

Diagnosis and Management Bronchopleural Fistula

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ABSTRACT

The diagnosis and management of bronchopleural fistula (BPF) remain a major therapeutic challenge for clinicians. It is associated with significant morbidity and mortality. Diagnosis and localisation of BPF is sometimes difficult and may require multiple imaging and bronchoscopies. Successful management of a fistula is combined with treatment of the associated empyema cavity. The first step, therefore, should be control of active infection and adequate drainage of the hemithorax. When deemed required, definitive surgical repair should be accomplished expeditiously, minimising the number of procedures performed. In cases of a small fistula or where the surgical risk is high, various bronchoscopic methods have been used to close the fistula. When treatment is protracted, secondary complications are more likely and survival is adversely affected. In this article, approaches to the diagnosis and treatment of BPF are discussed, with particular emphasis on bronchoscopic management options. [Indian J Chest Dis Allied Sci 2010;52:97-104]

Key words: Bronchopleural fistula, Fiberoptic bronchoscopy, Surgery, Diagnosis.

INTRODUCTION

Bronchopleural fistula (BPF) is a sinus tract between the bronchus and the pleural space that may result from a necrotising pneumonia/empyema (anaerobic, pyogenic, tuberculous, and fungal), lung neoplasms, blunt and penetrating lung injuries or may occur as a complication of procedures, such as lung biopsy, chest tube drainage, thoracocentesis or may complicate radiation therapy. More commonly, however, it arises as a complication of lung surgery: following failure of the bronchial stump to heal. This failure to heal may be from improper initial closure, inadequate blood supply, infection at the bronchial stump, or residual malignant tumour at the bronchial stump. The incidence of BPF varies from 4.5% to 20% after pneumonectomy and 0.5% after lobectomy.¹ A recent multivariate analysis² studying the risk factors for BPF in patients undergoing pulmonary resections for lung cancers identified right-sided resection, pneumonectomy (especially, right pneumonectomy), mediastinal lymph node resection, high dose pre-operative radiation therapy, and residual or recurrent carcinoma at the bronchial stump as technical factors predisposing to BPF. The increased risk of BPF associated with right pneumonectomy is attributable to the more extensive resection required in right pneumonectomy.³ Non-operative factors

included diabetes mellitus, hypoalbuminemia, cirrhosis and steroid administration. It has been suggested that post pneumonectomy ventilation for more than 24 hours is also a risk factor for the development of BPF.⁴ The BPF can cause significant morbidity, prolonged hospitalisation and even mortality. Mortality rates varies between 18 percent to 67 percent.⁵ The most common cause of death is aspiration pneumonia and subsequent acute respiratory distress syndrome or development of tension pneumothorax.^{1,6} The management of BPF is one of the most complex challenges encountered by the chest physicians.

CLINICAL PRESENTATION

Bronchopleural fistula typically manifests seven to fifteen days following a lung resection, though more delayed presentations have been reported. Among the several proposed classifications, Varoli *et al*⁷ classified fistulas according to the time of onset after the operation: early [1 to 7 days], intermediate [8 to 30 days], and late fistulas [more than 30 days]. These almost always occur within three months after surgery.^{5,8} Bronchopleural fistulas developing as a complication of pleuropulmonary infections may develop at any point of time during the course of illness.

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The symptoms and signs of cough and changes in the air-fluid pattern on chest radiograph are critical as warning signs of BPF. Other manifestations include fever with serosanguinous or purulent sputum. Acute respiratory distress may occur if a large fistula results in aspiration to the contralateral lung or if a tension pneumothorax develops. Many cases are associated with empyema. The diagnosis must be suspected when there is a persistent post-operative air-leak (immediate post-operative period) or when there is a new or increasing air-fluid level or disappearance of pleural fluid on chest radiographs (if patient has no chest tube in place). With a delayed BPF, a new air fluid level appears in a previously opacified haemithorax.

