Article Review

Persistent Air Leak

Dwi Anggita[1,2], Edward Pandu Wiriansya[1,2], Arif Santoso[1], Harry Akza Putrawan[1]

[1]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Hasanuddin, Makassar, Indonesia
[2]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Muslim Indonesia, Makassar, Indonesia

Abstract

In cases of pneumothorax in the chest tube, the presence of air in the pleural cavity that lasts more than 5 to 7 days can be suspected as a persistent air leak (PAL), especially if an increased amount of air is obtained accompanied by the appearance of bubbles in the water seal drainage (WSD) system. This is the most common complication after surgery (8–26%), although it can be primary spontaneous pneumothorax (PSP) (26%) or secondary spontaneous pneumothorax (SSP) (39%). One condition that often causes difficulties in PAL therapy is infection due to direct contact with the fistula. The presence of PAL is associated with higher morbidity and mortality, prolonged chest tube inserted, and longer hospitalization. Observations of air production in PAL are expected to occur spontaneously within 4 days, if the leak persists, pleurodesis is recommended. If it was possible, surgery is needed to close the leak. Bronchoscopy treatment is only recommended in special circumstances where surgery is contraindicated or the patient refuses the surgical procedure.

Keywords: alveolar-pleural fistula, bronchopleural fistula, persistent air leak

Corresponding Author:
Dwi Anggita | Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Hasanuddin, Makassar, Indonesia | dwi.anggita@umi.ac.id

Submitted: March 2nd, 2023
Accepted: March 3rd, 2024
Published: April 30th, 2024

J Respirol Indones. 2024
Vol. 44 No. 2: 161–9
https://doi.org/10.36497/jri.v44i2.432

INTRODUCTION

Persistent air leak (PAL) is any air keak that continues for more than 5 to 7 days in pneumothorax condition. Alveolar-pleural fistula (APF) or a broncho-pleural fistula (BPF) may be the root of this issue. The most typical PAL is postoperative (8–26%), although it can also happen after spontaneous pneumothorax brought on by an underlying lung condition such as a lung infection, difficulties with mechanical ventilation, or chest injury.[1–3]

Alveolar-pleural fistula refers to the junction between the pleural space and the alveoli. As air leaks from the lungs into the pleural space as a result of this interaction, a pneumothorax will form. The pneumothorax will become worse if this association persists because airflow from the lung parenchyma into the pleural space occurs. Following the insertion of the chest tube, bubbles occurred in the Intercostal drainage (ICD) system. If the bubbles are prolonged and last more than 5 to 7 days, then there is a persistent air leak.[2]

Having a direct connection between the bronchi and the pleural cavity is known as a BPF. BPF is split into two main groups, namely central and peripheral BPF, based on the location of the fistula.[4] Peripheral BPF involves the connection between the pleura and the airways beyond the segmental bronchi or lung parenchyma. On the other hand, central BPF involves the connection between the pleura and the tracheobronchial tract. Broncho-pleural fistula is also referred to as APF in certain literature.[5]

The healing process in cases of pneumothorax takes a long time until PAL can occur. The cause can be primary spontaneous pneumothorax (PSP) (26%) or secondary spontaneous pneumothorax (SSP) (39%). The average duration of air leaks in PSP is 5.2 days with a length of stay of 4–7 days, while the average duration of air leaks in PSS is 9.9 days with a length of stay between 12–16 days.[6]

Persistent air leaks can result from trauma or the spontaneous rupture of a pleural bleb but are mainly linked to/associated with lung surgery. When air accumulates extensively in the pleural space and remains undrained, it leads to a gradual loss of lung capacity and an increase in pleural pressure.[7]

The complications of PAL arise from contamination of the pleural space through direct communication with an unsterile tracheobronchial tree. Additionally, it occurs in a mismatch between ventilation and perfusion and makes it difficult to sustain Positive end-expiratory pressures (PEEP) during mechanical ventilation. A prolonged use of the chest tube, a longer hospital stay, and greater morbidity and death are all associated with PAL.[1] The overall mortality rate in PAL is 67%. In cases of PAL due to non-traumatic causes, the mortality rate is greater (92%).[2]

