Review Article

Post-resectional bronchopleural fistula: aetiology, clinical management and future perspectives: a narrative review

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Background and Objective: The aim of this review is to focus on post-resectional broncho-pleural fistula pathophysiology, clinical management, surgical approach and future perspectives of treatment. Bronchopleural fistula (BPF) is a pathological communication between the airways and the pleural cavity that may occur after pulmonary resection and chest traumas or following complications of thoracic infections or disruption of lung parenchyma bullae. The final scenario of defective bronchial suture healing after major pulmonary resection may result in a life-threatening ventilatory and infective disaster.

Methods: This is an unsystematic narrative review of previously published information about post-operative BPF. The research was done by accessing the following databases: MEDLINE; Cochrane database of systematic reviews. Delimiting search terms were: broncho-pleural fistula; lung resection; lung cancer; operative bronchoscopy; open window thoracostomy; stem cell technology. Inclusion criteria were: papers written in English about post-resectional broncho-pleural fistula from the above-mentioned databases [2000–2023].

Key Content and Findings: this review will focus on post-resectional broncho-pleural fistula pathophysiology, clinical management, surgical approach and future perspectives of treatment.

Conclusions: Although quite rare, BPF represents a life-threatening condition with a significant mortality rate; it thus still represents one of the most feared complications by thoracic surgeons. Significant independent risk factors for postoperative BPF development were right side, low preoperative albumin values, the use of EndoGIA stapler and bronchial stump diameter. In the case of BPF not amenable to minimally invasive endoscopic repair, open window thoracostomy (OWT) remains the most effective therapeutic approach. Minimally invasive endoscopic approach—in particular with stem cell local bronchoscopic application—represents a valuable and promising therapeutic option for small calibre BPF.

Keywords: Broncho-pleural fistula; lung resection; lung cancer; operative bronchoscopy; open window thoracostomy (OWT)

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Introduction

Background

Bronchopleural fistula (BPF) is a pathological communication between the airways and the pleural cavity that may occur after pulmonary resection and chest traumas or following complications of thoracic infections or disruption of lung parenchyma bullae (1).

The incidence of post-resectional BPF in thoracic surgery is reported to range from 1% to 4%, while the mortality rate extends from 12.5% to 71.2%. It may be due to deficient bronchial closure, obstacles to bronchial stump healing or stump colonisation by residual tumour cells (2). The final scenario of defective bronchial suture healing after major pulmonary resection may result in a life-threatening ventilatory and infective disaster (3). Bronchial suture dehiscence still represents one of the most dangerous postoperative complications in thoracic surgery (4) and—although many technical safety measures are routinely taken by surgeons while managing bronchial stump during anatomical lung resections—BPF remains a major issue to be prevented and to be solved whenever it occurs (5).

Since the origins of modern thoracic surgery, many salvage surgical procedures have been proposed as rescue treatments for BPF, ranging from muscle flap coverage, completion pneumonectomy and several types of thoracoplasty (1). Open pleural drainage represents the best therapeutic strategy to control the infection caused by BPF. First advocated by Robinson for treating chronic pleural empyema and then by Eloesser as an option for treating tuberculous empyema, this strategy was then modified by Clagett and Geraci as a two-step staged procedure for post-pneumonectomy empyema and then described by Alexander as extrapleural subperiosteal thoracoplasty (6). Although effective in many challenging cases, these operations represent the most mutilating, aggressive and psychologically disabling procedures a patient can experience. With the advent of the antibiotic era—dramatically modifying the approach to pleural infections—and later on flexible and video-bronchoscopy, many endoscopic strategies have been advocated as less invasive alternative treatments of BPF, among which bronchial stenting and local products injections have been the most frequently reported (7,8). Nevertheless, only small diameter BPF have been successfully managed by an exclusive endoscopic approach and the reported overall failure percentage is not negligible (9).

Recent progress of cell therapy and bioengineering procedures for pulmonary diseases has advanced rapidly in the last decade (10). Several reports disclosed that stem cells can locally interact with the microenvironment and can produce reparative effects on damaged bronchial tissue (11-13).

Nevertheless, although cellular therapy represents a promising management option for postoperative bronchial fistula healing, before it can be routinely applied as a standard clinical treatment, further investigations are required and standard surgical and conservative options still represent the gold standard approach.

