs), sealants, and autologous blood patch (ABP), have emerged as promising alternatives for refractory PAL. These interventions offer a targeted and minimally invasive approach to seal the fistulous connection, promoting faster recovery and reducing the need for surgical interventions.

Conclusions: PAL is a clinical challenge, and their management requires a tailored approach based on the underlying cause and severity. Bronchoscopic interventions have shown efficacy in cases of refractory PAL. Early recognition, multidisciplinary collaboration, and a personalized treatment plan are essential for optimizing outcomes in patients with PAL.

Keywords: Persistent air leak (PAL); alveolar-pleural fistula; bronchopleural fistula (BPF); conservative management; bronchoscopic intervention

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Introduction

Background

Persistent air leak (PAL) is a medical condition related to alveolar-pleural fistula, cause by a leakage from the lung parenchyma into the pleural cavity. This can also result from bronchopleural fistula (BPF), where and abnormal connection between the airways and the pleural cavity. If this connection persists, there will be flow of air from the lung parenchyma to the pleural space and worsening of the pneumothorax (1). The conventional treatment by intercostal drainage can resolve a majority of pneumothorax and air leak. However, if the leakage persists for more than 5 to 7 days, it is termed a PAL (2). The main causes of PAL are secondary spontaneous pneumothorax, necrotizing pneumonia, barotrauma from mechanical ventilator, following chest trauma or after chest surgery (3). This article describes the treatment of PAL by conservative and bronchoscopic management.

Definition of PAL

PAL is defined as the presence of persistent air leakage for greater than 5 to 7 days (2). In some studies, PAL is defined in patients with spontaneous pneumothorax who have air leakage exceeding 48 hours (4). The use of the 5-day time cutoff for PAL is based on studying the expected duration of hospitalization in post-lung surgery patients (5).

The severity of PAL is classified by Cerfolio (6) using the observation of air leakage volume during inhalation, exhalation, or continuous leakage through the chest tube, as outlined in *Table 1*.

The severity classification can be observed from the water seal system of the intercostal chest drainage. Three chambers are present in the majority of systems. The patient's drainage—either blood or water—is collected in the first chamber. The second chamber is a closed water system that allows air to exit from the pleural space during exhalation, preventing air entering during inhalation. The air bubbling in the second chamber in the water seal system serves as an indicator of PAL. The third chamber can be connected to wall suction to increase negative pressure in the pleural cavity. The measurement of air leak is indicated by numbers ranging from 1 to 7 in dry suction systems or 1 to 5 in wet suction systems (7), as shown in *Figure 1*. Higher numbers represent increased air leak volume.

Quantification of a pneumothorax in PAL is usually subjective Subsequently, the use of digital chest drainage has become more widespread for measuring the volume of air leakage (8). This system displays the air volume in milliliters per minute and the difference in pleural pressure in centimeters of water per second (maximum – minimum pleural pressure). PAL is defined using digital chest drainage when there is an air leakage volume exceeding 15 to 20 milliliters per minute for more than 5 days. A systematic review has demonstrated that the use of digital drainage devices, as opposed to conventional drainage devices, resulted in decreased durations of chest tube placement and shorter hospital stays (9).

Table 1 Cerfolio classification of air leaks

Grade	Description
Grade 1, FE	During any forced expiration only
Grade 2, E	Expiratory only
Grade 3, I	Inspiratory only
Grade 4, C	Continuous bubbling present in the air leak chamber during both inspiration and expiration

Aims of narrative review

The primary objective of this review is to critically assess and review the existing literature on bronchoscopic interventions for the management of PAL, encompassing techniques such as endobronchial valves (EBVs), sealants, autologous blood patch (ABP), and emerging technologies. Additionally, aiming to contribute to the current knowledge base and guide clinical decision-making, this review addresses the evolving field of bronchoscopic management of PAL. I present this article in accordance with the Narrative Review reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-46/rc).

Methods

Research on PubMed/MEDLINE and Scopus database from inception until 28th August, 2023 was conducted to analyze research that examined both the incidence and treatment strategies of PAL (*Table 2*). The following keywords were used: bronchoscopic management, bronchopleural fistula, endobronchial valve, sealant, blood patch pleurodesis, spigot, air leak, PAL, management, comparative study. The author systematically reviewed English-language literature, comprising both full-