DIAGNOSIS

The diagnosis of BPF is often obvious from the clinical presentation, particularly in the presence of a chest tube. Plain radiographs may reveal features suggestive of a BPF. Radiological features that are suggestive of the presence or the development of a BPF include: (1) steady increase in intrapleural air space, (2) appearance of a new air fluid level, (3) changes in an already present air fluid level, (4) development of tension pneumothorax, and (5) a drop in the air fluid level exceeding 2cm (if patient has no chest tube in place).⁹⁻¹¹ In computed tomography, apart from demonstration of a pneumothorax, pneumomediastinum and underlying lung pathology (Figure 1), the demonstration of actual fistulous communication may be possible in a subset of patients.^{12,13} Using standard and thin section non-contrast scans, Westcott and Volpe¹³ could demonstrate the fistula in 10 out of their 20 patients. In most of these cases, the

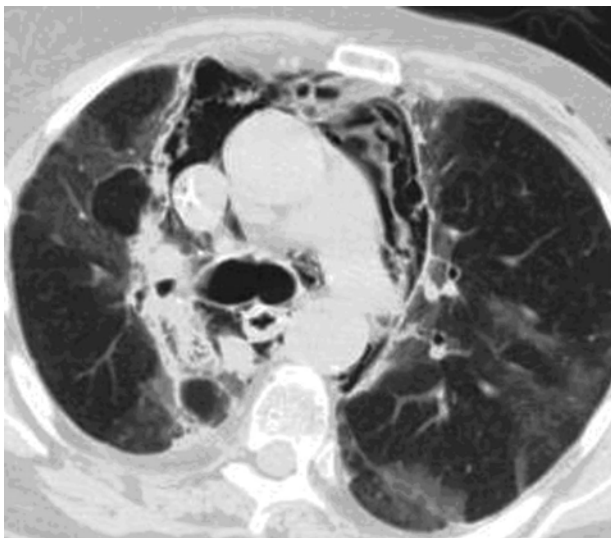


Figure 1. CT chest showing air in medial pleural space as well as pneumomediastinum in a patient with bronchomediastinal fistula.

fistulous tract was located peripherally and in only one case the air-leak was in the setting of a lung resection. Three-dimensional reconstruction from the volume acquisition using the spiral technique has also been used successfully to demonstrate BPF in its entirety.¹⁴ Evidently these radiological modalities are and will remain important supplements to bronchoscopy and bronchoscopic techniques for demonstrating and localising a BPF.

Fiberoptic bronchoscopy (FOB) and associated procedures have been used to localise/confirm BPF. The FOB and selective bronchography can be utilised to localise the site of the fistula.^{15,16} In some cases, direct visualisation of the fistula opening may be possible (Figure 2). The presence of BPF is also suggested by the return of continuous bubbles on bronchial wash (Figure 3). In patients where a BPF is not clearly visible on bronchoscopy, bronchography at the suspected site can be utilised to localise the site of the fistula.¹⁶ Selective instillation of methylene blue into segmental bronchi with its subsequent appearance in the chest drainage can also confirm

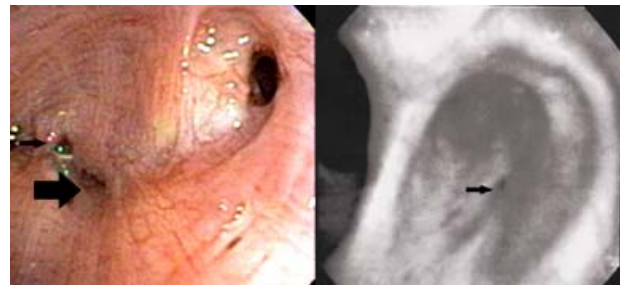


Figure 2. Bronchopleural fistula with the fistula opening being visible on fiberoptic bronchoscopy.

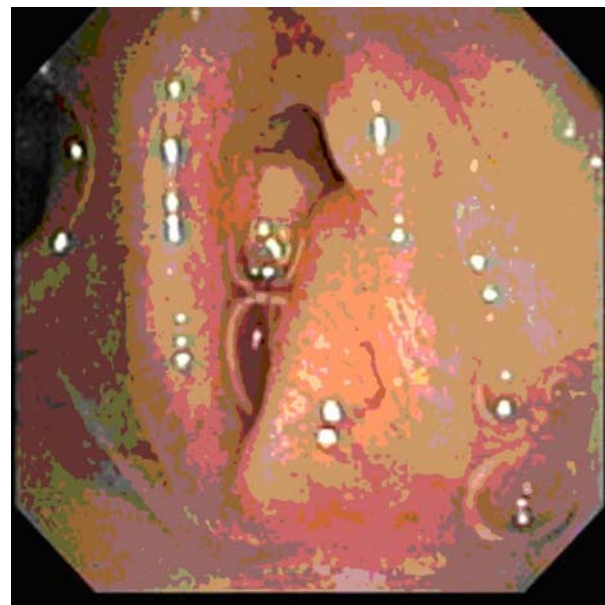


Figure 3. Healthy looking left upper lobe bronchial stump showing return of continuous bubbles on bronchial washing raising suspicion of BPF.