Objectives

The aim of this unsystematic narrative review is to focus on post-resectional broncho-pleural fistula pathophysiology, clinical management, surgical approach and future perspectives of treatment. We present this article in accordance with the Narrative Review reporting checklist (available at https://shc.amegroups.com/article/view/10.21037/shc-23-9/rc).

Methods

This is an unsystematic narrative review of previously published information about post-resectional broncho-pleural fistula pathophysiology, clinical management, surgical approach and future perspectives of treatment.

Sources of information

Research was done by accessing the following databases: MEDLINE; Cochrane database of systematic reviews.

Delimiting search terms

Delimiting search terms were: broncho-pleural fistula; lung resection; lung cancer; operative bronchoscopy; open window thoracostomy; stem cell technology.

Selection criteria employed

Inclusion criteria were: papers written in English about post-resectional broncho-pleural fistula from the above-mentioned databases [2000–2023] (*Table 1*).

Discussion

Lung cancer is the second most commonly diagnosed

Table 1 The search strategy summary

Items	Specification
Date of search	Last update: February 16th 2023
Databases and other sources searched	MEDLINE; Cochrane database of systematic reviews
Search terms used	Broncho-pleural fistula; lung resection; lung cancer; operative bronchoscopy; open window thoracostomy; stem cell technology
Timeframe	2000–2023
Inclusion criteria	Papers written in English about surgical treatment of malignant pleural mesothelioma
Selection process	Two senior researchers, independently

malignant tumour and the first cause of neoplastic death worldwide (14). Surgical resection represents the best therapeutic option for early- stage fit patients or in low-grade tumours (15,16); it may effectively contribute to local control disease in locally advanced stages within a multidisciplinary approach (17).

Moreover, it can be considered as a further option in very selected oligometastatic patients (18). With the advent of minimally invasive approaches (robot-assisted and video-assisted procedures), thoracic surgeons can be more frequently involved in diagnostic procedures of undiagnosed solitary or multiple pulmonary nodules (19), although bronchoscopic procedures or transthoracic computed tomography (CT) guided biopsy still remains the best diagnostic options (20,21).

Pathophysiology

Major anatomic lung resection—and in particular pneumonectomy, which is the resection of the whole lung—might be complicated by post-resectional BPF development: this condition is a pathological connection between the airways and the pleural cavity which usually leads to pleural empyema due to the contamination of the sterile pleural cavity by airway resident bacteria. Although quite rare, BPF represents a life-threatening condition with a significant mortality rate; it thus still represents one of the most feared complications by thoracic surgeons (13). BPF may also occur in non-surgical scenarios, like end-stage neoplastic disease, advanced infectious diseases like tuberculosis and following major thoracic traumas.

Mazzella *et al.* retrospectively reviewed the clinical data of 733 patients undergoing pneumonectomy for lung cancer from 1999 to 2014 focusing on pre-, intra- and postoperative data: they observed 60 cases of BPF (8.2%). Significant independent risk factors for postoperative BPF development were right side, low preoperative albumin values and the use of EndoGIA stapler for suturing the bronchial stump (1). Early BPF (occurring within 14 days after the operation) was more frequently treated by thoracotomic (12 cases) than thoracoscopic (2 cases) approach for debriding necrotic tissues and repairing the bronchial stump. Late BPF (occurring later than 14 days after the operation) was managed by endoscopic delivery of fibrin glue (3 cases), endobronchial stenting (1 case) or chest drainage and pleural cavity washing by povidone-iodine solutions (15 cases). Open window thoracostomy (OWT)—which consists of an opening into the chest wall by rib resection, allowing continual drainage, washing and dressing of the cavity to optimize wound granulation and closure over time—was performed in 27 cases (1).

Fuso *et al.* retrospectively reviewed the clinical data of 835 patients undergoing anatomical pulmonary resections in a 10-year period [786 lobectomies (94.1%) and 49 pneumonectomies (5.9%)]. They reported eighteen patients (2.2%) who developed a postoperative BPF: 11 in the lobectomy group (1.4%) and 7 in the pneumonectomy group (14.3%). In four cases they observed BPF occurring after bilobectomy, representing the highest incidence of this complication within the non-pneumonectomy cohort (36%). Among the 18 patients who developed fistula, two died (11.1%) (22).