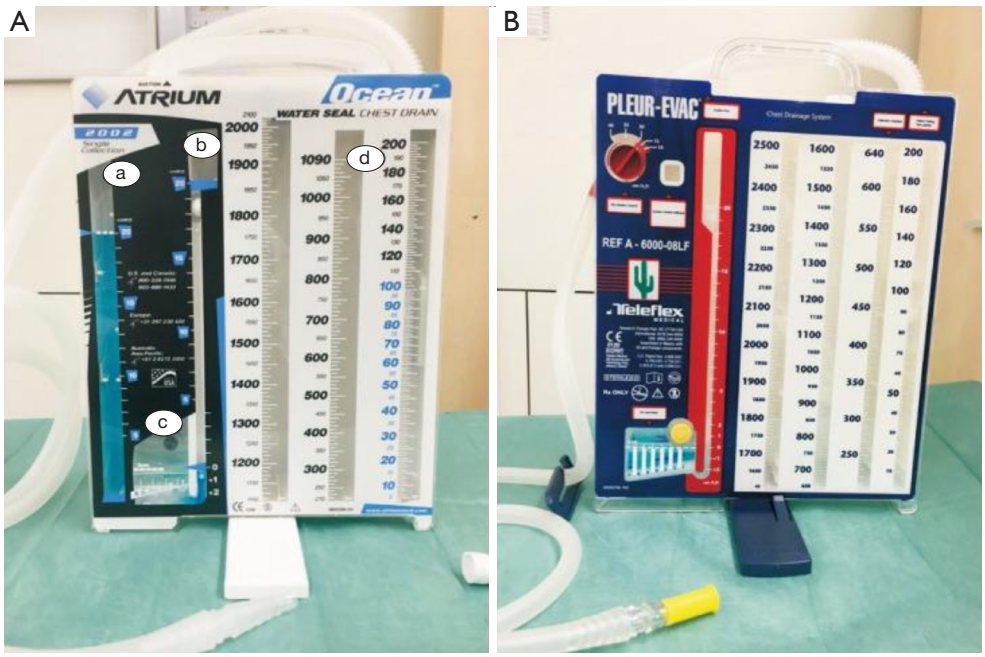

Figure 1 Three-chamber: wet suction system (A); dry suction system (B). Note the suction (a), water seal (b), air leak meter (c) and drainage (d).

Table 2 The search strategy summary

Item	Specification
Date of search	28th August, 2023
Databases and other sources searched	PubMed/MEDLINE, Scopus
Search terms used	("bronchoscopic management" [MeSH]) AND "air leak" [MeSH]
	("bronchoscopic management" [MeSH]) AND "persistent air leak" [MESH] AND "bronchopleural fistula" [MeSH]
	("bronchoscopic management" [MeSH]) AND "endobronchial valve" [MESH] AND "air leak" [MeSH]
	("Sealant" [MeSH]) AND "PAL" [MeSH]
	("Blood patch pleurodesis" [MeSH]) AND "PAL" [MeSH]
	("Spigot" [MeSH]) AND "PAL" [MeSH]
	("persistent air leak" [MeSH]) AND "management" [MeSH]
	("persistent air leak" [MeSH]) AND "comparative study" [MeSH]
Timeframe	Inception of database–28th August, 2023
Inclusion and exclusion criteria	Inclusion criteria: English language; available full-text or abstract; studies including patients ≥18 years old
	Exclusion criteria: non-English language; pediatric population studies
Selection process	Data search and selection, assembly of data, interpretation: P.R.

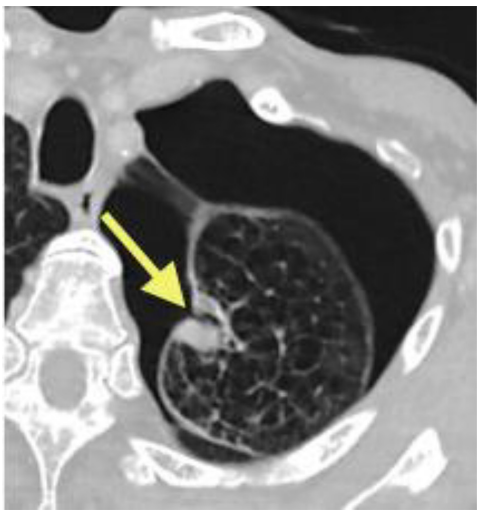

Figure 2 CT scan of the chest revealing a connection between a peripheral branch of the left upper lobe and the pleural space (arrow) in patient with PAL. CT, computed tomography; PAL, persistent air leak.

text articles and abstracts, without any publication type restrictions. Subsequently, a thorough evaluation of all identified materials was conducted to select studies meeting the criteria for inclusion in the final analysis.

Incidence of PAL

A pneumothorax during mechanical ventilation is associated with serious complications and a high mortality rate. In a retrospective 4-year study among critically ill patients, including those in internal medicine, surgery, and cardiology departments (10), 39 out of 1,700 patients (2.2%) developed PAL with a mortality rate of 67%.