Management of PAL is still challenging. Some guidelines recommend conservative therapy with chest tube drainage, then if it is unsuccessful, surgical repair is the gold standard for treatment. However, if surgery cannot be performed due to several conditions, conservative treatment options can be done although they are still less effective. [2]

CLASSIFICATION

The most popular classification, the Cerfolio classification, which rates PAL according to the volume of air leak and whether the leak is expiratory or continuous, is one of several proposed classifications that take the opportunity to quantify the severity of PAL in the postoperative condition.[2]

Table 1. Cerfolio Classification [2]

Grade	Maneuver
Grade 1, FE	During forced expiration only, typically when asking the patient to cough
Grade 2, E	Expiration only
Grade 3, I	Inspiration only
Grade 4, C	Continuous bubbling present in the air leak chamber during both inspiration and expiration

Note: FE=Forced expiration; E=expiration; I=inspiration; C=continues

Observing the water seal area in the three-chamber drainage system allows for further classifications. The patient's fluids or blood are collected in the first chamber. The water is located inside the second chamber. This forces air to leave the pleural space during exhalation and prevent air from entering during inhalation. Air leaks are indicated by the presence of bubbles in the WSD system. When using three-chamber drainage, the amount of air leakage is usually indicated by the presence of bubbles in the air leak control, which measures it in a column from 1 to 7. The size of the air leak is seen by the extent of the bubbles in the column. The larger the size of the leak, the larger the column the bubbles reach. In general, if the air leak is less than 20 ml/min, the chest tube can be removed safely.[2]

RISK FACTORS

Risk factors that depend on the underlying etiology such as PAL in spontaneous pneumothorax are underlying lung disease, older age and the presence of a large diameter bulla are risk factors for disease severity.[8] Pleural adhesion and diffuse emphysema predominate in the upper lobe test. Pulmonary function and pulmonary diffusion predispose to the occurrence of PAL.[9]

A recent study indicates that many risk factors, particularly BPF, have been linked to the onset of PAL. Three categories of risk factors are distinguished: those relating to the patient, those relating to surgery, and those relating to the patient's anatomy. Age (over 60 years), gender (male), neoadjuvant radiation therapy, diabetes mellitus, malnutrition, smoking, long-term use of steroids or other immunosuppressive therapy, underlying lung disease like chronic obstructive pulmonary disease (COPD), and the requirement for postoperative mechanical ventilation are a few examples of patient-related risk factors.[5,10]

The use of mechanical ventilation following pneumonectomy surgery is frequently linked to surgical risk factors. Despite advancements in surgical methods, pulmonary surgery procedures continue to be a major source of air leakage.[11] Therefore, to prevent bronchial leaks, extubation

should be performed as early as possible after surgery.[5]

Fever, steroid use, *H. influenzae* in sputum, an elevated erythrocyte sedimentation rate, and anemia are preoperative risk factors. The postoperative risk factors involved were fever, steroid use, leukocytosis, tracheostomy, and bronchoscopy for suctioning of sputum or mucous blockage.[12]

Risk factors associated with defined anatomical weakness for right-sided pneumonectomy include:[5]

1. Based on cadaveric research, the most typical configuration is two left-sided and one right-sided bronchial artery supply.
2. In contrast to the right main bronchus, the left main bronchus is protected by the aortic arch, unlike the right main bronchus which is exposed to mediastinal tissue.
3. Compared to the left main bronchus, the right main bronchus is wider and more vertical. This condition facilitates the retention of secretions in the right main bronchus.

CLINICAL PRESENTATION

The acute stage, clinical presentation of PAL can be a life-threatening condition due to a tension pneumothorax or shortness of breath due to lung compression. Sudden onset of dyspnea, hypotension, subcutaneous emphysema, cough with purulent sputum expectoration, tracheal and mediastinal displacement, ongoing air leaks, and diminished or absent pleural effusion on chest radiographs are symptoms for the postoperative cases of PAL.[13]

The subacute presentation is characterized by fever and a minimally productive cough.[12] The chronic presentation is associated with an infected pleural space and manifests as cough, fever, and malaise with varying degrees of respiratory distress.[11]

