Online Appendix A3   BTS Guideline for Pleural Disease

Section A   Spontaneous pneumothorax

Question A3   Evidence Review and Protocol

A3   In adults with spontaneous pneumothorax and ongoing air leak (excluding post-surgical patients), which treatments are better than ongoing chest tube drainage alone at improving clinical outcomes?

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Question Evidence Review

A3   In adults with spontaneous pneumothorax and ongoing air leak (excluding post-surgical patients), which treatments are better than ongoing chest tube drainage alone at improving clinical outcomes?

Background

Most spontaneous pneumothoraces will resolve once the air leak has ceased. However, some patients will have persistent/prolonged air leak (PAL) and/or failure of the lung to re-expand on chest X-ray (CXR). There are several treatment options including application of thoracic suction, converting to larger-bore chest drain, blood patch or chemical pleurodesis, endobronchial valves or thoracic surgery.

Outcomes

Length of hospital stay, recurrence of pneumothorax, re-admission, need for further pleural procedures, complications, pain and breathlessness, quality of life and mortality

Evidence review

The initial literature search identified 65 potential studies, but only three were deemed relevant to the review. These included one randomised controlled trial (RCT) of suction for pneumothorax, which compared digital suction (15 cm H_2O) with wall delivered suction (15 cm H_2O), but without a control arm of standard care (no suction). The definition of "air leak" was >20mL/min as measured on digital suction rather than the typical description of "persistent air leak" of air leak present after at least 48 hours and all patients were placed on digital suction for one hour prior to randomisation.[1] The remaining two RCTs investigated "blood patch" therapies for patients with PAL. Ibrahim et al compared instillation of 50mL autologous blood in 23 patients with secondary spontaneous pneumothorax (SSP) at day 3 post drain insertion, to standard care (n = 24) and Zhang et al performed a three-arm RCT of 150 patients with secondary spontaneous pneumothorax (SSP) and PAL >7 days: 50 were treated endobronchial autologous blood (with thrombin, ABP), bronchial occlusion with silicone spigots (BOS) and standard care with ongoing drainage alone.[2,3]

Length of hospital stay

Length of hospital stay was reported in all studies. Meta-analysis was not possible between the studies as interventions were not comparable, with comparative results displayed in Table A5a.

Table A5a: Comparison of length of hospital stay for differing treatments of spontaneous pneumothorax and ongoing air leak (excluding post-surgical patients) in adults

Study	**Treatment**	**Length of hospital stay** (days) (mean ± SD)	***p***
Jablonski 2014[1]	Digital suction	5.1 ± 1.1	<0.0005
	Wall suction	7.0 ± 2.0	
Ibrahim 2018[2]	Chest drain	15.0 ± 2.6	<0.001
	ABP (via chest drain)	10.0 ± 2.2	
Zhang 2019[3]	BOS	7.3 ± 1.6	<0.016*
	ABP (endobronchial)	8.1 ± 1.6	
	Chest drainage	10.1 ± 2.0	

* For both BOS or endobronchial ABP versus chest drainage

ABP – autologous blood plus thrombin patch; BOS – bronchial occlusion using silicone spigots

In Zhang et al[3], length of hospital stay was significantly shorter with both endobronchial autologous blood plus thrombin patch (ABP) and bronchial occlusion using silicone spigots (BOS) compared to standard care of chest drain with underwater-seal drainage. In Ibrahim et al[2], length of hospital stay was significantly shorter with ABP instilled via chest drain compared to standard care of chest drain with underwater-seal drainage. In Jablonski et al[1], digital wall suction led to lower length of hospital stay compared to standard wall suction.

Recurrence of pneumothorax, re-admission and need for further pleural procedures

No studies reported on the need for further pleural procedures, re-admission or long-term pneumothorax recurrence.

Complications

Complications were reported in two studies and a summary of the results is shown in Table A5b.[2,3]

Table A5b: Comparison of post-treatment complications following different treatment strategies for spontaneous pneumothorax and ongoing air leak (excluding post-surgical patients) in adults

Study/Complication	Treatment groups			*p*
	% Patients (no. patients)			
Ibrahim 2018[2]	Autologous blood		Chest drainage	
Fever	13% (3/23)		21% (5/24)	NS
Infection	9% (2/23)		17% (4/24)	NS
Zhang 2019[3]	Autologous blood	Bronchial occlusion	Chest drainage	
Cough†	28% (14/50)	44% (22/50)	36% (18/50)	NS
Temporary haemoptysis	100% (50/50)	100% (50/50)	12% (6/50)	<0.0016*
Fever	10% (5/50)	16% (8/50)	18% (9/50)	NS
Spigot displacement	NA	8% (4/50)	NA	NA

* Endobronchial autologous blood versus chest drainage and bronchial occlusion versus chest drainage; no significance between endobronchial autologous blood and bronchial occlusion

† >30 mm on visual analogue scale (VAS)

NA – not applicable; NS – not significant

Pain and breathlessness

Chest pain was only reported in one study where 24% of patients (13/50) receiving treatment with endobronchial autologous blood, 36% (18/50) of patients receiving treatment with bronchial occlusion and 42% (21/50) receiving treatment with chest drainage alone experience pain measured as >30 mm on the visual analogue scale (VAS), but there was no significance between the groups.[3] No study reported on breathlessness.