PAL is commonly observed in patients following thoracic surgery, particularly after lobectomy and lung volume reduction surgery (LVRS), with incidence rates of up to 26% and 46%, respectively (11). In a study by Rivera and colleagues, the incidence of PAL in patients after LVRS, lobectomy, and wedge resection was found to be 46%, 8.3%, and 3.3%, respectively (12). Using a digital drainage device in patients after lobectomy, air leakage volume exceeded 50 milliliters per minute or a large pleural pressure difference measured over 6 hours postoperatively, was predictive of a PAL (13).

Nonsurgical procedures, such as needle aspiration or transbronchial biopsy, result in a low incidence of pneumothorax. However, the incidence of pneumothorax after transbronchial biopsy is minimal, with an incidence rate as low as 0.009%; therefore, the incidence rate for PAL is very low (14).

Risk factors and etiology of PAL

The causes of PAL are categorized into those resulting from surgical procedures, such as pneumonectomy, lobectomy, and LVRS. Other non-surgical causes include thoracentesis, transthoracic needle biopsy or aspiration, necrotizing pneumonia, pulmonary tuberculosis infection, barotrauma from mechanical ventilation, and spontaneous pneumothorax (15).

Risk factors for developing PAL in the post-lobectomy surgery group include chronic obstructive pulmonary disease (COPD), female gender, low forced expiratory volume in 1 second (FEV1), smoking history, diabetes mellitus, and steroid use (3).

Risk factors for PAL in the post-LVRS group include low FEV1, low diffusing capacity of the lungs for carbon monoxide (DLCO), pleural adhesion identified during surgery, and upper lobe emphysema (3).

Complications of PAL

Complications of PAL include inadequate lung expansion, ventilation/perfusion mismatch, infection of the pleural cavity, increased hospitalization rates, and mortality (1).

Diagnosis and localization

The localization of the culprit airway leading to the pleural defect in patients with PAL can be achieved through various methods as discussed below.

Chest computerized tomography (CT) scan

High-resolution CT of the chest serves two primary objectives in patients with PAL. The first objective is to visualize the characteristics of BPF, whether it is of the central or peripheral type, by examining the points where the visceral pleura shows contrast injection deficits (as shown in *Figure 2*). The second objective is to assess fissure completeness. Fissure integrity can be assessed by directly visualizing high-resolution chest CT images of the lobar fissures or by using chest CT image analysis software (such as LungQ; Thirona). Fissure integrity exceeding 90% indicates minimal collateral ventilation and suggests responsiveness to bronchoscopic management for PAL (16).

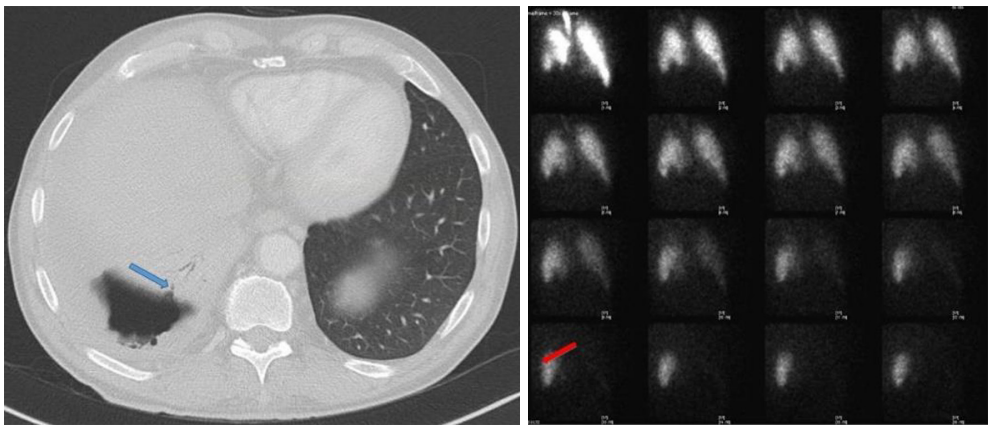

Figure 3 Image from ^{99m}Tc-DTPA ventilation scintigraphy demonstrates localized radiotracer in the lower right hemithorax (red arrow), aligning with the location of PAL in a patient with right hydropneumothorax (blue arrow). ^{99m}Tc-DTPA, technetium-99m-tagged diethylenetriaminepentaacetic acid; PAL, persistent air leak.

Methylene blue injection

The injection of methylene blue has been reported in post-lobectomy surgery patients. This can be performed either retrograde, involving the injection of methylene blue through the pleural cavity and bronchoscope to inspect sites of air leakage, or anterograde, the identification of methylene blue instilled through bronchoscopy into the pleural space would confirm the existence of a fistula but would not determine its exact location (17).

