Online Appendix D6 BTS Guideline for Pleural Disease

Section D Pleural malignancy

Question D6 Evidence Review and Protocol

D6 For adults with malignant pleural effusion, is surgical pleurodesis or surgical decortication better than talc slurry pleurodesis at improving clinical outcomes?

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Question Evidence Review

D6 For adults with malignant pleural effusion, is surgical pleurodesis or surgical decortication better than talc slurry pleurodesis at improving clinical outcomes?

Background

In adults with malignant pleural effusion (MPE), talc pleurodesis via slurry or poudrage, indwelling pleural catheters (IPC) and aspiration are common treatment options and widely available. However, surgical intervention is a treatment option in those able to tolerate surgery and this review questioned if there are relative benefits of using a surgical approach in MPE compared to the above "physician" approach. The only direct randomised comparative study is the MesoVATS study, a study comparing the role of video-assisted thoracoscopic partial pleurectomy versus talc pleurodesis in patients with malignant pleural mesothelioma[1], but this study was not included in this guideline as it is covered in the BTS Guideline for the investigation and management of pleural mesothelioma.[2]

Outcomes

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

Evidence Review

The initial literature search identified 28 papers and four studies were deemed relevant[3-6], but only one study compared surgery versus talc slurry pleurodesis[3].

Quality of life

One prospective (non-randomised) cohort study compared quality of life scores in patients managed by video-assisted thoracoscopic surgery (VATS) plus talc pleurodesis, VATS plus IPC, IPC only or talc slurry via chest drain.[3] No mechanical pleurodesis procedures were performed during VATS. Patient-reported satisfaction scores were measured pre-treatment and at 2- and 6-weeks post-treatment using the functional assessment of chronic illness therapy–palliative (FACIT-Pal). The summarised results are shown in Table D6a with each group showing a significant average increase in patient quality of life per day, but there were no significant differences between groups.

Table D6a: Quality of life score comparison between different methods of malignant pleural effusion management

Management strategy	**Patient number**	**Average change in score* / day** [95% CI]	***p***
VATS plus talc pleurodesis	18	0.36 [0.06, 0.66]	0.02
VATS plus IPC	20	0.21 [-0.03, 0.46]	0.08
IPC only	27	0.16 [-0.04, 0.35]	0.11
Talc slurry via chest drain	39	0.32 [0.09, 0.54]	0.007

* Using FACIT-PAL – Functional Assessment of Chronic Illness Therapy - Palliative Care

IPC – Indwelling pleural catherer; VATS – video assisted thoracoscopic surgery

Length of hospital stay

Three studies reported on length of hospital stay, but no study directly compared surgical management against talc slurry pleurodesis.[4,5] Trotter et al reported a longer average stay for patients undergoing VATS plus talc pleurodesis (10.4 ± 7.3 days, mean ± SD, 202 patients), but these were compared to average time taken to removal of an intercostal drainage in non-study patients (5.7 ± 4.3 days).[4] Results are summarised in Table D6b.

Table D6b: Length of hospital stay summary for different methods of malignant pleural effusion management

Management strategy	**Patient number**	**Length of hospital** (days)	
VATS plus chemical* pleurodesis[5]	355	5.58 ± 1.87	(mean ± SD)
		5.0 [3-10]	(median [range])
Minimal lateral thoracotomy plus chemical† pleurodesis[5]	210	6.99 ± 1.22	(mean ± SD)
		7.0 [4-11]	(median [range])
VATS plus talc pleurodesis[6]	611	5.8 [4-31]	(median [range])
VATS plus talc pleurodesis[4]	200	10.4 ± 7.3	(mean ± SD)
		[2-50]	([range])
Intercostal drain[4]	-	5.7 ± 4.3	(mean ± SD)

* 283 patients had talc pleurodesis, 72 patients had alcohol pleurodesis

† 159 patients had talc pleurodesis, 51 patients had alcohol pleurodesis

VATS – video assisted thoracoscopic surgery

Need for re-intervention

Three studies reported on the need for re-intervention, but meta-analysis was not possible. Cardillo et al reported that VATS was repeated in two subjects at 12+ months following the initial VATS and talc pleurodesis procedures[6] and Trotter et al reported that one patient required thoracotomy with decortication following VATS pleurodesis, but no timeframe was provided[4]. Walker et al reported that additional interventions were greater in the talc slurry and chest drain group early post-surgery, but additional interventions were more equally distributed across the study groups (VATS plus talc pleurodesis, VATS plus IPC and IPC only) at later follow-ups. However, as the re-intervention data had been combined with the complication data, the re-intervention only data could not be extracted.[3]

Symptoms (breathlessness, chest pain)

Two studies reported on pain and one study reported on breathlessness. For pain, one study used the World Health Organization (WHO) three step cancer pain relief scale[7], where Step 1 indicates the use of non-steroidal anti-inflammatory drugs for mild or moderate pain, Step 2 indicates the use of opioid drugs for moderate to severe pain and Step 3 indicates the use of opioids and/or adjuvant analgesics for severe, non-controlled pain. Measurements were made during the first three days post-thoracotomy or post VATS and results showed that all VATS patients required Step 1 only, whereas 70% of the thoracotomy patients required Step 2.[5] In the second study, post-treatment pain scores were collected from 44/104 patients using the Eastern Cooperative Oncology Group (ECOG) pain score, a numerical scale with 1 being 'no pain' and 10 being 'worst pain imaginable'. Data showed that 12/20 (60%) patients with IPC only and 3/4 (75%) with VATS plus IPC had an ECOG pain score of 4 or less. In contrast, 12/20 patients undergoing talc slurry via a chest drain ECOG pain scores of 5 or greater. No pain scores were obtained from those undergoing VATS plus talc pleurodesis.[3]