The patient often coughs up purulent sputum. A tension pneumothorax or a big fistula may cause acute respiratory distress. Empyema commonly develops in several chronic PAL cases. The most crucial indicator of a continuous air leak on a chest X-ray is a change in the height of the air fluid. PAL should be considered if there is a persistent postoperative air leak, fresh air fluid, or if the pleural effusion vanishes on the chest radiograph.[13]

DIAGNOSIS

The approach to the diagnosis of PAL is not only to establish the diagnosis but also to estimate the exact size and location of the air leak, understand its relationship to adjacent mediastinal structures, and identify secondary complications. The diagnosis of PAL may be made by bronchoscopy, chest X-rays, or chest CT scans, among other techniques.[14]

Chest X-ray

The simplest test to detect air leaks is a chest X-ray. Specific signs for the diagnosis of PAL include the existence of a tension pneumothorax, an increase in intrapleural air, and the appearance of a new level of air fluid. The appearance of subcutaneous emphysema, a new pneumothorax, a pneumothorax that is larger or displays a lower air-fluid level in the hydropneumothorax, a transfer of the mediastinum to the contralateral side, and any of these symptoms may be indicators of PAL. Therefore, if this image is discovered on a chest X-ray, more tests are required. The diagnosis of postoperative PAL usually shows a shift in the pleural fluid margin, whereas a decreased air-fluid level in the pleural cavity does.[14]

Bronchoscopy

The bronchoscopy technique is very important for the diagnosis of air leaks and can determine the location and size of air leaks.

Figure 1. Fistula on bronchoscopy in a patient after right lower lobectomy[14]

The bronchoscopy will show a fistula in the bronchi if the lesion is more centrally located[15], as in Figure 1 which shows the presence of a small fistula on bronchoscopy in a patient after right lower lobectomy.[14] Bronchoscopy should be done to evaluate the terminals of the bronchial branches if clinical suspicion is discovered or if radiological markers appear that suggest PAL.[5]

Bronchoscopy cannot provide a clear view of the fistula if the lesion is more peripheral. The localization method for PAL related to bronchoscopy is by administering anterograde methylene blue (MB) through a surgical wound and a chest tube. An alternate method for identifying the location of the source of the air leak is to insert the MB into the pleural drainage catheter after some time has passed while carefully monitoring all of the bronchial trees via bronchoscopy.[1,15]

This is carried out in conjunction with bronchoscopy-based bronchial visualization. The diagnosis will be confirmed by careful examination of the dye entering the tracheobronchial tree from the afflicted airway. This approach has the special benefit of not requiring the observation of chest drainage system bubbles.[1]

Figure 2. Methylene blue was seen in the anterior segment of the right upper lobe [15]

The approach is to dilute MB to the necessary volume in either 5% dextrose or normal saline in water.[1] The MB dose used for pleural fistula localization is 1 ml of MB equivalent with 10 mg diluted using 250 ml normal saline solution or 5% dextrose. Each case can be given as much as 80 mL of diluted MB.[15]

Because the dye will follow the largest leak to the smallest leak and only identify one fistula at a time, this method considers that the injection of methylene blue may not be able to localize multiple air leaks individually.[1]

Computed tomography scan thorax

Bronchoscopy and thoracic computed tomography (CT) help determine the diagnosis, identify the cause of the problem, and locate the fistula tract. For improved healing, patients with centrally located fistulas larger than 5 mm must undergo surgery. Many bronchoscopy procedures have been developed to treat PAL in addition to determining the diagnosis and location of the fistula. According to some research, peripheral air leaks with a size of 5 mm can be treated using bronchoscopy, particularly in patients who are frail and at high risk for surgery [16].

There is significant debate surrounding the diagnosis made by chest CT scan. Mediastinal emphysema, parenchymal infiltration, and expansion of the pleural cavity can all be seen on a CT scan. A fistula can be definitively diagnosed by periodic imaging of the bronchi or lung parenchyma into the pleural space (Figure 3) [5].