Ventilation scintigraphy

Ventilation scintigraphy with various radioactive tracers, including technetium-99m (^{99m}Tc) albumin colloid fog inhalation, ^{99m}Tc sulfur colloid, and ^{99m}Tc-labeled diethylenetriamine penta-acetate, can be utilized. When there is a BPF, the radioactive tracer is observed to distribute within the postpneumonectomy or pleural space following inhalation (as shown in *Figure 3*). A study involving 28 postpneumonectomy patients showed a sensitivity of 78% and a specificity of 100% for detecting BPF using ^{99m}Tc-diethylenetriamine penta-acetate aerosol (18).

Sequential balloon occlusion

Sequential balloon occlusion via flexible bronchoscopy is a useful method for identifying the bronchial segment or subsegment contributing to the alveolo-pleural fistula or small BPF. A balloon [e.g., a Fogarty balloon 5 Frech (Fr) in size] is placed through the working channel, and positioned in the subsegmental bronchus. The balloon is inflated to an optimal size to fully occlude the airway opening. The occlusion is maintained for a duration 4 to 5 complete breath cycles. If the leak diminishes by more than 50%, the test is considered positive, suggesting that the tested subsegmental bronchi is likely contributing to PAL. Additionally, this test indicates a high likelihood of fissure integrity exceeding 90%, minimal collateral ventilation, and a favorable chance of successful EBV placement (19).

Another method involves the use of a pressure transducer catheter (Chartis, Pulmonx, Inc., Redwood City, California, USA) (20). The Chartis system comprises a catheter equipped with an inflatable balloon at the end, which can be inserted through the 2.8 mm or larger working channel of a bronchoscope. When the balloon is inflated, it temporarily occludes the airway, enabling evaluation of airflow from the occluded lobe. The Chartis console analyzes and displays measurements of expired airflow volume, pressure, and resistance. Unique airflow patterns are then used to assess collateral ventilation status.

Treatment

The treatment of patients with PAL, for whom surgical intervention is contraindicated, can be achieved through conservative management via prolong intercostal drainage or bronchoscopic intervention.

Conservative management

The conservative management of PAL includes chest tube insertion, close monitoring of symptoms, and applying

thoracic suction. Three factors must be considered in this approach: the volume, duration, and trend of the air leak. For instance, a prolonged and substantial air leak may reduce the likelihood of resolving PAL, while a short-duration and low-volume air leak may have a higher potential of successful conservative treatment (21).

In the post-lung surgery patient group, a study investigated the use of chest tube placement under a water seal system for the first 24 hours postoperatively, comparing placing the chest tube to wall suction. The findings revealed a significantly reduced risk of PAL at 72 hours with the water seal approach, observed in 13 out of the total 14 patients included in the study (13).

If the treatment with chest tube drainage in a water seal system fails to expand the lung and stop the air leak, connect to wall suction with a negative pressure of 20 centimeters of water and reassess after an additional 48 hours. If the air leak decreases to grade 1 or measures less than 20 milliliters per minute, the chest tube can be removed. This mechanism is believed that negative pressure reduces trapped air in the pleural space, promoting apposition of the inner and outer layers of the pleura (22).

If the insertion of a chest tube followed by wall suction is ineffective, consider discharging the patient with a Heimlich valve (ambulatory one-way valve) to shorten the hospitalization period. In a study involving 107 patients after LVRS due to emphysema (23), 25 patients with PAL beyond 5 days were treated with Heimlich valve, irrespective of the size of the pneumothorax. All patients received daily pulmonary rehabilitation. The study results showed a significant reduction in hospitalization duration by 46%, with only one patient returning to the hospital with subcutaneous emphysema. This study highlights the safety of using the Heimlich valve for outpatient management in patients with PAL. Another study by Cerfolio and colleagues (24) demonstrated the safety of removing chest tubes in patients with ongoing PAL and using Heimlich valve after hospital discharge, with no complications such as subcutaneous emphysema or an increase in pneumothorax size.

In summary, conservative management includes placing a chest tube under a water seal system, discharging patients with a one-way valve, or combining these various treatment methods—all of which are beneficial for treating PAL. However, in some cases, these treatments may not be effective, and alternative approaches may be necessary.

Bronchoscopic intervention

The assessment of patients with prolonged air leak and suitability for bronchoscopic intervention requires evaluation of the quantity of air leakage and identification of the location of air leakage. The measurement of air leakage can be done using a digital chest drainage system, with a threshold of more than 20 milliliters per minute over a duration exceeding 5 to 7 days, as defined by PAL criteria. Alternatively, an air leak meter on a scale of 1 to 7, 1 to 5, or according to the Cerfolio classification system can be employed. Determining the location of air leakage can be achieved through various methods mentioned earlier, with sequential balloon occlusion being a commonly used and convenient approach.

Identification of the location of air leakage can be performed using the following two methods.