Walker et al used FACIT-Pal shortness of breath scores to assess the impact of MPE management on breathlessness. Ranking breathlessness over the preceding seven days, results showed a significant average increase of 0.02 [0.007, 0.02] scores per day [95% confidence intervals] (p=0.0007) across the whole group (VATS plus talc pleurodesis, VATS plus IPC, IPC only or talc slurry via chest drain). No statistically significant differences were reported between groups, but the authors implied that VATS and pleurodesis offered the most sustained improvement.[3]

Complications

Three studies reported on complications experienced with surgical management of MPE. Brega-Massone et al reported that 2% of patients who underwent VATS and chemical pleurodesis experienced complications, whereas this increased to 7% in those who underwent thoracotomy and chemical pleurodesis.[5] Cardillo et al

and Trotter et al both focused on patients undergoing VATS plus talc pleurodesis and reported that 3% and 15% of their participants respectively experienced complications.[4,6] Although Walker et al did comment on complications, their data included re-intervention data and was quoted as 5-31% across all groups (VATS plus talc pleurodesis, VATS plus IPC, IPC only or talc slurry via chest drain).[3] Complications included empyema, persistent effusion, prolonged air leak and wound infection.

Pleurodesis rates

Pleurodesis success rates were reported for surgical MPE management strategies in three retrospective case series studies.[4-6] The results are summarised in Table D6c.

Table D6c: Comparison of pleurodesis success rates for surgical talc pleurodesis malignant pleural effusion management techniques

	% pleurodesis success rate (no. patients)			
	All		**Non-expandable lung only**	
Study	**VATS**	**Thoracotomy**	**+ Decortication**	**No decortication**
Brega-Massone 2004[5]	88% (248/283)	75% (120/159)		
Cardillo 2002[6]	93% (558/602)	-	97% (28/29)	13% (2/15)
Trotter 2005[4]	88% (178/202)	-		

VATS – video assisted thoracoscopic surgery

All studies reported a ≥88% success rate with VATS and talc pleurodesis. Brega-Massone et al reported a lower recurrence in the VATS and talc group, with 88% having evidence of effusion at 5 months compared to 75% in the minimal lateral thoracotomy and talc pleurodesis group.[5]

Evidence statements

There was insufficient evidence to accurately address the question and published evidence was in highly selected, non-randomised patients

Surgical and non-surgical treatments for MPE may improve quality of life and reduce breathlessness (**Ungraded**)

Surgical MPE treatments may require a longer stay in hospital compared to talc slurry pleurodesis (**Ungraded**)

VATS with talc pleurodesis may reduce the need for early post-surgery re-intervention (**Ungraded**)

Pleurodesis failure rates may increase in MPE patients with non-expandable lung if thoracoscopic decortication is not performed (**Ungraded**)

Recommendation

- ➢ In selected patients considered fit enough for surgery, either surgical talc pleurodesis or medical talc slurry can be considered for the management of malignant pleural effusion patients. The relative risks, benefits and availability of both techniques should be discussed with patients to individualise treatment choice (**Conditional** – by consensus)

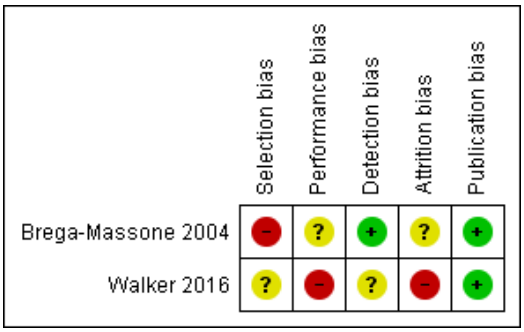
Good Practice Point

- ✓ Informed decision making should include the role of surgery versus ambulatory management with an IPC for the management of malignant pleural effusion in selected patients
- ✓ Decortication surgery may improve pleurodesis success in malignant pleural effusion patients with non-expandable lung, but the risks and benefits of IPC and surgical treatment should be discussed with patients, and treatment individualised according to circumstances (for example, fitness to undergo thoracic surgery)

Research Recommendations

- Further research is needed into assessing the clinical benefits of surgery in non-selected adult patients with malignant pleural effusion
- Further research is needed into assessing the clinical benefits of combined video-assisted thoracoscopic surgery (VATS) and indwelling pleural catheters (IPC)

Risk of bias summary



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4. Trotter D, Aly A, Siu L, Knight S. Video-assisted thoracoscopic (VATS) pleurodesis for malignant effusion: an Australian teaching hospital's experience. *Heart, Lung & Circulation.* 2005;14(2):93-97.
5. Brega-Massone PP, Lequaglie C, Magnani B, Ferro F, Cataldo I. Chemical pleurodesis to improve patients' quality of life in the management of malignant pleural effusions: the 15 year experience of the National Cancer Institute of Milan. *Surgical Laparoscopy, Endoscopy & Percutaneous Techniques.* 2004;14(2):73-79.
6. Cardillo G, Facciolo F, Carbone L, et al. Long-term follow-up of video-assisted talc pleurodesis in malignant recurrent pleural effusions. *European Journal of Cardio-Thoracic Surgery.* 2002;21(2):302-305; discussion 305-306.
7. *World Health Organization. Cancer pain relief.* Geneva: World Health Organization; 1996.

Question Protocol

Field	Content
Review Question	For adults with malignant pleural effusion, is surgery better than talc slurry pleurodesis 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 surgical intervention more effective?
Eligibility criteria – population / disease / condition / issue / domain	Adults (18+) with malignant pleural effusion
Eligibility criteria – intervention(s)	Surgery (talc, abrasion or pleurectomy)
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 '*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	Talc slurry through an intercostal tube remains the standard of care. What is the evidence that informs this practice?