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Opinion

Management of Persistent Air Leak

Santiago Serna [1,*], Marium Khan [1], Krupa Shingada [1], Shreya Podder [1], Harpreet Singh [1], Bryan S. Benn [2], Steven Verga [1], Elizabeth Malsin [1] and Jonathan S. Kurman [1]

[1] Division of Pulmonary & Critical Care, Medical College of Wisconsin, 8701 Watertown Plank Rd, Milwaukee, WI 53226, USA; markhan@mcw.edu (M.K.); kshingada@mcw.edu (K.S.); shreya.podder@uchicagomedicine.org (S.P.); hasingh@mcw.edu (H.S.); sverga@mcw.edu (S.V.); emalsin@mcw.edu (E.M.); jkurman@mcw.edu (J.S.K.)

[2] Pulmonary Department, Integrated Hospital Care Institute, Cleveland Clinic, Cleveland, OH 44195, USA; bennb@ccf.org

* Correspondence: sserna@mcw.edu; Tel.: +414-955-7040

Abstract

Alveolar–pleural or broncho-pleural fistulas, leading to persistent air leaks (PALs), are associated with prolonged hospitalization and substantial morbidity. While guidelines advocate surgical repair as the primary treatment, its efficacy is limited. For patients recently subjected to thoracic surgery or those for whom surgery is contraindicated due to severe illness, viable treatment alternatives have been lacking. This article reviews the newer and less invasive treatment options for PALs. Further research is crucial, including randomized controlled trials comparing these options, and long-term monitoring of intervention outcomes is warranted.

Keywords: bronchoscopy; persistent air leak; bronchoalveolar fistula; endobronchial valve; pneumothorax; air leak; pleural defect; Zephyr; Chartis; Spiration

1. Introduction

Pneumothorax, characterized by the presence of air in the pleural space, is a frequently encountered clinical problem [1]. It arises from chest wall injuries, termed traumatic pneumothorax, or occurs spontaneously without preceding trauma, known as spontaneous pneumothorax. The latter is further classified into primary spontaneous pneumothorax (PSP), affecting individuals with presumably healthy lungs, and secondary spontaneous pneumothorax (SSP), which develops in individuals with underlying lung pathology. A distinct category includes iatrogenic pneumothorax, which occurs following medical or surgical procedures such as thoracentesis, transthoracic needle aspiration for lung biopsy, or central venous line procedure [2]. Additionally, with advancements in bronchoscopic interventions, post-endobronchial valve pneumothorax is now recognized as a post-procedure complication with specific management recommendations [3].

Air typically enters the pleural space due to a fistula between pulmonary parenchyma (alveolar or bronchial spaces) and the pleura or due to gas-forming organisms in the pleural space. An air leak is defined as the flow of air into the pleural space, most commonly due to abnormal communication between subsegmental or peripheral segments of the bronchial tree and the pleural space (alveolar–pleural fistula). Less commonly, it occurs due to an abnormal connection between the segmental bronchus or more central airways and the pleural space (broncho-pleural fistula) [4].

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While most instances involving air leaks typically resolve with intrapleural catheter drainage, some may not follow this pattern and can significantly contribute to morbidity, mortality, and hospital length of stay. Typically, when an air leak continues beyond 5–7 days after intrapleural catheter placement, it is defined as a persistent air leak (PAL) and often necessitates additional treatment beyond pleural drainage and watchful waiting, especially in patients with secondary spontaneous pneumothorax [5].

Air leaks may further be defined by their severity. The most utilized system is the Cerfolio Classification System, which uses a grading scale from 1 to 4 [6]. This grading system utilizes the presence of bubbles noted within the collection chamber, which is attached to the thoracostomy tube and is further described in Table 1. Grade 1 is defined as an air leak present with only forced expiration, such as during a cough; grade 2 is an air leak with expiration only; grade 3 is an air leak with inspiration only; and grade 4 is described as a continuous leak within inspiration and expiration [7].

Table 1. Cerfolio classification system.

Grade	Description
Grade 1—FE	Only during forced expiration
Grade 2—E	Expiratory only
Grade 3—I	Inspiratory only
Grade 4—C	Continuous

PAL may be seen following primary or secondary pneumothoraxes, pulmonary infections, complications from mechanical ventilation or following lung thoracic surgery [8]. As PALs are associated with increased healthcare costs, prolonged hospitalization and significant mortality and morbidity, identifying management strategies for PALs is crucial.

