Postoperative bronchopleural fistula repair: Surgical outcomes and adverse factors for its success

Young Ho Yang1 | Seong Yong Park1,2 | Ha Eun Kim1 | Byung Jo Park1 | Chang Young Lee1 | Jin Gu Lee1 | Dae Joon Kim1 | Hyo Chae Paik1

INTRODUCTION

A bronchopleural fistula (BPF) is a communication between the main stem, lobar, or segmental bronchus and the pleural space1 and is one of the fatal complications after pulmonary resection. The estimated prevalence rate was reported to be 1%–4%, with a 16%–72% mortality rate.2–4 There are certain patient characteristics and surgical techniques that can increase the incidence of BPF; these include neoadjuvant therapy, destroyed or infected lung tissue from inflammatory disease, an immunocompromised host, insulin-dependent diabetes, pneumoniaeomy (specifically rightsided pneumonectomy), a long bronchial stump, devascularization of the bronchial stump, residual cancer at the bronchial margin, prolonged ventilation, or reintubation after resection, and surgical inexperience.5–8

There are many studies regarding the risk factors for an occurrence of BPF, but few studies have focused on the factors related to the failure of surgical BPF repair. Although there have been developments in the surgical techniques and perioperative patient management, the treatment for postoperative BPF is still technically challenging for the thoracic surgeon. Various methods and techniques can be used for a BPF repair, such as primary suture, additional pulmonary resection, and reinforcement using muscle, pericardial fat, or omental flap.
However, no large study or randomized trials have been conducted to date, and as a result, there is a lack of evidence regarding the optimal treatment strategies. Therefore, the purpose of this study was to investigate the results of postoperative BPF repairs and to identify the adverse risk factors for a successful BPF repair.

**METHODS**

**Ethical statement**

This study was approved by the Severance Hospital Institutional Review Board (4–2021–1048; September 19, 2021). Informed consent was not required for this retrospective study.

**Patients**

A total of 39 patients that had a BPF after pulmonary resection or lung transplantation were surgically treated between January 2010 and June 2020 at the Department of Thoracic Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea. Their age, sex, comorbidities, indication of primary surgery, site of the BPF, requirements of mechanical ventilation (MV) at the time of the BPF repair, methods of the BPF repair, use and type of flap, failure of the BPF repair, and mortality were investigated retrospectively using medical records. A chronic steroid user was defined as a patient who had an oral prednisolone prescription of >5 mg and duration of treatment >1 month, which was based on the National Institute for Health and Care Excellence guidance for patients at risk of systemic side effects.9

**Surgical indications and treatment**

A BPF was defined as any communication between the bronchial tree and the pleural cavity that was confirmed either clinically, by bronchoscopy or high-resolution computed tomography. Surgery was indicated when the size of the BPF was >8 mm,10 or when a BPF was not improved with pleural drainage and conservative care. The surgical repair was performed through a posterolateral thoracotomy. The technique of surgical repair was either a primary suture closure of the bronchial stump or an additional pulmonary resection. When performing a primary repair or bronchoplasty, the necrotic tissue around the BPF was removed and the surrounding fresh tissue was manually repaired with polydioxanone 3–0 suture (Ethicon) using simple interrupted stitches. When an additional pulmonary resection was performed, more proximal part than the BPF location was additionally resected with mechanical stapler (Covidien Endo GIA Ultra Universal staplers, Medtronic). Afterwards, the air leakage test was performed. After confirming that the BPF restoration site was intact, the stump site was reinforced with a vascularized pedicle flap (e.g., omental or muscle flap) as needed.

**Definition of success**

The success of BPF repair was defined as discharge of the patient without a drain with visual occlusion of BPF associated with the absence of an air leak, recurrence of BPF and thoracic cavity infection. Failure included death within 3 months postoperatively, the need for a surgical procedure, or the development of a chronic fistula. In-hospital mortality was defined as death during hospitalization after surgery, and overall mortality was defined to include in-hospital mortality, mortality after readmission and death at other hospitals.