(I) Sequential balloon testing: this method not only allows for the evaluation of the location of air leakage but also enables the assessment of collateral ventilation. It serves as an indicator of fissure completeness when there is a significant reduction of air leakage by more than 50% during sequential balloon testing (assessed by observing air bubbles per minute or measuring with a digital drainage system) (25). This suggests a higher success rate if bronchoscopic intervention is performed. However, if the reduction in air leakage is less than 50%, there may be significant collateral ventilation, such as an incomplete lung fissure between the target lobe and an adjacent lobe. This indicates a lower success rate for procedures like EBV placement. Thus, the balloon should be moved to the proximal airway to localize the pathologic lobe.

(II) High-resolution CT of the chest: this imaging modality allows for the assessment through direct visual examination of BPF or alveolopleural fistula.

In summary, for bronchoscopic interventions to achieve a high success rate in patients with PAL, it is essential to perform sequential balloon occlusion testing with a reduction in air leakage of more than 50% (16).

EBVs/intrabronchial valve (IBV)

EBV and IBV are one-way valves (*Figure 4*) (1) that can be inserted into the airways through flexible bronchoscopy to occlude sites of PAL. The valve operates unidirectionally, controlling the airflow to prevents air from entering the distal bronchus beyond the valve. Meanwhile, air or secretions in the distal bronchus can exit through the proximal part of the valve. The U.S. Food and Drug Administration (US FDA) has approved devices from two

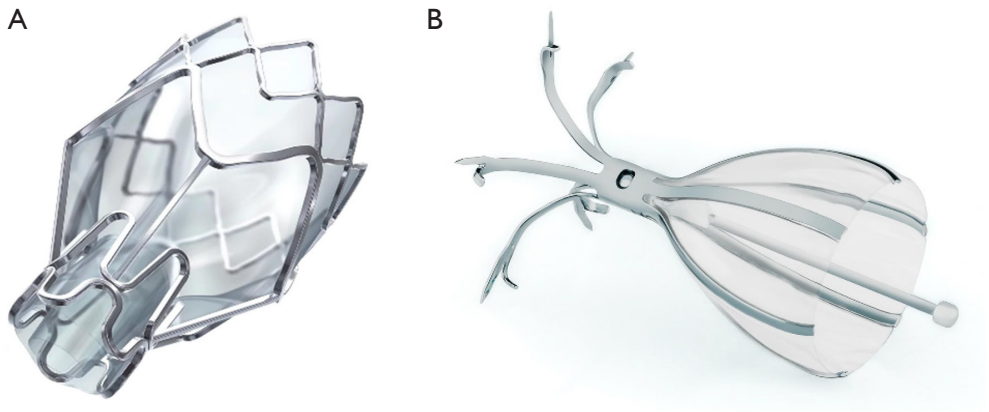

Figure 4 Zephyr endobronchial valve (A) and spiration intrabronchial valve (B). Image courtesy of Olympus Respiratory and Pulmonx, Inc.

companies, the Zephyr EBV (Pulmonx, Inc.) and Spiration IBV (Spiration Inc., Redmond, Washington, USA) for lung volume reduction in patients with emphysema. Additionally, the US FDA has approved IBV Spirations for treating patients with PAL after lung surgery, supported by studies demonstrating the effectiveness in reducing the air leaks (25).

The procedure of placing the IBV device consists of three steps (26): air leak isolation, airway sizing, and valve deployment. For isolation, balloon occlusion is performed, and the IBV system is designed in various sizes to accommodate both main bronchi and sub-segmental bronchi. Once the IBV is appropriately positioned, the complete air leak response is observed by monitoring 4 to 5 complete breath cycles to assess whether the air leak has decreased. Previous studies have indicated that an average of 2 to 3 valves per lobe is required for the treatment of PAL in one lung (25).

In a study by Travaline and colleagues (27) involving a total of 40 patients with PAL resulting from mechanical ventilation, pulmonary infection, lung biopsy, and pneumothorax, all patients underwent EBV placement (Zephyr, Pulmonx). The study found a 92% reduction in pneumothorax and air leak (37 patients), with 47.5% (19 patients) achieving resolution of PAL. Complications after EBV placement were observed in six patients, including valve migration, pulmonary infection, oxygen desaturation, and methicillin-resistant *Staphylococcus aureus* colonization. Additionally, Gillespie and colleagues (28) studied seven patients with PAL, averaging a 4-week duration of pneumothorax. All patients received IBV placement, resulting in complete resolution of PAL, and four patients were discharged within 3 days. Both studies have limitations, such as the absence of a control group, and further follow-up studies may be necessary in the future.

Based on observational evidence and case reports (27,28), placement of IBV and EBV devices in PAL patients has shown success in the treatment of PAL in certain groups. EBV placement is another alternative for treatment in PAL patients who are poor surgical candidates (29,30). Valves are removed when PAL resolves, typically within 6 to 8 weeks.

