Best evidence topic - Pulmonary

Are bronchoscopic approaches to post-pneumonectomy bronchopleural fistula an effective alternative to repeat thoracotomy?

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Summary

A best evidence topic in cardiothoracic surgery was written according to a structured protocol. The question addressed was whether bronchoscopic or other minimal access approaches to the closure of bronchopleural fistulae (BPFs) were effective compared to a conventional re-thoracotomy. Our search identified 1052 abstracts, from which we identified six case series of greater than two post-pneumonectomy bronchopleural fistula patients. These series included reports of bronchial stenting, glue occlusion and scar obliteration of fistulae. No thoracoscopic techniques were reported except in case report form. The author, journal, date and country of publication, patient group studied, study type, relevant outcomes, results, and study weaknesses of these papers are tabulated. We identified 85 post-pneumonectomy bronchopleural fistulae reported in the literature who underwent bronchoscopic procedures to attempt repair. There was a 30% cure rate using a range of bronchoscopic techniques in these series. Bronchoscopic techniques included cyanoacrylate or fibrin glue application, YAG laser therapy, injection of the vein sclerosant polidocanol and tracheo-bronchial stenting. The mortality was 40% in these patients reflecting the very high mortality with this complication. Many patients required multiple bronchoscopic procedures and also further drainage procedures of their empyemas. Bronchoscopic treatment has so far only been reported in small case series but may offer further treatment options in patients too unwell to undergo re-thoracotomy.

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Keywords: Bronchopleural fistula; Pneumonectomy; Thoracic surgery

1. Introduction

A best evidence topic was constructed according to a structured protocol. The protocol is fully described in the ICVTS [1].

2. Clinical scenario

You perform a right pneumonectomy for a cT2 cN1 cM0 non-small-cell lung cancer, in a 77-year-old diabetic with a history of ischaemic heart disease.

On the sixth postoperative day he deteriorates, with a copious productive cough, worsening gas exchange, pyrexia and rising inflammatory markers. Chest X-ray shows a fall in fluid level, and fibreoptic bronchoscopy confirms a bronchopleural fistula (BPF), with dehiscence of one third of your staple line. The intercostal drain you site recovers 700 ml of purulent fluid. You feel that he would not survive a repeat thoracotomy and wonder if a bronchoscopic approach might work?

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3. Three-part question

In [patients with a bronchopleural fistula] is a [minimal access or bronchoscopic approach superior to conventional re-thoracotomy] for BPF closure in terms of [survival].

4. Search strategy


[exp Bronchial fistula/OR bronchopleural fistula.mp OR bronchial dehiscence.mp OR exp respiratory tract fistula/] AND [exp thoracoscopic/OR thoracoscopy.mp OR exp thoracic surgery, video-assisted/OR exp surgical procedures, minimally invasive/OR minimally invasive.mp OR minimal access.mp] AND [outcome.mp OR outcome$.mp OR exp intraoperative complications/OR exp empyema OR empyema.mp OR complication$.mp OR exp treatment outcome/]. The Cochrane Register of Systematic Reviews was also searched for relevant studies. Results were restricted to studies on human subjects published in the English language.

5. Search outcome

The search identified 1052 abstracts in Medline and EMBase. Abstracts were hand-searched, and several identified
### Table 1