### TABLE 1  Patient baseline characteristics

| Variables | Total N = 39 |
|-----------|-------------|
| **Age**   | 60.2 ± 10.8 |
| **Male**  | 33 (84.6%)  |
| **Comorbidity** |                 |
| Diabetes mellitus | 13 (33.3%) |
| Connective tissue disease | 5 (12.8%) |
| Chronic steroid user | 10 (25.6%) |
| **Mechanical ventilation at the time of primary surgery** | 6 (15.4%) |
| **Indication of primary surgery** |                 |
| Pulmonary resection | 25 (64.1%) |
| Lung cancer | 13 (33.3%) |
| Benign lung disease | 12 (48%) |
| Lung transplantation | 14 (35.9%) |
| Idiopathic pulmonary fibrosis | 10 (71.4%) |
| Bronchiectasis | 1 (7.1%) |
| Connective tissue disease related ILD | 3 (21.4%) |
| **Site of BPF** |                 |
| Bronchial anastomosis | 11 (28.2%) |
| Bronchial stump | 26 (66.7%) |
| Peripheral BPF | 2 (5.1%) |
| Mechanical ventilation at the time of BPF repair | 13 (33.3%) |
| **Method of BPF repair** |                 |
| Primary repair | 27 (69.2%) |
| Additional resection | 12 (30.8%) |
| Completion pneumonectomy | 8 (66.7%) |
| Lobectomy or bilobectomy | 2 (16.7%) |
| Wedge resection | 1 (8.3%) |
| Bronchoplasty | 1 (8.3%) |
| Failure of BPF repair | 16 (41.0%) |
| In-hospital mortality | 12 (30.8%) |

Abbreviations: BPF, bronchopleural fistula; ILD, interstitial lung disease.
Statistical analysis

Continuous variables are expressed as the mean ± standard deviation or median (interquartile range, IQR), and categorical data were expressed as frequencies and percentages. The Chi-square or Fisher’s exact tests were used to compare the categorical variables between the two groups. A stepwise multivariable logistic regression model was used for statistically significant variables (p < 0.2) in the univariate model. Multivariable analysis was performed using a logistic regression model to evaluate the effects of multiple variables on BPF repair. A p-value < 0.05 indicated statistical significance. Statistical analyses were performed using the SPSS version 25.0 (SPSS Inc.) software.

RESULTS

Patient baseline characteristics

The mean age of patients was 60.2 ± 10.8 years and there were 22 male patients (84.6%; Table 1). During the study period, 63 (0.7%) of the 8,635 patients who underwent pulmonary resection surgery developed BPF. The BPF was developed in 16 (4.9%) of the 324 lung transplant patients. Among them, 25 patients (4 pneumonectomies, 18 lobectomies, and 3 sublobar resections) in pulmonary resection surgery and 14 patients (1 single lung, 9 bilateral lungs, and 4 bilateral lungs with lobectomy of the donor lung) in lung transplantation received surgical treatment for BPF. A pectoralis major and 3 latissimus dorsi; Table 2). There was only one abdominal complication of a diaphragmatic hernia related to the omental harvest. The in-hospital mortality rate was 30.8% (12/39), and the overall mortality rate was 56.4% (22/39). Eleven patients died due to septic shock, six of pneumonia, two of chronic respiratory failure, one of lung cancer, and two of unknown causes. The overall success rate of BPF repair was 59% (23/39). The patients that required MV at the time of BPF repair had a significantly lower success rate when compared to those without (15.4%, 2/13 vs. 80.8%, 21/26, respectively; p < 0.001; Table 3).