Spigots

The use of bronchial occlusion with silicone for treatment of BPF began in 1991 (31) when Watanabe *et al.* developed the Watanabe spigots (EWS®, Novatech, Grasse, France). These devices, made of silicone, were used in the treatment of 60 patients with PAL, primarily caused by postoperative air leak. The success rate of the treatment was 80%. The spigots are coated with barium sulfate for radiographic visibility. The devices have tapered ends and available in three sizes (*Figure 5*). The occlusion procedure involves introducing the spigot through the working channel of a flexible bronchoscope using biopsy forceps or grasping forceps and then advanced within the bronchus until firmly wedged. This process is repeated if additional airways need occlusion. Spigots are removed when PAL resolves, typically within 3 to 4 weeks.

A case series study by Kaneda *et al.* (32) reported in 21 patients with PAL treated with EWS. The study found that 6 out of 21 patients (29%) achieved success after the initial spigot placement. Meanwhile, 12 patients (57%) experienced reduced air leak but required a second spigot placement or pleurodesis. Another study by Zhang *et al.* (19) investigated 50 patients with PAL lasting more than 7 days due to secondary spontaneous pneumothorax. The spigots

Figure 5 Three sizes of EWS size L, M, S (from left to right). ϕ, diameter; EWS, endobronchial Watanabe spigot.

were placed in the segmental bronchi with PAL, resulting in overall success in treatment of PAL in 42 patients (84%) compared to a conservative group with a success rate of 60%. Currently, EWS is registered in Japan for PAL and pneumothorax treatment but has not received FDA approval. Complications associated with spigot placement include fever, cough, spigot dislodgement, and pulmonary infection (32).

Bronchoscopic ABP

The process of performing bronchoscopic ABP involves using a balloon or Fogarty catheter to occlude the responsible bronchus. Sequential balloon occlusion is performed, and a positive result is achieved when the air leak decreases by more than 50%. Subsequently, the patient's blood, in a volume of 20 to 30 milliliters, is aspirated and injected through the balloon or Fogarty catheter. Thrombin in a dosage of 2,000 to 3,000 IU may also be injected simultaneously to enhance clot formation. Following the injection of ABP, the bronchus is occluded for a duration of 5 minutes. If there is a PAL in other areas of the bronchus, the same steps can be repeated. The instillation of ABP through flexible bronchoscopy induces blood clot formation, inflammation, and occlusion of the bronchus, leading to an improvement in air leak conditions. In a case series study in Japan (33), involving emphysematous patients with PAL despite spigot placement, a total of 9 cases underwent ABP with the addition of instilled thrombin through flexible bronchoscopy, guided by fluoroscopy. A blood volume of 25 milliliters was injected into the space around the spigot at the target air leak bronchus. Seven out of the nine patients achieved success with ABP. Another study by Zhang and colleagues (19) investigated patients with PAL for more than 7 days. In this study, 50 patients received ABP via a 5 Fr balloon catheter, injected a volume of 20 to 30 milliliters along with 2,000 to 3,000 IU of thrombin, and occluded the airway for 5 minutes. The overall success rate in treatment of PAL was 82%, compared to a 60% success rate in the conservative treatment group.

Complications resulting from bronchoscopic ABP include fever, cough, pulmonary infection, and hemoptysis (19). According to a meta-analysis study (2), no statistically significant differences in complications were found when compared to conservative treatment for PAL.

Occlusive material

Tissue adhesives

Cyanoacrylate compound initially used in surgical skin closure. Scappaticci and colleagues (34) successfully treated BPF with associated PAL in patients after pneumonectomy, with a total of 20 cases and a success rate of 70% (14 out of 20 cases). Success factors included BPF size less than 5 millimeters. Another study by Chawla and colleagues (35) treated BPF with PAL in patients after pneumonectomy, total 9 cases with a success rate of 89% (8 out of 9 cases). Success factors in this study included BPF size less than 8 millimeters.

Another substance within this classification, describe for BPF management, is the adhesive resulting from the combination of bovine serum albumin and glutaraldehyde (BioGlue®, CryoLife, Kennesaw, GA, USA). Two case series, comprising a total of four patients, involved instillation through either a flexible or rigid bronchoscope, with all cases successfully achieving closure that persisted for up to 5 months post-procedure (36).

Hemostatic agent

Fibrin glue (Tisseel®; Baxter, Deerfield, Illinois, USA) is the most extensively studied sealant for treating BPF post-surgery. Its mechanism of action is based on thrombogenesis and consists of two components, fibrinogen and thrombin. This triggers a process leading to the formation of fibrin, which seals the site of BPF. Within the lung, endogenous plasmin is generated to degrade the fibrin produced by the sealant. To address this, aprotinin, an anti-plasmin agent, is added to the fibrin glue formulation. This addition helps delay the fibrin degradation process for up to 14 days (37).