and localise a BPF (Figure 4). In cases where the site is not clear it can also be determined with a bronchoscope for placing a balloon-tipped catheter into the selected airways and inflate it. If the bronchus contributes to the fistula, balloon occlusion decreases or eliminates the air leak. Capnography can also be used to identify the bronchial segment related to BPF. The end tidal carbon dioxide is measured by connecting a capnograph to a polyethylene catheter

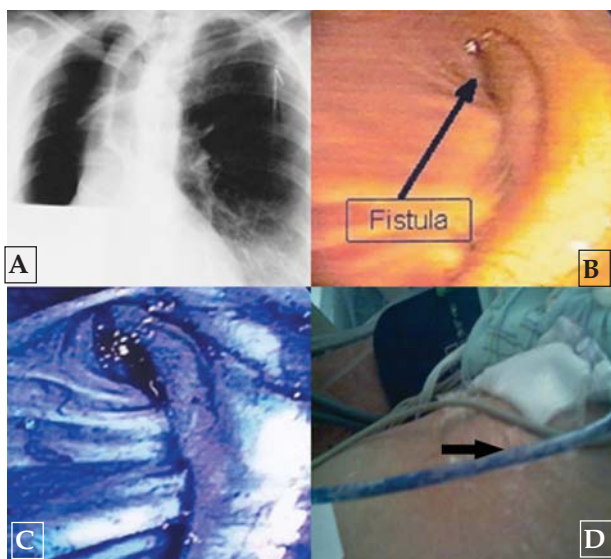


Figure 4. Post pneumonectomy bronchopleural fistula, (A) right hydro-pneumothorax, (B) FOB showed a possible fistulous opening at the right bronchial stump, (C) methylene Blue injected at the suspected site, (D) appearance of dye in the pleural drainage system confirmed the diagnosis.

passed through the bronchoscopic channel and placed systematically into different bronchi. The presence of a BPF is suggested by the absence of the capnographic tracing in a particular segment or subsegment by logic of its communication to the atmosphere from the chest tube which has been previously disconnected from under water drainage.

Other than bronchoscopy, several other techniques have been used to confirm the diagnosis of a BPF or to localise it. Several studies have reported the role of ventilation scintigraphy in this setting.^{17,18} Greyson and Rosenthal¹⁹ were the first to report scintigraphy with ^{99m}Tc-albumin colloid fog inhalation as a simple and accurate test for the detection of BPF. Many other case reports or case series have confirmed the value of ventilation scintigraphy using radioactive gases, like ⁸¹mKr or ¹³³Xe, or radioactive aerosols using ^{99m}Tc albumin, ^{99m}Tc-DTPA, and ^{99m}Tc sulfur colloid.^{17,20-22} In a prospective study, Raja *et al*²³ performed 20 scintigraphy studies in 11 lung cancer patients with suspected BPF after pulmonary resection. Using ¹³³Xe as the preferred agent and bronchoscopy as the gold standard technique for detection of BPF, these authors

reported a sensitivity of 83% and a specificity of 100% in the diagnosis of BPF. The limitations of ventilation scintigraphy include the possibility of false negative results because of: (a) small fistula that can temporarily collapse or get occluded by a mucus plug during the imaging or (b) slow diffusion of the tracer through a small fistula being missed during the brief scanning period. If aerosols are used, difficulty in interpretation of images may occur in ventilation studies because of deposition of tracer in the tracheobronchial tree, particularly in patients with chronic obstructive airway disease.^{23,24} Several authors have also tried to localise a BPF using radiolabelled aerosol inhalation with planar and single photon emission tomography (SPECT) imaging.^{20,24,25} However, these imaging modalities would require substantial time and patient's cooperation to breathe aerosol through a mouthpiece.²⁴ These studies have also been criticised on the ground that the aerosol tends to deposit in areas of turbulence, and therefore, may lead to false positive results and/or mis-localisation of fistula, particularly in patients with obstructive airways.²³ A further limitation of scintigraphic studies remains that the estimation of the size of BPF is only indirect from the kinetics of tracer gas during different phases of the study.²³ Therefore, though scintigraphy may be useful as a non-invasive technique for early detection of a suspected BPF and follow-up, it has no advantage in cases where bronchoscopic and surgical interventions are being considered because of adverse consequences of the fistula. Lillington *et al*²⁶ have used injection of small boluses of ¹³³Xenon into several segmental bronchi during bronchoscopy and looking for appearance of radioactivity in the chest tube drainage for localisation of BPF before bronchoscopic intervention. We do not see any advantage of this technique, as it will involve additional complexities in handling radioactive tracer materials in a bronchoscopy suite and a longer procedure time. While, any of the above-mentioned techniques can be useful alone or in combination with other techniques, none of them provides direct confirmation and visualisation of the fistula.