Risk factors for surgical BPF repair

In the univariate analysis, chronic steroid use (hazard ratio [HR], 5.19; 95% confidence interval [CI]: 1.16–28.7; p = 0.039), MV at the time of BPF repair (HR, 23.1; 95% CI: 4.5–185.6; p < 0.001), and additional resection at the time of BPF repair (HR, 0.36; 95% CI: 0.07–1.51; p = 0.183) were independent prognostic factors. Furthermore, in the multivariable analysis, MV at the time of BPF repair (HR, 16.65; 95% CI: 3.02–140.43; p = 0.003) remained independent prognostic factors (Table 4).
A BPF may develop at any point of time during the course of illness. Intermittent mandatory ventilation modes with low tidal volumes, PEEP, respiratory rates, and shorter inspiratory times are appropriate. The patients who were on MV at the time of BPF repair were more likely to require a ventilator after surgery. On this basis, continuous positive pressure ventilation, with high airway pressure being applied to the BPF repair site, was thought to interfere with and impede the healing of the BPF repair site. Therefore, the possibility of weaning the patient off MV after surgery should be determined and considered when the timing of the surgery is planned. In patients who require continued ventilatory care postoperatively for hypoxia or hemodynamical instability, it would be preferable to delay surgery until extubation is possible. In the event that ventilator weaning is not possible after BPF surgery, it is suggested to reduce the mean airway pressure, positive end expiratory pressure (PEEP) to reduce the peak airway pressure, tidal volume to reduce the peak inspiratory pressure, and the proportion of minute ventilation provided by the ventilator. Intermittent mandatory ventilation modes with low tidal volumes, PEEP, respiratory rates, and shorter inspiratory times are appropriate.

In a BPF repair, vascularized tissue is often used to buttress the stump. Satisfactory results have been reported with the use of omental, muscular,19–21 pericardial,22,23 and diaphragmatic24 flaps for BPF repair. We prefer to use an omental flap to reinforce the stump site after a postoperative BPF repair. The omental flap has several advantages. First, because the omentum is large and atypical, it is suitable for filling irregular spaces and attaching to stumps. However, a disadvantage is that an additional incision is required. The omental flap group demonstrated a greater trend toward the success of BPF repair than the muscle flap group in the patients without MV at the time of repair (p = 0.07). Despite the theoretical advantages of the omental flap, there was no statistically significant difference in our study. This is thought to be because the small number of patients in the muscle flap group, and that the ventilator factor had a great influence. Therefore, additional studies are needed regarding the appropriate flap for BPF repair.

### DISCUSSION

BPF is one of the most serious complications after pulmonary resection that has been reported to occur in approximately 0.4%–1.5% after lobectomy and 1.5%–15% after pneumonectomy. A BPF may develop at any point of time during the course of illness. Although the incidence of BPF has decreased with the development of surgical techniques and perioperative management, patients with BPF have a relatively high mortality rate that remains a challenge for thoracic surgeons. Surgical treatment is indicated for both early (within 2 weeks) and late (after 2 weeks) postoperative patients under the care of thoracic surgeons. Several endoscopic procedures that have been proposed to close a BPF, including the application of glues, sclerosant agents, plugs placement and endoscopic prosthesis (Amplatzer devices, Dumon silicone stent, and self-expandable metallic stents). However, in the case of large BPF (>8 mm), the surgical method is strongly recommended.

Several studies have suggested risk factors for developing a postoperative BPF. However, little is known about the related adverse factors of a successful BPF repair. In our study, multivariable analysis showed that MV at the time of BPF repair had a negative effect on the success of the BPF repair. Furthermore, there was no statistical significance reached for the presence of diabetes mellitus and chronic steroid use, the type of primary surgery, additional resection required at the time of BPF repair, bronchial stump reinforcement with flap, and time between surgery and diagnosis of BPF.

### TABLE 4 Univariate and multivariate analysis for surgical BPF repair

| Variables                           | Univariate | Multivariate |
|-------------------------------------|------------|--------------|
|                                     | OR (95% CI) | p-value      | OR (95% CI) | p-value      |
| Age                                 | 1.04 (0.98–1.12) | 0.215        | 3.20 (0.46–24.01) | 0.233        |
| Sex                                 | 1.47 (0.25–11.72) | 0.678        |              |              |
| Diabetes mellitus                   | 0.52 (0.12–2.04) | 0.360        |              |              |
| Chronic steroid use                 | 5.19 (1.16–28.7) | 0.039        | 16.65 (3.02–140.43) | 0.003        |
| Lung transplantation (vs. lung resection) | 1.12 (0.29–4.27) | 0.862        |              |              |
| MV at the time of BPF repair        | 23.10 (4.5–185.6) | <0.001      |              |              |
| Additional resection at the time of BPF repair | 0.36 (0.07–1.51) | 0.183        | 0.53 (0.06–3.68) | 0.530        |
| Reinforcement with flap             | 1.05 (0.15–8.77) | 0.960        |              |              |
| Time to surgery from diagnosis of BPF | 1.00 (0.99–1.01) | 0.741        |              |              |