Hydrogel (Coseal®; Baxter), composed of polyethylene glycol, has been studied in 22 patients with PAL not resulting from surgical causes. In 19 patients (86%), air leaks were successfully stopped, with an average time of approximately 2 days post-treatment completion. The

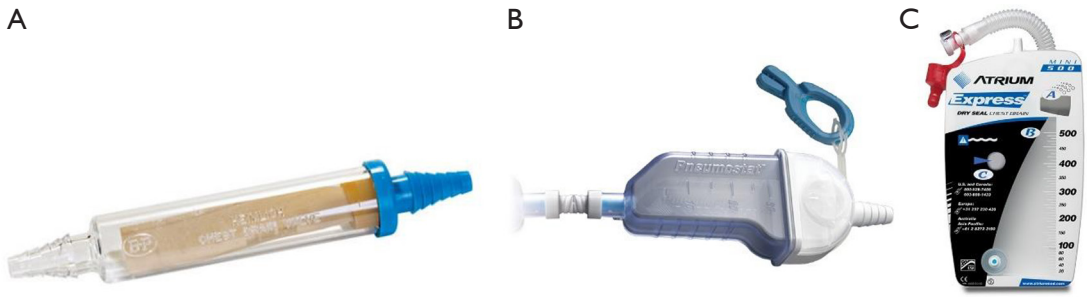

Figure 6 Ambulatory attachable devices (from BTS 2023 definition): Heimlich valve (A), Pneumostat chest drain valve (B), mobile dry seal drain (C). BTS, British Thoracic Society.

average time for chest tube removal was approximately 4 days (38).

From the aforementioned data, fibrin glue can be used to treat post-lung surgery patients with BPF smaller than 8 millimeters with PAL, with a success rate of 55% (39). The procedure requires rigid bronchoscopy. As for hydrogel, it can be employed to treat BPF not resulting from surgery, measuring less than 8 millimeters, and associated with PAL, with a success rate of 86%. The procedure can perform via flexible bronchoscopy (36).

Submucosal injections

The administration of sclerosing agents via submucosal injection induces a collagen formation reaction, causing inflammation beneath the bronchial wall and resulting in a tissue bulking effect that aids in sealing the leak. These selected agents possess biocompatible properties but are not biodegradable. Silver nitrate can be injected through a flexible bronchoscope, achieving a success rate of 80% in treating PAL arising from BPF post lung surgery (40). Varoli *et al.* (41) reported a success rate of 66% in treating 35 patients with BPF after lung surgery using the submucosal injection of polidocanol. Silver nitrate and polidocanol exhibit efficacy in treating PAL arising from BPF following lung surgery, with average success rates of 94% and 66%, respectively. These treatments can be performed through a flexible bronchoscope (36).

Amplatzer device

The septal defect occlusion device, also known as the Amplatzer device (Abbott, Abbott Park, Illinois, USA), is an equipment used in the treatment of atrial septal defects. It has been adapted for the management of BPF following surgery, with an average success rate of 82% (42). Due to its larger size, this device is commonly used in the treatment of larger BPFs in the main bronchus or surgical incision site.

Pleural intervention

Ambulatory drainage devices

The use of a one-way flutter valve reduces the hospitalization duration for patients. This can be achieved with devices such as the Heimlich valve, chest drain valve, or mobile dry seal drain (*Figure 6*). These devices are applicable to patients with PAL with full lung expansion, as confirmed by radiographic imaging. Additionally, the Heimlich valve serves as a rescue treatment following bronchoscopic intervention, addressing complications such as empyema resulting from prolonged chest tube placement, dislodged chest tubes, and tension pneumothorax due to valve occlusion (43).

Chemical pleurodesis

Sclerosant or pulmonary adhesion agent is a chemical substance that induces inflammation. When introduced into the pleural space, it promotes inflammation and adhesion of pleural surfaces, preventing the occurrence of air leaks. Commonly used sclerosing agents include talc, doxycycline, tetracycline, minocycline, bleomycin, and OK-432 (a mixture of low-virulence *Streptococcus pyogenes*). In a study by Liberman *et al.* (11), talc pleurodesis was successful in treating PAL in 40 out of 41 patients after thoracic surgery. Another retrospective study in patients with primary spontaneous pneumothorax after surgery with PAL revealed a success rate of 38 out of 60 patients treated with minocycline pleurodesis and 18 out of 19 patients treated with OK-432 pleurodesis, as reported by Watanabe *et al.* (31). In cases of PAL with secondary spontaneous pneumothorax, where surgery is not feasible, talc pleurodesis was successful in 16 out of 17 patients, with a success rate of 94%

Chemical pleurodesis requires apposition between the visceral pleura and parietal pleura. Therefore, the pleurodesis