Recently, we have described computed tomography bronchography (CTB) as a new technique for diagnosing and demonstrating a difficult BPF.²⁷ We performed FOB and injected 20 to 30mL of a water-based nonionic low osmolar iodinated contrast medium iohexol (OMNIPAQUE™, GE healthcare) at the suspected fistula site either through a catheter or directly through the working channel of the bronchoscope. A CT was performed immediately with targeted reconstruction of images in different planes. Using standard axial and sagittal sections, we could demonstrate the fistulous communications clearly (Figure 5). We see several advantages of this new

technique compared to other bronchoscopic/non-bronchoscopic techniques: (1) it is fast, less cumbersome and highly accurate; (2) using volumetric data acquisition, the images can be reconstructed in different planes to provide a better visualisation of the anatomy of the fistulous tract; (3) relationship of the fistula tract with other mediastinal structures can be delineated with high confidence, thereby being a good technique for diagnosing complex bronchopleuromediastinal fistulas; (4) OMNIPAQUE™ has excellent safety record as a radiocontrast agent²⁸ without any known effect on pulmonary function. The disadvantage of the procedure remains the need to transport the patient for CT. Therefore, it may be difficult to perform on patients in intensive care requiring high levels of ventilatory support.

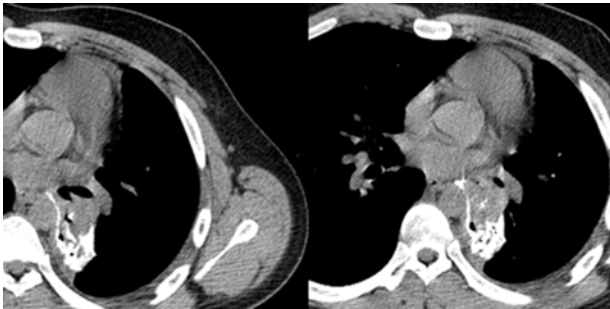


Figure 5. CT bronchography showing leakage of contrast from left lower lobe bronchus to medial pleural space.

Management

The first principle of therapy is to address any immediate, life-threatening conditions, such as endobronchial contamination, pulmonary flooding and tension pneumothorax. This is accomplished by placing the patient with the affected side dependent and performing adequate pleural drainage. In general, suture reclosure of the bronchial stump with vascularised flap coverage is curative for the fistula presenting acutely, usually fewer than two weeks after surgery.²⁹ Definitive repair accomplished expeditiously, minimise the number of procedures required in this setting.³⁰

Patients who present with a BPF developing late or those who develop the fistula as a complication of suppurative pleuropulmonary diseases are initially managed medically. Medical management should include dependent drainage and reduction of the pleural space, antibiotics, nutritional supplementation and adequate ventilator management if ventilated.⁶ The disease course is understandably more complicated for patients who are on ventilators with the BPF.³¹ It can present a significant therapeutic challenge, a challenge related to keeping airway pressures at or below the critical opening pressure of

the fistula in order to promote fistula healing, yet still providing adequate alveolar ventilation for sufficient gas exchange.³² Since air-leaks through bronchopleural fistulae may range from <1 to 16 L/min,³³ there are several potential adverse effects of BPF in mechanically ventilated patients including, incomplete lung expansion, loss of effective tidal volume or positive end-expiratory pressure, inability to remove carbon dioxide in addition to prolonged ventilatory support.^{6,34} The large air leak via BPF can also result in autotriggering of the ventilator that can lead to serious adverse effects, including severe hyperventilation and inappropriate escalation of sedatives and/or neuromuscular blockers (administered to reduce spontaneous breathing efforts).³⁵ Chest tube and ventilator management of BPF center around the principles of obtaining adequate pleural space decompression to allow for lung re-expansion and minimising the airflow through the fistulous tract in order to allow healing. Although this has never been subjected to a prospective study, a retrospective analysis of 39 cases supports the contention that patients with the smallest air-leak have the best prognosis.³¹ The volume of flow through a BPF is a function of the size of the air-leak [resistance] and the transpulmonary pressure gradient [airway pressure minus pleural pressure]. Increased chest tube suction proportionally increases transpulmonary pressure and thus increases the flow through a BPF.^{31,34,36} Many authors have advocated the use of the least possible chest tube suction (or a water seal alone) to reduce tidal volume loss through the fistula.^{34,37,38} In addition, the mean airway pressure should be reduced as much as possible [minimal or no PEEP, low peak airway pressures, reducing the proportion of minute ventilation provided by the ventilator (intermittent mandatory ventilation modes with low machine tidal volumes and respiratory rates), and shorter inspiratory times]. Various other techniques are described to decrease the air leak including independent lung ventilation (either with two ventilators or differential lung ventilation using a single ventilator and a variable-resistance valve attached to one lumen of a bifurcated endotracheal tube) and high frequency ventilation.^{30,39-42}