Abbreviations: BPF, bronchopleural fistula; CI, confidence interval; MV, mechanical ventilation; OR, odds ratio.
This study had some limitations. First, this was a retrospective, single-center study with a relatively small sample due to the low incidence of postoperative BPF with only some of them treated surgically. Second, the type of BPF repair was performed mainly on the surgeon’s preference. Nevertheless, our study is considered meaningful as it offers novel suggestive factors related to the success of BPF repair in the current situation where little is known about the risk factors related to prognosis after surgical treatment of postoperative BPF.

There was a high overall mortality after BPF repair and a low success rate of BPF repair. The use of mechanical ventilation at the time of BPF repair was significantly related to the failure of BPF repair, whereas etiology, chronic steroid usage, and additional pulmonary resection were not related. The omental flap group demonstrated a greater trend toward a successful BPF repair when compared to the muscle flap group.

CONFLICT OF INTEREST
The authors declare no conflicts of interest for this article.

ORCID
Young Ho Yang https://orcid.org/0000-0002-0977-0525
Seong Yong Park https://orcid.org/0000-0002-5180-3853
Ha Eun Kim https://orcid.org/0000-0001-9240-2215
Chang Young Lee https://orcid.org/0000-0002-2404-9357
Jin Gu Lee https://orcid.org/0000-0003-2767-6505
Dae Joon Kim https://orcid.org/0000-0002-2182-010X
Hyo Chae Paik https://orcid.org/0000-0001-9309-8235