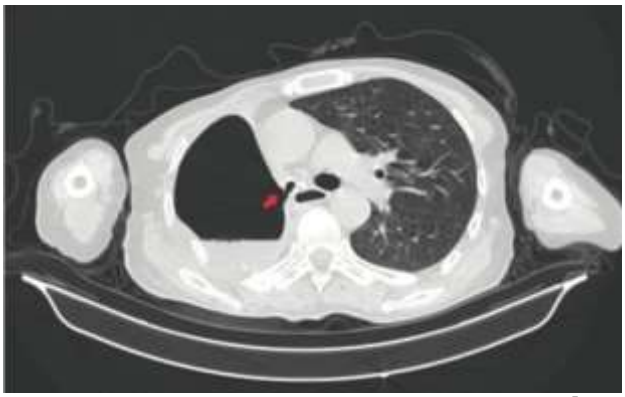

Figure 3. Bronchopleural fistula on the right hemithorax[5]

MANAGEMENT

While analyzing an air leak, the amount, duration, and trend of the leak should all be considered. A larger, longer-lasting air leak, for example, has a reduced chance of resolution, whereas a smaller air leak that gets better every day is more likely to mend spontaneously. Most

postoperative air leaks might disappear with their own, even if it takes weeks.[2]

The treatment of PAL frequently necessitates longer hospital stay, difficult surgical procedures, and extensive follow-up. The management of life-threatening illnesses like sepsis, tension pneumothorax, and respiratory failure is the first stage of treatment. To minimize the danger of pneumonia and respiratory failure, it is important to protect the contralateral lung against pleural fluid aspiration. Thus, it is necessary to insert a chest tube to guarantee that the pleural area is drained. Broad-spectrum antibiotic therapy is depending on the results of the culture. In 16 of 17 effective cases of pleural fistula, investigations using conservative therapy, such as pleural irrigation, drainage and reduction of the pleural cavity, antibiotics, and nutritional supplementation, have been documented.[5]

Treatment for PAL ranges from medical management to bronchoscopy procedures for critically ill patients and surgical intervention for those at the highest risk. In patients with PAL, 4 days of observation are recommended for spontaneous closure of the defect. Pleurodesis surgery is advised if the air leak lasts for longer than 4 days. Bronchoscopy is only advised as a therapeutic option when surgery is not an option or when the patient declines the operation. Similar recommendations were made in the 2010 British Thoracic Society (BTS) guidelines, which state that in situations of PAL or failure of the lung to re-inflate after 3-5 days, a surgical opinion should be sought. Regarding situations in which surgery is not an option, there are no specific recommendations.[1,2]

There are a variety of minimally invasive PAL care strategies available for people who are inoperable or choose not to have surgery. Since the first documented successful management of endobronchial fistulas, numerous alternative materials have been tested. Each has its setbacks, and reported success rates are quite variable. It is crucial to emphasize that there have been no randomized controlled studies to identify the most safe and effective treatment approach.[1]

As a result, there are currently no recommendations, algorithms for treatment, or consensus among experts regarding the optimal kind of therapy. The preferred course of treatment is frequently conservative management with continuous chest tube drainage, and if further intervention is necessary, it should be based on the individual clinical signs of each patient.[1]

Chest Tube

Chest tubes can be used to treat air leaks, but there are also potential risks. Chest tubes can have adverse effects, including tidal volume loss, and irregular changes in ventilator cycles from inspiration to expiration, particularly when mechanical ventilation is employed. Moreover, applying negative pressure to a chest tube may increase flow through the fistula tract and delay healing and closure.[12]

Patients with high-flow air leakage and empyema drainage require a chest tube. A chest tube can also be used to occlude during the inspiratory phase or enhance positive intrapleural pressure during the expiratory phase in patients who are undergoing mechanical ventilation.[12]

To maintain PEEP, this intervention aims to both decrease air leakage during expiration and to decrease airflow near the leak during the last inspiration. This method has also been used in conjunction, and it might be especially important for patients with ARDS or other disorders where PEEP is required to keep oxygen levels up. Any air leaks must be able to drain through a chest tube that is large enough. A sclerosing agent can be applied through a chest tube to perform pleurodesis.[12]

Heimlich Valve

The Heimlich valve is another alternative to shorten the hospital stay if the insertion of a chest tube into the water drainage system is unsuccessful in stopping the air leak. The tiny one-way valve gives the patient more flexibility. Every patient with PAL receives a Heimlich valve to allow early hospital discharge, regardless of the size of the air leak. Each patient got daily chest tube therapy and pulmonary rehabilitation. Chest tubes can be removed from PAL

patients using the Heimlich valve as long as they do not exhibit subcutaneous emphysema symptoms and the pneumothorax does not enlarge, according to another study.[17]