After one to three weeks, a surgical re-intervention can be attempted in suitable cases. Patients who present with a BPF at times more remote from resection are unlikely to have direct reclosure of their fistula. Surgical closure of the fistula is attempted by either an anterior, transpericardial approach thoracotomy with muscle flap to fill the pleural space, or muscle flap coverage of the fistula with a limited thoracoplasty to obliterate the pleural space.⁴³ A detailed discussion of surgical options and techniques is beyond the scope of this article. It is clear,

however, that these procedures are associated with high morbidity, mortality and cost. Many of these patients may be poor candidates for a second thoracic operation of this magnitude. If the patient's general condition is poor (as is often the case), bronchoscopic treatment appears an efficient and established alternative.¹ It is a viable first option in small bronchopleural fistulas⁴⁴ that are less than 5mm in diameter. Endoscopic closure of the BPF has low cost, ease, and reduced rate of trauma. The procedure is easy to learn and is performed on an out-patient basis with minimal cost and discomfort to the patient and can be performed in both stable and critically ill patients. The BPF can be closed endoscopically as long as one is sure that there is no evidence of active ongoing infection in the pleural cavity.

A plethora of bronchoscopic procedures have been reported in the literature for the management of a BPF. These include:

1. Bronchoscopic placement of glutaraldehyde-sterilised lead shot,⁴⁵ gel foam and tetracycline,⁴⁶ autologous blood patch,⁴⁵ tissucol (Immuno Co., Vienna, Austria), gelatin-resorcinol mixture, oxidised regenerated cellulose (Surgicel),⁴⁷ albumin-glutaraldehyde tissue adhesive [BioGlue],⁴⁸ cryoprecipitate fibrin glue,^{1,15,49-56} N-butyl-2-cyanoacrylate⁵¹ at the fistula site. There is no strong evidence in the literature to choose any one agent over another. Most of these products are commercially available, but the two-component cryoprecipitate fibrin glue deserves special mention. It can easily be assembled by the treating physician in any hospital. It is a dual component biological adhesive whose action mimics the final stage of clotting whereby fibrinogen (present in the form of cryoprecipitate), in the presence of factor XIII, thrombin, and calcium, polymerises to form a fibrin clot, which is gradually adsorbed by the fibrinolysis.⁵⁷ It is important to note that the two fibrin components should be applied directly to the fistulae site and allowed to mix at the desired location as the clot formation will begin to develop within seconds. The two component fibrin-cryoprecipitate glue is delivered at the fistula site through a double lumen catheter inserted via the operative channel of the bronchoscope; [calcium gluconate and cryoprecipitate along with topical thrombin (1000 IU /mL)] creating a fibrin clot that occludes the fistula. A total of 1.0 cc of the each of the solutions needs to be injected;
2. Use of bronchial blockade;⁵⁸⁻⁶¹ use of intrabronchial valves (some of them primarily designed for bronchoscopic lung volume reduction);⁶²⁻⁶⁴ endobronchial placement of vascular embolisation coils;⁶⁵ use of endovascular metallic ring-shaped coil in combination with a sealant;^{66,67}
3. Placement of stents;⁶⁸⁻⁷⁰ other reported methods

have been the use of a dumon stent placed in the bronchial stump to prevent air leak and closure of the bronchopleural fistula^{68,69} (Figure 6);

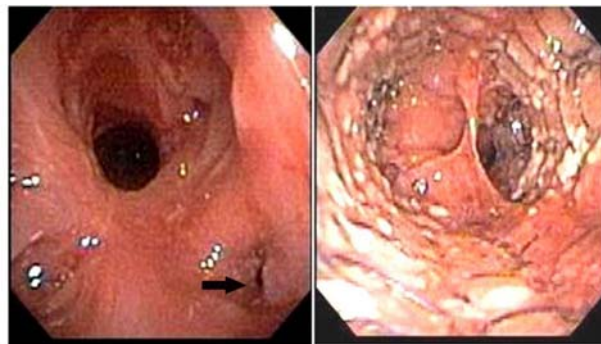


Figure 6. Bronchomediastinal fistula, before and after stent placement.