2. Epidemiology

Although underlying chronic obstructive pulmonary disease (COPD) can account for up to 70% of SSP, other pulmonary pathologies may also be prone to the development of pneumothorax, thereby increasing the possibility of PAL. These include cystic fibrosis, necrotizing pneumonia, pneumocystis carinii infection, lung cancer, pulmonary fibrosis and cystic lung diseases such as lymphangioleiomyomatosis (LAM) [9]. Certain connective tissue diseases, such as Marfan syndrome and Ehlers–Danlos syndrome, may also increase the risk of development of pneumothorax and subsequent PAL [9].

PAL may be observed following thoracic surgery such as lung volume reduction surgery (LVRS) for emphysema or lung resection for malignancy. The incidence of PAL is 8–45% after LVRS [10]. In the National Emphysema Treatment Trial for LVRS, 552 of the 580 patients enrolled developed a PAL within 30 days post-operatively [11].

In those undergoing lobectomy, risk factors for developing a PAL include the presence of COPD, female gender, lower forced expiratory volume in one second (FEV_1), smoking history, diabetes mellitus and chronic steroid use [8]. With LVRS, PAL was more likely to occur with a lower diffusion capacity (DLCO) along with FEV_1, pleural adhesions, or upper lobe predominance of their emphysema [8]. In a retrospective study evaluating patients with PAL, there was a statistically significant increase in the odds of intervention being required among those who had an $FEV_1 < 40\%$, DLCO < 50%, steroid use and serum albumin less than 3 g/dL [12].

3. Guidelines for Management

According to the American College of Chest Physicians (ACCP) consensus statement, the recommendation is to observe the spontaneous closure of a bronchopleural fistula for four days. After this, PAL should be evaluated for surgical closure and pleurodesis to prevent pneumothorax recurrence [13]. A second chest tube is not recommended. Thoracoscopy is the preferred management method with a strong recommendation [13]. It was also recommended that patients not undergo chemical pleurodesis with sclerosing agents except in situations where surgery is contraindicated or if patients refuse surgical management [13]. The consensus statement recommended against bronchoscopic management [13]. The updated 2023 British Thoracic Society (BTS) guidelines for pleural disease recommend consideration of autologous blood pleurodesis and endobronchial therapies for the management of PAL in non-surgical candidates [14]. However, no single intervention is universally preferred due to limited high-quality evidence supporting a single approach [14].

While consensus statements recommend surgical evaluation, less invasive strategies include bronchoscopic deployment of various materials for bronchial occlusion. These include sealants, such as fibrin glue or synthetic hydrogel [15,16]; silicone spigots designed to occlude segmental bronchi [17]; metal endovascular coils that can be repurposed for endobronchial occlusion [18]; and self-expanding covered metallic airway stents [19] (Table 2). Among these bronchoscopic interventions, endobronchial valves (EBVs) have the most robust published experience, albeit largely consisting of case reports and case series, likely reflecting their standardized design, reproducibility, and increased adoption. Accordingly, a more detailed discussion is provided below.

Table 2. Endobronchial therapies for the management of PAL.

Intervention	Study	Number of Subjects	Technical Success	Clinical Success	Comments
EBV	Gkegkes et al., 2015 [20]	39	NR	67% (26/39 within 24 h)	Reversible; valve removal required after PAL resolution.
EBV	Ding et al., 2017 [10]	52	NR	62% (31/50 within 24 h)	Reversible; valve removal required after PAL resolution
Silicone Spigots (EWS)	Watanabe et al., 2003 [17]	60	97% (58/60)	78%	40% complete cessation; 38% reduction in air leak
Metallic Coils + Glue	Watanabe et al., 2003 [18]	5	100%	80%	Primarily peripheral BPF
Customized Metal Stent	Han et al., 2018 [19]	148	97% (143/148)	49%	Post-surgical, granulation tissue formation in 34%
Fibrin Glue	Hollaus et al., 1998 [16]	29	NR	55%	BPF < 8 mm; required rigid bronchoscopy
Hydrogel	Mehta et al., 2015 [15]	22	NR	86%	Non-surgical

Abbreviations: PAL, persistent air leak; BPF, bronchopleural fistula; EWS, endobronchial Watanabe spigot; NR, not reported; EBV, endobronchial valve.

4. Other Treatments for PAL

Pleurodesis is the process by which fusion of the visceral and parietal pleural layers is promoted in order to obliterate the pleural space and eliminate the possibility of recurrent pleural effusion or pneumothorax [21]. When a sclerosing agent, which serves as a chemical irritant, is placed within this space, there is activation of the inflammatory pathway and coagulation cascade, and a decrease in pleural fibrinolytic activity. Fibrin links then develop

between the pleural layers, producing a mesh-like framework and ultimately obliterating the pleural space [21]. Talc is considered an excellent sclerosant in pleurodesis with a high success rate and a favorable side effect profile. Other agents include doxycycline, iodopovidone and silver nitrate [21]. Doxycycline or talc slurry is the preferred agent in the ACCP consensus statement [13].