REFERENCES
1. Hammad WA. Results of surgical closure of bronchopleural fistula with vascularized tissues. J Egyptian Soc Cardio-Thoracic Surg. 2016; 24(2):200–6.
2. Bazzocchi R, Bini A, Grazia M, Petrella F. Bronchopleural fistula prevention after major pulmonary resection for primary lung cancer. Eur J Cardiothorac Surg. 2002;22(1):160.
3. Asamura H, Naruke T, Tsuchiya R, Goya T, Kondo H, Suesamuro K. Bronchopleural fistulas associated with lung cancer operations: univariate and multivariate analysis of risk factors, management, and outcome. J Thorac Cardiovasc Surg. 1992;104(5):1546–56.
4. Boudaya MS, Smadhi H, Zrini H, Mohamed J, Ammar J, Mestiri T, et al. Conservative management of postoperative bronchopleural fistulas. J Thorac Cardiovasc Surg. 2013;146(3):575–9.
5. Cerfölio RJ. The incidence, etiology, and prevention of postresectional bronchopleural fistula. Semin Thorac Cardiovasc Surg. 2001;13(1):3–7.
6. Sirbu H, Busch T, Aleksic I, Schreiner W, Oster O, Dalichau H. Bronchopleural fistula in the surgery of non-small cell lung cancer: incidence, risk factors, and management. Ann Thorac Cardiovasc Surg. 2001;7(6):330–6.
7. Sonobe M, Nakagawa M, Ichinose M, Ikegami N, Nagasawa M, Shindo T. Analysis of risk factors in bronchopleural fistula after pulmonary resection for primary lung cancer. Eur J Cardiothorac Surg. 2000;18(5):519–23.
8. Sfyridis PG, Kapetanakis EI, Baltayianis NE, Bolanos NV, Anagnostopoulos DS, Markogiannakis A, et al. Bronchial stump butressing with an intercostal muscle flap in diabetic patients. Ann Thorac Surg. 2007;83(3):967–71.
9. Mundell L, Lindemann R, Douglas J. Monitoring long-term oral corticosteroids. BMJ Open Quality. 2017;6(2):e000209.
10. Lois M, Noppen M. Bronchopleural fistulas: an overview of the problem with special focus on endoscopic management. Chest. 2005; 128(6):3955–65.
11. Deschamps C, Bernard A, Nichols FC III, Allen MS, Miller DL, Trastek VF, et al. Empyema and bronchopleural fistula after pneumonectomy: factors affecting incidence. Ann Thorac Surg. 2001;72(1):243–8.
12. Chawla RK, Madan A, Bhardwaj P, Chawla K. Bronchoscopic management of bronchopleural fistula with intrabronchial instillation of glue (N-butyl cyanoacrylate). Lung India. 2012;29(1):11.
13. Scappaticci E, Ardissone F, Ruffini E, Baldi S, Mancuso M. Postoperative bronchopleural fistula: endoscopic closure in 12 patients. Ann Thorac Surg. 1994;57(1):119–22.
14. Dal Agnol G, Vieira A, Oliveira R, Figuereoa PAU. Surgical approaches for bronchopleural fistula. Open J Thorac. 2017;8:94–5.
15. Bribriesco A, Patterson GA. Management of postpneumonectomy bronchopleural fistula: from thoracoplasty to transsternal closure. Thorac Surg Clin. 2018;28(3):332–35.
16. Greason KL, Miller DL, Clay RP, Deschamps C, Johnson CH, Allen MS, et al. Management of the irradiated bronchus after lobectomy for lung cancer. Ann Thorac Surg. 2003;76(1):180–5.
17. Grotberg JC, Hzyr RC, De Cardenas J. Bronchopleural fistula in the mechanically ventilated patient: a concise review. Crit Care Med. 2021;49(2):292–301.
18. Salik I, Vashisht R, Fau-Abramowicz AE, Abramowicz AE. Bronchopleural Fistula. [Updated 2021 May 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534765/
19. Arnold PG, Paierlo PC. Intrahepatic muscle flaps. An account of their use in the management of 100 consecutive patients. Ann Surg. 1990;211(6):656.
20. Stamatis G, Freitag L, Wencker M, Greschuchna D. Omentotomy and muscle transposition: two alternative methods in the treatment of pleural empyema and mediastinitis. Thorac Cardiovasc Surg. 1994; 42(04):225–32.
21. D’Andrea EA, Venuta F, De Giacomo T, Ricci C. Intercostal pedicle flap in tracheobronchial surgery. Ann Thorac Surg. 1999;68(2):630–1.
22. Taghavi S, Marta GM, Lang G, Seebacher G, Winkler G, Schmid K, et al. Bronchial stump coverage with a pedicled pericardial flap: an effective method for prevention of postpneumonectomy bronchopleural fistula. Ann Thorac Surg. 2005;79(1):284–8.
23. Klepetko W, Taghavi S, Pereszlenyi A, Birsan T, Groetzen J, Kupilik N, et al. Impact of different coverage techniques on incidence of postpneumonectomy stump fistula. Eur J Cardiothorac Surg. 1999; 15(6):758–63.
24. Mineo TC, Ambrogli V. Early closure of the postpneumonectomy bronchopleural fistula by pedicled diaphragmatic flaps. Ann Thorac Surg. 1995;60(3):714–5.
25. Goldsmith HS, Griffith AL, Kupferman A. Catsimponas N. Lipid angiogenic factor from omentum. JAMA. 1984;252(15):2034–6.
26. Kanamori T, Watanabe G, Yasuda T, Nagamine H, Kamiya H, Koshiba Y. Hybrid surgical angiogenesis: omentotomy can enhance myocardial angiogenesis induced by cell therapy. Ann Thorac Surg. 2006;81(1):160–7.
27. Litbarg NO, Gudehitthu KP, Sethupathi P, Arruda JA, Dunea G, Singh AK. Activated omentum becomes rich in factors that promote healing and tissue regeneration. Cell Tissue Res. 2007;328(3):487–97.
28. Morgan E, Lima O, Goldberg M, Ferdman A, Luk S, Cooper J. Successful revascularization of totally ischemic bronchial autografts with omental pedicle flaps in dogs. J Thorac Cardiovasc Surg. 1982;84(2):204–10.
29. Puskas JD, Mathisen DJ, Grillo HC, Wain JC, Wright CD, Moncure AC. Treatment strategies for bronchopleural fistula. J Thorac Cardiovasc Surg. 1995;109(5):989–96.