Quality of life

Quality of life was not reported in any studies.

Mortality

Only one study reported on mortality following treatment with autologous blood or standard chest drainage for the treatment of SSP and PAL, but no patient deaths were reported in either treatment arm.[2]

Evidence statements

Length of hospital stay appears to be shorter following autologous blood pleurodesis treatment, regardless of delivery method, for pneumothorax and persistent air leak in adults when compared with chest drainage (**Ungraded**)

There was no evidence to suggest that the application of suction is beneficial to treat pneumothorax and persistent air leak in adults

Limited evidence suggests that endobronchial therapies may have the potential to treat pneumothorax and persistent air leak (**Ungraded)**

Recommendations

There is insufficient evidence to make any recommendations on the best treatment method for pneumothorax and persistent air leak in adults.

Good Practice Points

✓ The risks and benefits of all treatment strategies options for pneumothorax with persistent air leak in adults should be discussed with the patient

✓ If a patient is not considered fit for surgery, autologous blood pleurodesis or endobronchial therapies should be considered for the treatment of pneumothorax with persistent air leak in adults

Research Recommendation

▪ Further studies are required to better define and determine the optimal management of pneumothorax with persistent air leak in adults

Risk of bias summary

References

1. Jablonski S, Brocki M, Wawrzycki M, Smigielski JA, Kozakiewicz M. Efficacy assessment of the drainage with permanent airflow measurement in the treatment of pneumothorax with air leak. *Thoracic & Cardiovascular Surgeon.* 2014;62(6):509-515.

2. Ibrahim IM, Elaziz MEA, El-Hag-Aly MA. Early Autologous Blood-Patch Pleurodesis versus Conservative Management for Treatment of Secondary Spontaneous Pneumothorax. *Thoracic & Cardiovascular Surgeon.* 2018.

3. Zhang HT, Xie YH, Gu X, et al. Management of persistent air leaks using endobronchial autologous blood patch and spigot occlusion: a multicentre randomized controlled trial in China. *Respiration.* 2019;97(5):436-443.

Question Protocol

Field	Content
Review Question	In adults with spontaneous pneumothorax and ongoing air leak (excluding post-surgical patients), which treatments are better than ongoing chest tube drainage alone at improving clinical outcomes?
Type of review question	Intervention review
Objective of the review	The objective of this question is to review the evidence of treatments for ongoing air leaks via chest tubes in non-surgical patients with spontaneous pneumothorax and compare these treatments against chest tube drainage alone.
Eligibility criteria – population / disease / condition / issue / domain	Adults (18+) with pneumothorax and ongoing air leak (excluding post-surgical patients)
Eligibility criteria – intervention(s)	Suction (digital and otherwise) Increasing drain size or number of drains Blood patch pleurodesis Chemical pleurodesis One way valve (applied to the chest tube) Endobronchial valves Surgical intervention (as defined above)
Eligibility criteria – comparators(s)	Ongoing chest tube drainage alone
Outcomes and prioritisation	Length of hospital stay Further treatment (pleural and surgical procedures) Pain / breathlessness Duration of air leak Complications Quality of life Mortality
Eligibility criteria – study design	RCTs Prospective comparative studies Case series of >100 patients

Other inclusion /exclusion criteria	Non-English language excluded unless full English translation
	Conference abstracts, Cochrane reviews, systematic reviews, reviews
	Cochrane reviews and systematic reviews can be referenced in the text, but **DO NOT** use in a meta-analysis
Proposed sensitivity / subgroup analysis, or meta-regression	None
Selection process – duplicate screening / selection / analysis	Agreement should be reached between Guideline members who are working on the question. If no agreement can be reached, a decision should be made by the Guideline co-chairs. If there is still no decision, the matter should be brought to the Guideline group and a decision will be made by consensus
Data management (software)	RevMan5 Pairwise meta-analyses Evidence review/considered judgement. Storing Guideline text, tables, figures, etc. Gradeprofiler Quality of evidence assessment Gradepro Recommendations
Information sources – databases and dates	MEDLINE, Embase, PubMED, Central Register of Controlled Trials and Cochrane Database of Systematic Reviews 1966 - present
Methods for assessing bias at outcome / study level	RevMan5 intervention review template and NICE risk of bias checklist (follow instructions in '*BTS Guideline Process Handbook – Intervention Review*')
Methods for quantitative analysis – combining studies and exploring (in)consistency	If 3 or more relevant studies: RevMan5 for meta-analysis, heterogeneity testing and forest plots (follow instructions in '*BTS Guideline Process Handbook – Intervention Review*')
Meta-bias assessment – publication bias, selective reporting bias	GRADEprofiler Intervention review quality of evidence assessment for each outcome (follow instructions in '*BTS Guideline Process Handbook – Intervention Review*')
Rationale / context – what is known	There was little evidence to support onward management of ongoing air leaks in spontaneous pneumothorax management at the time of the last BTS guidelines (particularly the optimal timing of surgery and what to do in those not fit for surgery). This question will review this evidence.