Other potential treatment strategies include pleurodesis with an autologous blood patch (ABP). This procedure is performed by obtaining a sample of the patient's own blood, typically 60 to 120 mL or 2 mL of blood per kilogram of body weight in a sterile manner [22,23]. This blood is immediately instilled into the chest tube, followed by a saline flush to prevent coagulation within the tube drainage system. The chest tube is then raised above the level of the insertion site and may be clamped briefly to allow for the blood to remain within the pleural space [8,22]. The mechanism of ABP is believed to differ from traditional chemical pleurodesis. It functions through a dual process: first, the instilled blood forms a direct sealant at the site of the air leak through clot formation; second, the subsequent pleural irritation and inflammation in response to fibrogenic activity promote adhesion between pleural surfaces, achieving pleurodesis [24]. This technique was first described by Robinson in 1987 for the management of PAL [25]. In this case series, 25 patients with a PAL were treated with one to three injections of autologous blood, which demonstrated successful air leak cessation among 85% of the patients [25]. Since then, several additional studies have demonstrated similar results with success rates of 92–93% [8,26]. Benefits of ABP include a more favorable side effect profile than sclerosing agents, which can precipitate allergic reactions or hypersensitivity reactions [27]. Additionally, use of ABP is associated with less pain, may be performed in aseptic conditions (outside of the operating room) and does not require anesthesia [27]. Complications with use of ABP are similar to those of pleurodesis with other agents, including tension pneumothorax or development of empyema. Importantly, the 2023 BTS guidelines recommend consideration of ABP pleurodesis for PAL, as evidence has demonstrated reduced hospital length of stay compared to chest drainage alone [14].

Advancements in bronchoscopy procedures have allowed for the development of additional treatment strategies for PAL. Endobronchial valves (EBVs) are small umbrella-shaped or duck-bill-shaped devices with one-way valves, designed to limit airflow to airways through a defect in the visceral pleura so that the margins of the defect can approximate and heal. Currently, there are four types of endobronchial valves described in the literature—the Zephyr EBV (PulmonX), the Spiration EBV system (Olympus), the Miyaazawa EBV (Novatech) and the MedLung EBV (Medlung). In the United States, both Zephyr and Spiration valves are FDA-approved for severe emphysema treatment, but only Spiration holds Humanitarian Device Exemption (HDE) approval for PAL (granted October 2008) [28]. The HDE designation requires institutional IRB approval and specialized informed consent clearly stating this is not an FDA-approved indication. Both systems have CE Mark approval in Europe for emphysema and air leak management.

The EBV system consists of a delivery catheter/sizer, which is inserted into the bronchoscope, a loader system, and the actual EBV. Once deployed, an EBV can be repositioned slightly or removed if needed. The process of placing an EBV includes air leak isolation, airway sizing and valve deployment [29]. PALs can be complex and involve more than one segment of the lung. Thus, isolation of the air leak is an important step in management of PAL using EBVs. The most reliable method to identify the culprit airway(s) is sequential balloon occlusion, moving from proximal to distal airways, while the drainage device is monitored for cessation or diminishment of air leak with occlusion of the affected segments. Alternatively, the Chartis assessment (Chartis system, PulmonX) can be used to detect the cessation of airflow with the occlusion of the affected segment [30]. Once the affected

segment(s) are identified, valve sizing is determined using airway sizing kits specific to the EBV being used. Following this, the delivery catheter system is used through the working channel of the bronchoscope to deploy the EBV. Once deployed, the drainage catheter system is monitored for 4–5 ventilatory cycles to monitor change and degree of air leak [8] (Table 1).

There is increasing evidence in the form of case reports, case series and review articles to support the use of EBVs in management of PAL. To date, no randomized controlled trials have been completed; the VAST trial was halted early because of problems with enrollment (ClinicalTrials.gov Identifier: NCT02382614). Despite this growing body of evidence, EBV therapy has important limitations that must be considered. The need to isolate the air leak is time-consuming and may fail due to collateral ventilation or inability to localize the culprit airway [31]. EBV insertion may also cause complications such as granulation tissue formation, pneumonia, or valve migration. Additionally, anatomic factors such as large (≥8 mm) central airway defects may preclude EBV deployment [31]. From a healthcare cost perspective, the cumulative cost of EBV—including procedure, valves, and hospitalization—may appear substantial; however, it is comparable to costs associated with prolonged intensive care and hospitalization of unresolved PAL [10,20]. Table 3 summarizes the efficacy of EBV for PAL from two comprehensive review articles by Gkegkes et al. and Ding et al. [10,20].