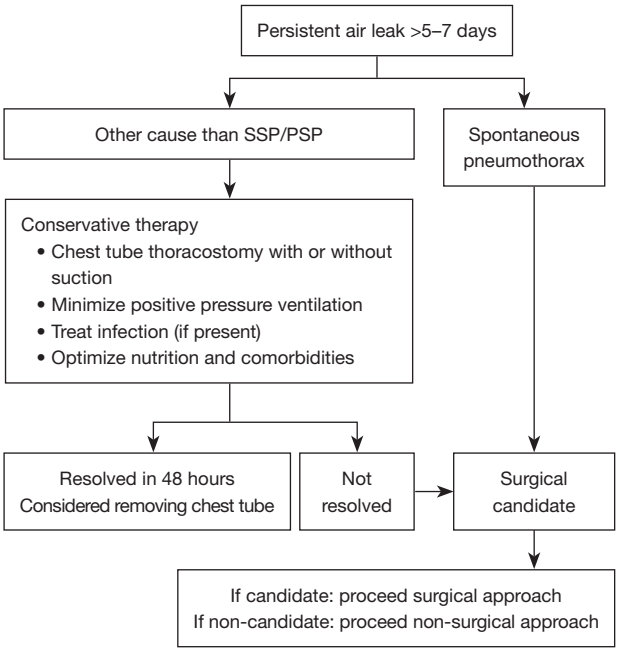

Figure 7 Algorithms management of persistent air leak. SSP, secondary spontaneous pneumothorax; PSP, primary spontaneous pneumothorax.

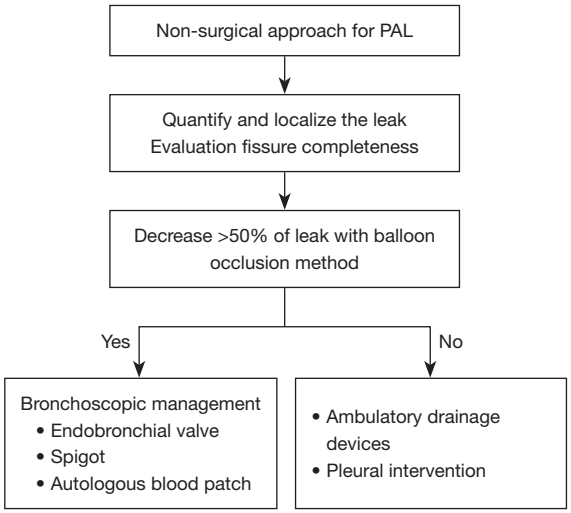

Figure 8 Algorithms management of persistent air leak with non-surgical approach. PAL, persistent air leak.

procedure should be reserved for patients with a minimal volume of pneumothorax or those without any pneumothorax under water seal drainage. Complications associated with the chemical pleurodesis process include chest pain, fever, acute exacerbation of pneumonia, and empyema. These complications are reported at a rate of 1% (11).

ABP pleurodesis (ABPP)

ABPP is an alternative technique used in patients with PAL, with or without complete lung expansion. Two randomized controlled trials and a systematic review comprising a total of 10 studies (44), including patients with PAL following lung surgery or pneumothorax, revealed success rates ranging from 92% to 93%. The proposed mechanism of action probably involves directly sealing the air leak and inducing pleural inflammation, leading to eventual pleurodesis.

The process of ABPP involves using the patient's whole venous blood, typically drawn from median cubital vein of forearm, in a quantity ranging from 50 to 100 milliliters or calculated as 1 to 2 milliliters per kilogram. Blood is injected into the pleural space through the intercostal drainage tube using a sterile method, followed by the infusion of 20 mL of saline. Subsequently, the chest tube is suspended over an intravenous pole for one to two hours to prevent blood drainage and potential tube blockage by thrombus, which might cause tension pneumothorax, especially in individuals requiring suction for pleural apposition (45).

Complications from ABPP include tension pneumothorax due to blood clots blocking the intercostal drainage tube, fever, and empyema. The incidence of complications is approximately 0–9% (46), and current analysis suggests that the incidence of complications related to infection does not show a statistically significant difference compared to the conservative treatment group (2).

Conclusions

PAL is a condition commonly observed following lung surgery, pulmonary infections, thoracic surgeries, prolonged use of ventilatory support, and spontaneous pneumothorax. The diagnostic criterion for PAL is the presence of prolonged air leak for more than 5 to 7 days. The recommended treatment for PAL involves surgical intervention, which reduces hospitalization duration and mortality rates. An alternative conservative approach is considered if surgical intervention is not feasible, involving the placement of a chest drainage tube. However, if PAL persists, bronchoscopic interventions are considered, including EBV placement, ABP, and the use of occlusive materials. Alternatively, pleural interventions such as chemical pleurodesis, ABPP, and ambulatory devices can be employed, as illustrated in *Figures* 7,*8*.

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Footnote

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