Heimlich valve is a one-way flutter valve that permits fluid and air to leave the pleural region without returning. The collection device that is connected to the other end of the Heimlich valve allows air to pass while collecting pleural fluid. A chest X-ray was taken after 24 hours, and the patient was sent home if there were no new or expanded pneumothoraxes or subcutaneous emphysema. The patient should be returned to suction or water seal if there is an issue with the chest X-ray. This method must be repeated every one to two days. Alternatives to more long-term treatment must be considered if relapses do occur.[1]

Figure 4. A Heimlich valve is installed at the left hemithorax in patient with PAL[18]

Following Heimlich valve discharge, it is recommended to conduct weekly chest radiographs. To assess the presence of PAL, patients should submerge the Heimlich valve tip in water while performing passive or forced breathing exercises. The absence of bubbles confirms PAL resolution and signals the safe removal of the chest tube. Regardless of the magnitude of the leak or the occurrence of a pneumothorax, the chest tube can be safely removed 2 weeks after discharge. Even though there was still an air leak, numerous pleural space adhesions that had formed by this point would have prevented the growth of a pneumothorax.[1]

This method provides some benefits, including simple placement, quick hospital discharge for patients, and no introduction of foreign materials into the pleural space. The inconvenience of leaving the patient with the chest tube in place (which frequently necessitates home care services and onsite care supplies), the discomfort and pain related to the chest tube, the risk of pleural infection secondary to the chest tube, and having to bring the patient back frequently are all limitations of this approach.[1]

Chemical Pleurodesis

To prevent repeated pleural effusion or pneumothorax, a procedure known as pleurodesis is used to create adhesion between the visceral and parietal pleura. Inflammation, fibrosis, and adhesions between the two pleural layers are caused by chemical irritation (chemical pleurodesis) or mechanical abrasion (mechanical pleurodesis). Chemical pleurodesis is frequently used in clinical settings to control air leaks, to stop a pneumothorax from recurring and to treat critical patients.[19].

Via a chest tube, a thoracoscopic procedure, or during surgery, chemical pleurodesis can be applied. Several sclerosants, such as talc, bleomycin, autologous blood patches[20], iodopovidone, and several other chemical substances, have been utilized in clinical practice. Tetracyclines and their derivatives, such as doxycycline and minocycline, have also been employed.[21]

When injected into the pleural space, a sclerosant triggers an inflammatory response that permits the pleural space to close, eliminates air leaking, and prevents recurrent pneumothoraxes. In a retrospective analysis, talc pleurodesis was successful in treating 40 of 41 post-lobectomy patients who had PAL.[22]

When considering the performance of chemical pleurodesis, it is important to note that it should only be carried out in cases where there is no or only a small pneumothorax remaining once the chest tube is

inserted into the aqueous drainage system. This approach ensures that the procedure is both effective and safe for the patient. Alternatively, chemical pleurodesis needs to be avoided since it can make it difficult for the lung to reinflate. Chest pain, fever, acute lung damage, and empyema are all side effects of chemical pleurodesis.[2]

Bronchoscopy

Flexible bronchoscopy is a recognized diagnostic and treatment option for PAL patients. Bronchopleurocutaneous fistula traces have been successfully viewed using fiberoptic bronchoscopy. However, a distal fistula has to occlude bronchial segments using a balloon to find one that leads to a fistula. Via bronchoscopy, some sealants have been placed directly into the fistula, including ethanol, lead plugs, fibrin, antibiotics, gel foams, and some other substances. In non-septic patients, small defects measuring less than 5 mm can be effectively managed through the use of endoscopic fibrin glue or silver nitrate.[23] The majority of leakage happens in peripheral situations, which increases the possibility of this strategy's effectiveness. For individuals who are unable to tolerate large thoracic surgical operations, it also provides an option.[2]