<table>
<thead>
<tr>
<th>Author, year, journal, country</th>
<th>Patient group</th>
<th>Outcomes</th>
<th>Key results</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Hollaus et al. (1998), Ann Thorac Surg, Austria, [2]</td>
<td>45 post-resection BPFs, 40 (89%) post-pneumonectomy, treated initially by bronchoscopic therapy. Fistulas &gt; 8 mm diameter excluded. All male, median age 60.29 years. No stump recurrences of malignancy</td>
<td>Mortality, progression to surgical treatment, resolution of fistula and empyema</td>
<td>9 patients (including 4 lobectomies) cured by endoscopic therapy alone (20% of total, 12.8% of pneumonectomy BPFs). 7 (15.6%) BPF resolved but chronic empyema remained. 16 (35.6%) went on to surgery, in-patient mortality 8 (20%). Further 17 post-discharge deaths in mean follow-up 779 days. Overall mortality 57%</td>
<td>Large retrospective series. Treated with fibrin glue alone (fistulae &lt; 3 mm) or fibrin and spongy calf bone (&gt; 3 mm). Mixed series including 5 (11%) lobectomies. Rates of cure (resolution of both BPF and empyema) low in post-pneumonectomy group, conversion to open surgery and mortality relatively high</td>
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<td>Varoli et al. (1998), Ann Thorac Surg, Italy, [3]</td>
<td>35 patients with post-resection BPF, 1 post-pneumonectomy, the remainder postlobectomy. 33 (94%) with associated empyema</td>
<td>Clinical resolution, time to clinical resolution, mortality</td>
<td>11 (58%) post-pneumonectomy fistulas ‘completely resolved’ within 2–8 weeks (mean 5.5). Healed fistulas ranged in size from 2–10 mm. 8 patients with ‘total’ dehiscence did not heal, all ‘intermediate’ or ‘late’ fistulas. 5 patients (26%) died within 2 weeks of fistula appearance</td>
<td>Retrospective series. Treatment with intercostal tube drainage for empyema, followed by repeated bronchoscopic submucosal injection of polidocanol (weekly). Definition of clinical resolution unclear. Some reporting of results does not differentiate between the post-pneumonectomy and post-lobectomy groups</td>
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<td>Han et al. (2006), Ann Thorac Surg, China, [4]</td>
<td>6 patients with post-resection BPF, 5 post-pneumonectomy, 1 post-lobectomy. Pleural drains sited pre-procedure. Stump length varied from 18–35 mm</td>
<td>Correct stent placement on bronchoscopic and helical CT, clinical resolution of BPF and empyema</td>
<td>Stents successfully placed in all patients. 4 of 5 post-pneumonectomy fistulas closed and empyema resolved (67%). In 1 other patient, fistula closed but empyema remained. No mortality at mean follow-up of 316 days (range 150–616)</td>
<td>Retrospective review. Radiological placement of covered metal stents, specifically designed with a blind-ended side arm to obstruct the stump. Device placed under topical anaesthesia. Complete medium-term follow-up with good results and complete survival in a small series. Size of fistulas treated not stated but presumably large</td>
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<td>Scappaticci et al. (2000), Ann Thorac Surg, Italy, [5]</td>
<td>12 post-pneumonectomy BPFs within a series of 20 post-resection BPFs, 6 early-onset and 6 late</td>
<td>Clinical resolution of BPF and empyema, survival</td>
<td>Of 6 early BPFs, 3 &lt; 5 mm closed successfully with resolution of associated empyema in one affected patient. In 3 BPFs &gt; 5 mm no resolution of BPF or associated empyemas. 2 died, 1 later successfully treated with surgery. In 6 late ‘small’ fistulas, 5 successfully treated endoscopically, 1 progressed to surgery. Overall BPF cure rate 66.7%, empyema cure rate 10% (1 of 10), survival 83%</td>
<td>Retrospective series. Bronchoscopic application of methyl-2-cyanoacrylate glue. Criteria for resolution of BPF and empyema not stated. Duration of follow-up not stated. Low cure rate for empyema- 0% in 6 late presentation BPFs</td>
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<td>Kiriymama et al. (2002), Ann Thorac Surg, Japan, [6]</td>
<td>6 post-pneumonectomy BPFs within series of 8 post-resection BPFs, 2 with stump recurrence of malignancy, 1 with stump aspergilloma. All fistulae &lt; 2 mm diameter. Onset from 1–9 months post-operatively. 5 of 6 (83%) had intercostal drain prior to bronchoscopy</td>
<td>Clinical resolution of BPF, survival, presence of ongoing clinical pleural space infection</td>
<td>All initially closed with laser therapy, but only 2 without recurrence (33%). Recurrences occurred 3–12 days later. Follow-up 1.2–108 months. 4 deaths (66%), 3 from recurrent malignancy, 1 from invasive aspergilloma. No pleural space infection in 5 of 6 (83%)</td>
<td>Retrospective case series. Nd:YAG applied to peri-fistula endothelium via the flexible bronchoscope under local anaesthesia and sedation. Authors note that all successes were at higher energy doses (15–20 W). Relatively low overall success rate</td>
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<td>Sabanathan and Richardson (1994), J Cardiothorac Surg, UK, [7]</td>
<td>3 post-pneumonectomy BPFs, 6 weeks (2 patients) to 32 weeks (1 patient) post-operatively. All with associated empyema, fistula size not stated</td>
<td>Resolution of BPF and empyema, progress to surgery, mortality</td>
<td>Treatment by immediate chest drain, followed by bronchoscopic closure with n-butyl-2-cyanoacrylate glue. Space then irrigated. Follow-up 3 months–3 years. No mortality, 2 progressed to omentopexy, all resolved</td>
<td>No mortality and resolution in all cases. However, 2 (66%) went on to open surgery by omentopexy, so the contribution of endoscopic gluing is unclear</td>
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for full manuscript assessment. No randomised trials, two narrative review articles, several case series and many case reports were identified for manuscript review. Reports of two patients or less were excluded from further study. Reports containing both post-lobectomy and post-pneumonectomy were assessed on their post-pneumonectomy content alone. The papers finally considered to be the best evidence are summarised in Table 1.

