

Online Appendix D3 **BTS Guideline for Pleural Disease**

Section D **Pleural malignancy**

Question D3 **Evidence Review and Protocol**

D3 **For adults with malignant pleural effusion, is pleural aspiration with no pleurodesis agent better than talc slurry at improving clinical outcomes?**

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Question Evidence Review

D3 For adults with malignant pleural effusion, is pleural aspiration with no pleurodesis agent better than talc slurry at improving clinical outcomes?

Background

Chest drain insertion with talc pleurodesis provides definitive management of malignant pleural effusion (MPE) by creating permanent fusion of the pleural layers. This requires hospitalisation with a chest drain *in situ* for a number of days. Pleural aspiration with no attempt at pleurodesis is an alternative approach and has the advantage of not requiring hospital admission but may permit fluid recurrence. Understanding which of these interventions has the most benefit for important clinical outcomes would permit rational treatment choices.

Outcomes

Quality of life, length of hospital stay, need for re-intervention, symptoms (breathlessness, chest pain), complications and pleurodesis rate

Evidence Review

The initial literature search identified 20 papers of which two were deemed relevant. The first study was a randomised controlled trial¹ and the second a retrospective analysis of the SEER (Surveillance, Epidemiology and End Results) database².

Quality of Life

None of the studies provided data on quality of life.

Length of Stay

Only the retrospective analysis of the SEER database provided information on hospital stay, comparing pleural aspiration and talc slurry pleurodesis. All patients underwent an initial pleural aspiration before study treatment and the results are summarised in [Table D3a](#).²

Table D3a: Length of hospital stay data following a second pleural aspiration or talc slurry pleurodesis after initial pleural aspiration

Treatment	Second pleural aspiration	Talc slurry pleurodesis
No. patients	10,019	1779
Median length of stay [IQR] (days)	1 [1-1] ^a	7 [7-7] ^a
Median in-patient days until death [IQR]	31 [15-67]	34 [18-68]

^a p<0.001; IQR – interquartile range

Re-intervention

The SEER analysis was the only study that provided information on re-intervention after pleural aspiration or talc slurry pleurodesis. Following initial pleural aspiration (n = 23,431), 45% required no further pleural procedures and 55% required a second procedure (of which 32% occurred within 14 days). The mean number of further pleural procedures was 1.44 in the pleural aspiration group and 0.75 in the talc slurry pleurodesis group.²

Symptoms

The only study to report symptoms was the randomised controlled trial. Of the 21 patients in whom the primary outcome was available, symptoms were only reported in those with successful pleurodesis (n = 16) and

measured using a subjective description. All (9/9) patients treated with talc slurry had subjectively improved breathlessness, compared with 86% (6/7) of those treated with pleural aspiration.¹

Complications

Two studies reported complications; the SEER analysis reported pneumothorax² and Sorensen et al reported infective complications¹.

The SEER analysis reported similar pneumothorax rates using pleural aspiration and talc slurry. Overall, patients treated with pleural aspiration required more pleural procedures than talc slurry and those treated with repeated pleural aspiration suffered pneumothorax more than with talc slurry. The reported pneumothorax rate per procedure was 9/1000 patients for pleural aspiration and <3.7/1000 patients for talc slurry, but as talc slurry involves fewer procedures, this translated to <190 treated with talc slurry to prevent one pneumothorax.²

Sorensen et al reported cases of staphylococcus bacteraemia in 1/9 cases with talc slurry (11.1%) and 1/7 cases with pleural drainage alone (14.3%). However, this study did not reflect normal practice as patients in the “pleural aspiration” arm were post thoracoscopy with a chest drain *in situ* for 72 hours rather than the more usual simple aspiration.¹

Pleurodesis rates

Sorensen et al reported a pleurodesis success rate of 100% in those treated with talc slurry (9/9) and 58% in those treated with pleural aspiration alone (4/7), but as above, the study did not reflect normal pleural aspiration practice.¹

Evidence statements

The evidence supporting this review was very limited.

Talc slurry pleurodesis may be associated with a longer hospital stay than pleural aspiration (**Ungraded**)

Talc slurry pleurodesis appears to reduce the need for re-intervention and reduces the overall number of complications compared with pleural aspiration alone (**Ungraded**)

Patients undergoing pleural aspiration as the first intervention will often require a second procedure, with approximately one third requiring this within 2 weeks (**Ungraded**)

Pleural aspiration appears to improve breathlessness (**Ungraded**)

Recommendation

- Management of MPE using talc pleurodesis (or another method) is recommended in preference to repeated aspiration especially with those with a better prognosis, but the relative risks and benefits should be discussed with the patient (**Conditional** – by consensus)

Good Practice Points

- ✓ Decisions on the best treatment modality should be based on patient choice
- ✓ Informed decision making should include the role of inpatient versus ambulatory management and the potential risk of requiring further pleural interventions

Research Recommendation

- Research is needed to assess factors that predict the re-accumulation of pleural fluid following an initial aspiration

Risk of bias summary

	Selection bias	Performance bias	Detection bias	Attrition bias	Publication bias
Ost 2018	?	?	+	?	+
Sorenson 1984	+	+	?	+	+

References

1.

Sorensen PG, Svendsen TL, Enk B. Treatment of malignant pleural effusion with drainage, with and without instillation of talc. *Eur J Respir Dis.* 1984;65(2):131-135.

2.

Ost DE, Niu J, Zhao H, Grosu HB, Giordano SH. Quality gaps and comparative effectiveness of management strategies for recurrent malignant pleural effusions. *Chest.* 2018;153(2):438-452.

Question Protocol

Field	Content
Review Question	For adults with malignant pleural effusion, is pleural aspiration with no pleurodesis agent better than talc slurry at improving clinical outcomes?
Type of review question	Intervention review
Objective of the review	One of a series of questions comparing the standard of care (chest tube and talc slurry) with another intervention. Is pleural aspiration alone as effective as an intervention?
Eligibility criteria – population / disease / condition / issue / domain	Adults (18+) with malignant pleural effusion
Eligibility criteria – intervention(s)	Pleural aspiration with no pleurodesis agent
Eligibility criteria – comparators(s)	Talc slurry pleurodesis
Outcomes and prioritisation	Quality of life Length of hospital stay Need for re-intervention Symptoms (breathlessness, chest pain) Complications Pleurodesis rates
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	Trapped lung Non-trapped lung Unknown
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 ' <i>BTS Guideline Process Handbook – Intervention Review</i> ')
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 ' <i>BTS Guideline Process Handbook – Intervention Review</i> ')
Meta-bias assessment – publication bias, selective reporting bias	GRADEprofiler Intervention review quality of evidence assessment for each outcome (follow instructions in ' <i>BTS Guideline Process Handbook – Intervention Review</i> ')
Rationale / context – what is known	Talc slurry through an intercostal tube remains the standard of care. What is the evidence that informs this practice?