Hollaus *et al.* retrospectively reviewed the clinical data of 209 patients receiving pneumonectomy in a 5-year period; among them, 15 patients developed BPF (7.2%). The authors performed a multivariate analysis including central tumour distance, diameter of the resection margin, gender, age, side, stage and tumour localisation (peripheral *vs.* central). Only the bronchial stump diameter remained a significant predictor for fistula development (23).

Skrzypczak *et al.* reported their institutional experience on 472 patients receiving pneumonectomies between 2006 and 2017; they observed 34 cases of BPF (7.47%), more prevalent after right pneumonectomies than after left ones (10.98% *vs.* 5.32% P=0.026) with a 90-day mortality rate of 35.3%. They did not observe any difference in BPF development among bronchial stump coverage with the parietal pleura, intercostal muscle flap and pericardial fat pad and only the right side was significantly associated with higher BPF development (24).

Surgical approach

In the case of major BPF, with almost complete bronchial stump destruction and anyway not amenable to minimally invasive endoscopic repair, OWT remains the most effective therapeutic approach (1). It consists of an opening of the chest wall by segmental resection of the lateral arch of several consecutive ribs (usually 2 or 3 ribs are resected) to achieve complete drainage of the purulent collection, thus allowing bronchial stump fistula closure by natural spontaneous healing. With regard to OWT timing, major bronchial disruption would require a timely procedure, before severe infections might develop; on the contrary, in case of small caliber fistula, potentially amenable of endoscopic approach, OWT should be considered only after minimally invasive approach failure.

Mazzella *et al.* reported their experience on OWT for postpneumonectomy BPF: they performed 27 OWT, 20 (74.1%) on the right side. OWT was subsequently closed by muscle flap in 7 patients by using the latissimus dorsi in 2 cases, the pectoralis major in one case and both of them in 4 cases. They did not observe any muscle flap necrosis or other major complications and final OWT closure was obtained in all patients without any further procedure (1).

Endoscopic treatments

In the case of small calibre fistula, several minimally invasive endoscopic approaches have been proposed (25-27). Sakata *et al.* reported 5 cases of post-resectional BPF (2 after pneumonectomy, 3 after lobectomy) in which fistula plugs were positioned by flexible bronchoscopy: successful closure was obtained by fistula plug alone in 3 cases while the other two required an endobronchial valve and muscle flap (28).

Han *et al.* reported their experience in post-resectional BPF closure by customized airway stenting. They treated 148 patients presenting BPF occurring after pneumonectomy (104 patients) or lobectomy (44 patients): BPF closure was effective at the first attempt in 143 patients (96.6%) as confirmed by tracheobronchography showing complete fistula closure. After a 10-week follow-up, 38% of post-pneumonectomy patients versus 85% of post-lobectomy patients were defined as "cured", presenting a full obliteration of the pleural cavity allowing a safe chest tube removal (29).

Bottoni *et al.* described their "lipofilling" technique for closing post-resectional broncho pleural fistula by utilizing bronchoscopic instillation of autologous fat tissue containing a large amount of mesenchymal stem cells, which are well known for their reparative effect (30,31). They reported a series of 8 patients with post-resectional BPF (6 after pneumonectomy, one after lobectomy and one after bilobectomy). The success rate for treated patients was 100% with 3 patients treated by single session and 5 patients requiring an additional analogous procedure (30). Our personal preclinical experience with a large animal model showed the efficacy of mesenchymal stem cell in closing small calibre BPF (12) and it was subsequently further confirmed in a clinical setting of post-pneumonectomy BPF (13).

Conclusions

In conclusion, bronchial suture dehiscence still represents one of the most dangerous postoperative complications in thoracic surgery and—although much technical safety measures are routinely taken by surgeons while managing bronchial stump during anatomical lung resections—BPF remains a major issue to be prevented and to be solved whenever it occurs.

Significant independent risk factors for postoperative BPF development were the right side, low preoperative albumin values, the use of EndoGIA stapler and bronchial stump diameter; bronchial stump coverage with the parietal pleura, intercostal muscle flap and pericardial fat pad did not have any impact on BPF development.

In the case of major BPF, with almost complete bronchial stump destruction and anyway not amenable to minimally invasive endoscopic repair, OWT remains the most effective therapeutic approach. Minimally invasive endoscopic approach—in particular with stem cell local bronchoscopic application—represents a valuable and promising therapeutic option for small calibre BPF (32,33).

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Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://shc.amegroups.com/article/view/10.21037/shc-23-9/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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