Endobronchial (EBV)/Intrabronchial (IBV) Valves

A flexible bronchoscope is used to insert the one-way EBV and IBV valves into the lobar, segmental, or subsegmental airways. This procedure aims to maintain normal distal secretion flow while preventing air from passing through the fistula. Using an airway gauge, the bronchi are measured after the airway leading to the abnormality has been identified. The airway lumen is measured using the balloon catheter and calibrated to determine the size of the valve. The chest tube drainage chamber needs to be watched for 4–5 ventilation cycles after the valve is installed to detect any changes in the air leakage rate. Past research has indicated that each PAL is typically controlled by 1–10 valves (on average: 2–3 valves).[2]

This valve is simply removed with forceps and is well tolerated. Rarely may air leaks stop right away once a valve is installed. The usual duration from valve installation to resolution of the air leak is 4–7 days, with a mean of 5 days, so spontaneous responses to remove the valve should be avoided in cases where the air leak persists for 1–2 days following placement.[1] For some patients whose conservative treatment has failed or who are poor surgical candidates, the insertion of EBV and IBV for PAL has been successful.[2]

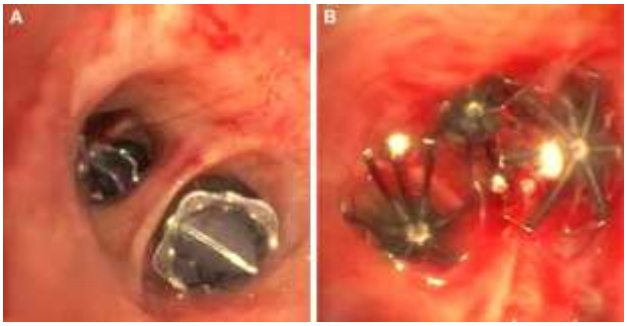

Figure 5. Endobronchial valve installation (right) in left lower lobe. Installation of an intrabronchial valve (left) in the left upper lobe[24]

Surgery

Although conducting a thoracotomy has a risk, the reported mortality has been low, and the success rate of surgical closure of the pleural fistula has been reported to be almost 95% of the cases. Omental flaps, transsternal bronchial closure, direct leak closure with intercostal muscle strengthening, thoracoplasty with or without extrathoracic chest wall muscle transposition, and open drainage are some surgical closure options. This method has also been applied in attempts to cure pleural fistula since the development of video-assisted thoracoscopy (VATS).[12]

It is advised to close the pleural fistula in steps. The Eloesser treatment for drainage of the chest cavity, which involved a muscle flap operation with minimum morbidity in a chronically ill patient, was performed on the patient in the initial stage. After that, the patients endured intensive nutritional and physical therapy until they were able to tolerate a second thoracic obliteration with an omental flap operation.[12]

CONCLUSION

Persistent air leak is still a challenge in management and has an impact on extending the

length of stay, increasing morbidity caused by BPF and APF. As the gold standard of care, recent guidelines advise conservative waiting with chest tube drainage followed by surgical repair. In contrast to a big or central pleural fistula, which is best treated through surgery or stent implantation, a minor distal pleural fistula is better treated through bronchoscopy. If PAL develops soon after surgery, re-closure is required. Multiple air leaks can be controlled with proper chest tube management, and switching to an outpatient drainage device (such as the Heimlich valve) can allow the leak to heal while avoiding the morbidity linked to prolonged hospitalization. Several case series have demonstrated that pleurodesis and IBV are effective treatments for PAL.

There has been no further research to determine which therapy options are the most effective, safe, or cost-effective for PAL, so management guidelines and treatment algorithms are less updated. Prolonged chest tube drainage is often the preferred treatment. In cases where further intervention is necessary, it is essential to customize the treatment to the individual patient and their specific clinical situation.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

None.

FUNDING

None.