Table 3. Summary of EBV for PAL review articles.

	Gkegkes et al., 2015 [20]	**Ding et al., 2017 [10]**
	***N* = 39**	***N* = 52**
Demographics		
Age (years), median (range)	57 (18–93)	60 (18–88)
Male	24/39	28/51
Female	15/39	23/51
Past medical history		
Immunosuppressive disease or treatment	36/39	NR
Lung disease	20/39	26/52
Lung infection	NR	11/52
Cancer	10/39	14/52
Smoker	10/39	NR
Cardiovascular disease	4/39	NR
Etiology of PAL		
Tension pneumothorax	NR	6/52
Spontaneous secondary pneumothorax or pneumothorax	12/39	23/52
Bronchopleural fistula	8/39	6/52
Iatrogenic pneumothorax	6/39	6/52
Alveolar–pleural/ transdiaphragmatic fistula	2/39	1/52
Parapneumonic pleural empyema	2/39	9/52
Broncho-cutaneous fistula	1/39	1/52
Lung tree perforation	1/39	NR

Table 3. *Cont.*

	Gkegkes et al., 2015 [20]	Ding et al., 2017 [10]
	N = 39	*N* = 52
Post-operative air leak	8/39	12/52
Type of EBV used		
Emphasys	25/81	32/122
IBV valve	23/81	59/122
Zephyr valve	23/81	31/122
Duration of air leak after EBV placement		
<24 h	26	31/50
24 h to <48 h	3	6/50
>48 h	10	13/50
Outcomes		
Removal of EBV	17/39	20/50
Reoccurrence of PAL	3/39	3/50
Migration of EBV	2/39	1/50
Expectoration of EBV	NR	1/50
COPD exacerbations	1/39	NR
Death not related to utilization of EBV	4/39	3/50

As previously discussed, EBVs are FDA-approved for bronchoscopic lung-volume reduction (BLVR) in severe emphysema. The most common complication of EBV is pneumothorax, which may present acutely and requires prompt chest-tube drainage when symptomatic [3]. PAL following EBV placement is managed according to a distinct algorithm. Expert consensus recommends initial removal of one or two valves to permit partial re-expansion of the target lobe and re-establish pleural apposition, which may facilitate spontaneous sealing of the leak [3]. If the air leak persists after valve removal, cross-sectional imaging can help localize the source and guide subsequent management. Options include mechanical or chemical pleurodesis, repeat bronchoscopic interventions, or surgical repair in selected patients. The choice is individualized based on the patient's clinical status and operative risk [3].

5. When to Intervene

Knowing when to intervene on an air leak is equally important. Conservative management is advised for the first 5–7 days unless the air leak is vigorous enough that it causes either hemodynamic or respiratory instability, in which case either surgical or bronchoscopic intervention should be pursued immediately.

Once an air leak extends beyond 5–7 days, and by definition becomes persistent, more aggressive management should be considered if there is no trend to improvement. Evidence of improvement includes progression with chest tube weaning, such as tolerating progressively longer water seal trials or transitioning from water seal to clamp trials. Alternatively, it may also manifest as decreasing air leak severity as quantified by a digital collection chamber or decreased bubbling in an analog collection chamber [32].

Surgical or bronchoscopic interventions should be employed for PAL if there is no trend toward improvement. Which of these interventions is pursued is largely dependent upon local expertise and equipment availability. If only surgical expertise is available,

then patient factors must also be accounted for, such as the ability to tolerate single-lung ventilation and at least partial resection of the parenchyma. Pulmonary function testing and some type of perfusion scan (V/Q or NM SPECT) should ideally be obtained to make this determination. In areas where both surgical and bronchoscopic options are available, the authors recommend the latter option based on a growing body of evidence, its minimally invasive nature, and its reversibility. Among the bronchoscopic modalities, endobronchial valves are preferred for the same rationale.

If valve insertion is performed, valve removal is recommended after approximately 6 weeks. By this time, the visceral pleural defect should have had sufficient time to approximate and heal. If pneumothorax recurs upon valve removal, then valves should be reinserted for another 6-week trial. If pneumothorax still recurs upon removal, then there is no utility to further valve trials, and surgical intervention is the only option.

6. Conclusions

PALs have been identified as a healthcare system burden due to increased length of stay and need for further interventions. Identifying patients who are at risk for PAL and utilizing effective management strategies is important to reduce this burden. EBVs provide a minimally invasive, effective alternative to surgical intervention. Updated guidelines may need to be considered in the near future based on mounting evidence supporting the use of EBVs as first-line therapy for PALs.

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