4. Bronchoscopic submucosal injection of absolute ethanol⁷¹ or polidocanol-hydroxypoliethoxydecane on the margins of the fistula using an endoscopic needle inserted through a flexible bronchoscope;^{7,72}
5. NdYAG laser has also been used to close small BPF but the technique has not been widely reported.^{15,53,73}

In performing many of these bronchoscopic procedures, use of a flexible bronchoscope is more advantageous, providing superior and precise access to a greater portion of the bronchial tree than the rigid bronchoscope.⁵³ All these agents act first as a plug mechanically sealing the leak and then later on induce an inflammatory process with mucosal proliferation and fibrosis, creating a permanent seal.¹⁶ It has also been shown that repair of fistula occurs by organisation of granulation tissue and granulomas caused by foreign bodies. Epithelialisation with typical respiratory epithelium has also been reported.⁷⁴ While there are no large-scale controlled trials to document the efficacy of the endobronchial procedures, the availability of multiple case reports and series suggest its efficacy in selected patients. Various endoscopic options are successful in 35% to 80% of cases^{8,75} and have been responsible for significantly reducing the morbidity and mortality from bronchopleural fistulae.^{15,51-53} A more recent analysis,⁷⁶ however, has shown success rates to be 30% and a mortality still around 40%, indicating the need for further refinement and improvement of these techniques.

While the above-mentioned techniques remain appropriate for closing the more proximal fistulae, i.e. communication between a main stem, lobar, or segmental bronchus and the pleural space, management of more peripheral fistulae, i.e. communication between the pulmonary parenchyma

distal to a segmental bronchus and the pleural space (sometimes called alveolopleural fistulae, APF) may require a different approach.⁷⁷ Options for surgical or bronchoscopic reclosure of such fistulae are limited. Careful management of chest tube drainage to minimise the air-leak and effective treatment of pleural infection may help some of these peripheral fistulae to heal. Some authors have reported successful use of adhesive glue in closure of post-traumatic peripheral BPF.⁷⁸ Placement of endobronchial valves⁶² or other kinds of endobronchial blockade to the corresponding segmental bronchi may also reduce the peripheral air leak allowing the APF to heal. Video-assisted thoracoscopic placement⁷⁹ as well as CT-guided percutaneous transthoracic application⁸⁰ of fibrin sealant have been used to seal pulmonary air leaks but the drawback of these techniques are the need of additional invasive procedure. Pleurodesis has also been successfully used to manage peripheral air leaks.^{81,82} In intractable cases, surgical decortication or repair remains an option. The management of BPF in summarised in figure 7.

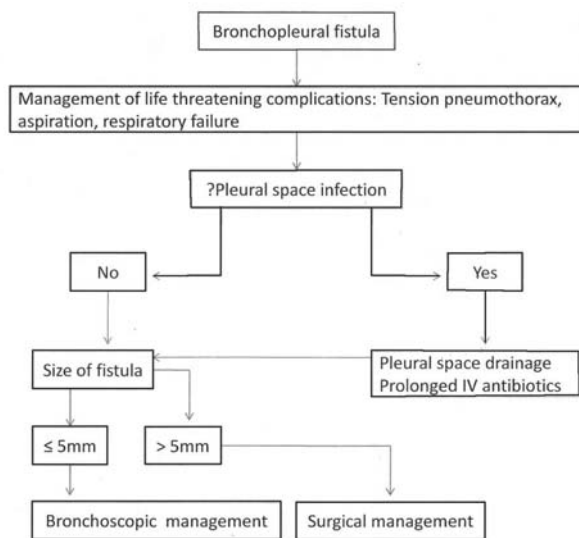


Figure 7. Management of bronchopleural fistula.

CONCLUSIONS

Bronchopleural fistula is associated with significant morbidity and mortality. Treatment of life threatening complications and pleural space infection should be instituted as early as possible. The management of an immediate post-operative fistula and large BPF is surgical. In cases of smaller (≤ 5 mm) fistula, a bronchoscopic closure can be attempted with satisfactory result. The choice of a particular bronchoscopic method should depend on the familiarity and experience of the bronchoscopist.

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