REFERENCES

1. Sakata KK, Reisenauer JS, Kern RM, Mullon JJ. Persistent air leak-review. Respir Med. 2018;137:213–8.
2. Dugan KC, Laxmanan B, Murgu S, Hogarth DK. Management of persistent air leaks. Chest. 2017;152(2):417–23.
3. Hoeijmakers F, Hartemink KJ, Verhagen AF, Steup WH, Marra E, Röell WFB, et al. Variation in incidence, prevention and treatment of persistent air leak after lung cancer surgery. European Journal of Cardio-Thoracic Surgery. 2022;61(1):110–7.
4. Okuda M, Go T, Yokomise H. Risk factor of bronchopleural fistula after general thoracic surgery. Gen Thorac Cardiovasc Surg. 2017;65(12):679–85.
5. Batıhan G, Can CK. Bronchopleural fistula: causes, diagnoses and management. Dis Pleura. 2020;1–14.
6. Walker SP, Hallifax R, Rahman NM, Maskell NA. Challenging the paradigm of persistent air leak: are we prolonging the problem? Am J Respir Crit Care Med. 2022;206(2):145–9.
7. Mentzer SJ, Tsuda A, Loring SH. Pleural mechanics and the pathophysiology of air leaks. J Thorac Cardiovasc Surg. 2018;155(5):2182–9.
8. Jiang L, Jiang G, Zhu Y, Hao W, Zhang L. Risk factors predisposing to prolonged air leak after video-assisted thoracoscopic surgery for spontaneous pneumothorax. Ann Thorac Surg. 2014;97(3):1008–13.
9. DeCamp MM, Blackstone EH, Naunheim KS, Krasna MJ, Wood DE, Meli YM, et al. Patient and surgical factors influencing air leak after lung volume reduction surgery: lessons learned from the National Emphysema Treatment Trial. Ann Thorac Surg. 2006;82(1):197–207.
10. Kurman JS, Hogarth DK. Minimally invasive persistent air leak management. AME Med J. 2018;3:80.
11. Shekar K, Foot C, Fraser J, Ziegenfuss M, Hopkins P, Windsor M. Bronchopleural fistula: an update for intensivists. J Crit Care. 2010;25(1):47–55.
12. Lois M, Noppen M. Bronchopleural fistulas: an overview of the problem with special focus on endoscopic management. Chest. 2005;128(6):3955–65.
13. Sarkar P, Chandak T, Shah R, Talwar A. Diagnosis and management bronchopleural

fistula. Indian J Chest Dis Allied Sci. 2010;52(2):97.
14. Dal Agnol G, Vieira A, Oliveira R, Figueroa PAU. Surgical approaches for bronchopleural fistula. Open Thoracic Surgery. 2017;84.
15. Sakata KK, Nasim F, Schiavo DN, Nelson DR, Kern RM, Mullon JJ. Methylene blue for bronchopleural fistula localization. J Bronchology Interv Pulmonol. 2018;25(1):63–6.
16. El-Sameed YA. Role of Bronchoscopy in Management of Bronchopleural Fistula. In: Interventional Bronchoscopy. Springer; 2013. p. 211–25.
17. Cerfolio RJ, Minnich DJ, Bryant AS. The removal of chest tubes despite an air leak or a pneumothorax. Ann Thorac Surg. 2009;87(6):1690–6.
18. Gogakos A, Barbetakis N, Lazaridis G, Papaiwannou A, Karavergou A, Lampaki S, et al. Heimlich valve and pneumothorax. Ann Transl Med. 2015;3(4).
19. Kurman JS. Persistent air leak management in critically ill patients. J Thorac Dis. 2021;13(8):5223.
20. Hugen N, Hekma EJ, Claessens NJM, Smit HJM, Reijnen MMPJ. Efficacy of an autologous blood patch for prolonged air leak: a systematic review. Ann Thorac Surg. 2022;114(3):1064–71.
21. How CH, Hsu HH, Chen JS. Chemical pleurodesis for spontaneous pneumothorax. Journal of the Formosan Medical Association. 2013;112(12):749–55.
22. Liberman M, Muzikansky A, Wright CD, Wain JC, Donahue DM, Allan JS, et al. Incidence and risk factors of persistent air leak after major pulmonary resection and use of chemical pleurodesis. Ann Thorac Surg. 2010;89(3):891–8.
23. Clark JM, Cooke DT, Brown LM. Management of complications after lung resection: prolonged air leak and bronchopleural fistula. Thorac Surg Clin. 2020;30(3):347–58.
24. Eberhardt R, Gompelmann D, Herth FJF, Schuhmann M. Endoscopic bronchial valve treatment: patient selection and special considerations. Int J Chron Obstruct Pulmon Dis. 2015;10:2147.