6. Discussion

Bronchopleural fistula is a disastrous complication following pneumonectomy, with high morbidity. Incidence after pneumonectomy in a recent series was 12%, and mortality with fistula was 67% [8]. Impaired respiratory mechanics, contralateral lung contamination and chronic pleural sepsis all contribute to its poor outcome. Conventional surgical strategies such as thoracoplasty or chest wall fenestration carry significant mortality in themselves, and long-term morbidity with pain and deformity. Reducing the morbidity of therapy with a minimal access approach is, therefore, appealing. The fistula site is accessible by bronchoscopy and/or thoracoscopy, which may avoid major surgery in these high-risk patients may reduce risk.

Our search strategy produced reports of several different procedures. They can be broadly categorised as (1) tracheobronchial stenting, (2) occlusion with glue or other materials, and (3) procedures to induce scar tissue formation at the fistula. We decided to exclude from our table series of two cases or less. Case reports of other treatments, including thoracoscopic closure, were excluded on these grounds. The search also identified two recent topic reviews [9, 10].

Endobronchial stenting has been used to isolate fistulas in several case reports, but our search identified only one series of more than two patients [4]. The authors used specially-designed covered metal stents (with a blind-ending arm to fit the bronchial stump) in six patients. The mortality rate at a mean follow-up of 316 days was 0%, with 67% of patients cured of both fistula and empyema. Patients in this series underwent follow-up CT scan and bronchoscopy to confirm adequate stent placement. This initial study is encouraging, although it is not population-based, making the effect of case-selection hard to quantify. It does, however, establish the feasibility of the technique in selected patients.

Fibrin glue occlusion was used in a large series of 45 post-resection fistulas (40 post-pneumonectomy) <8 mm in diameter [2]. Only 20% of cases were cured with this technique, with resolution of both fistula and empyema. However, the majority had an adverse outcome, with 20% dying as in-patients, 35.6% progressing to surgery and 15.6% left with a chronic empyema. Another series using synthetic glue in 12 post-pneumonectomy fistulas had a better fistula resolution rate (66.7%) and survival of 83%, but disappointingly only 10% of empyemas resolved [5]. The authors’ impression was that small and late-presentation fistulas responded better to glue, although the numbers were too small for statistical analysis. Sabanathan [7] also used cyanoacrylate glue in three patients, with no mortality, but resolution of BPF and empyema was only achieved in one patient (33%). The other two required open omentopexy.

Lastly, reported scar-forming techniques have included the Nd:YAG laser [6] and sub-mucosal injection of the vein sclerosant polidocanol [3]. Resolution of BPF ranged from 33% to 58%, and mortality from 26% to 66%. Both of these techniques involved repeated bronchoscopic interventions in most patients. Other techniques included bronchoscopic submucosal alcohol injection [11] and thoracoscopic gluing or clipping [12].

The pooled mortality in amongst 90 patients reported in these five series (including five BPFs following lobectomy) is 39.6%. Of 85 post-pneumonectomy BPFs reported in these series, 30.1% were cured of both BPF and associated empyema (when present) by bronchoscopic treatment alone.

These outcomes could clearly still be improved. Fistula size, time of onset from surgery, bronchial stump length and aetiology of stump failure (e.g. tumour recurrence) vary. It may be that some strategies are useful for specific types of BPF. For example, several authors have suggested that glue and scarring techniques seem better suited to smaller fistulas [2, 3, 5]. Concentrating on fistula subsets with specific techniques may improve results.

7. Clinical bottom line

In 85 post-pneumonectomy BPFs there was a 30% cure rate using a range of bronchoscopic techniques. The mortality was approximately 40% reflecting the very high mortality with this complication. Bronchoscopic treatment has so far only been reported in small case series but may in the future offer further treatment options in patients too unwell to undergo re-thoracotomy.
References


