Online Appendix C5 BTS Guideline for Pleural Disease

Section C Pleural infection

Question C5 Evidence Review and Protocol

C5 For adults with pleural infection, which surgical approach provides the best clinical outcomes?

Contents

Question Evidence Review

C5 For adults with pleural infection, which surgical approach provides the best clinical outcomes?

Background

A significant proportion of patients with pleural infection fail to improve following optimal medical therapy, prompting surgery. Different surgical approaches can be used to access the infected space, broadly classified into endoscopic techniques, termed video-assisted thoracoscopic surgery (VATS) or open techniques, termed thoracotomy. This review assessed the relative evidence for the optimal surgical approach in patients with pleural infection.

Outcomes

Mortality, need for repeat intervention, quality of life, patient symptoms, length of hospital stay and complications

Evidence review

The initial literature review identified 34 potentially relevant studies, of which eight were relevant to the review. These included three prospective cohort studies[1-3] and five retrospective cohort studies[4-8].

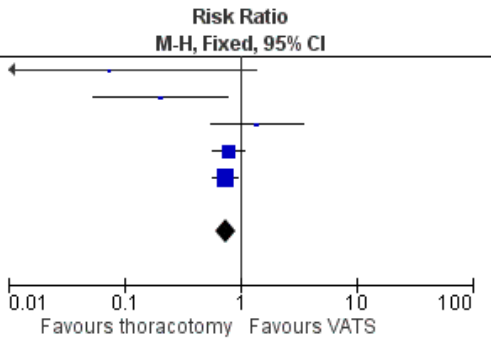
Mortality

'Peri-operative', 28-day or 30-day mortality was reported in seven studies[1-5,7,8], but two studies reported no mortality in both experimental arms[1,2], so were excluded from the meta-analysis. Meta-analysis showed a slightly reduced mortality rate following VATS (35 per 1000 (29 to 42)) when compared with thoracotomy (47 per 1000 patients) for the treatment of pleural infection (Figure C5a).

Figure C5a: Mortality (VATS versus thoracotomy)

	VATS		Thoracotomy			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Cardillo 2009	0	185	4	123	2.3%	0.07 [0.00, 1.36]
Luh 2005	4	194	4	40	2.8%	0.21 [0.05, 0.79]
Reichert 2018	10	110	7	107	3.0%	1.39 [0.55, 3.52]
Semenkovich 2018	71	1313	83	1219	36.8%	0.79 [0.58, 1.08]
Towe 2019	122	4435	106	2881	55.0%	0.75 [0.58, 0.97]
Total (95% CI)		**6237**		**4370**	**100.0%**	**0.75 [0.62, 0.91]**
Total events	207		204			

Heterogeneity: Chi² = 7.80, df = 4 (P = 0.10); I² = 49%
Test for overall effect: Z = 2.95 (P = 0.003)



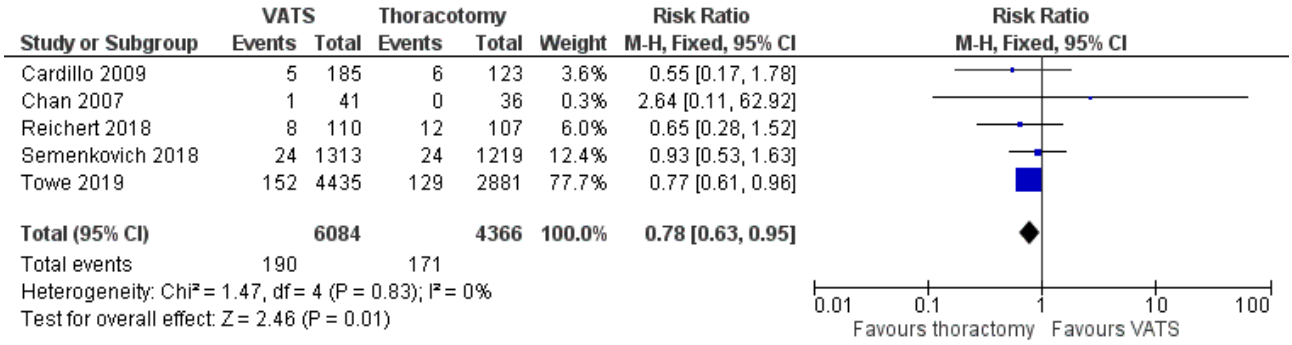
Need for repeat intervention

The need for repeat intervention was reported in five studies and meta-analysis showed that the need for repeat intervention following VATS (31 per 1000 (25 to 37)) was very similar to that following thoracotomy (39 per 1000 patients) (Figure C5b).[1,3,4,7,8]

Quality of Life

Quality of life was not reported in any of the studies.

Figure C5b: Need for repeat intervention (VATS versus thoracotomy)



Patient symptoms

Patient symptoms were reported in two studies[1,4], but the outcomes and reporting methods differed, precluding meta-analysis. Both studies reported pain scores using a 10-point ordinal scale and a summary of the results is shown in Table C5a.

Table C5a: Comparison of pain scores following VATS or thoracotomy for the treatment of pleural infection in adults

		Pain score*			
Study	**Time**	**VATS**	**Thoracotomy**	**Data type**	***p***
Post-operative					
Cardillo 2009[4]	Day 1 and Day 6†	5.0	6.0	Median	<0.0001
Chan 2007[1]	Post-surgery	3.9 ± 2.3	5.3 ± 2.0	Mean ± SD	0.041
Follow-up					
Cardillo 2009[4]	6 months	2.0	2.0	Median	0.7
Chan 2007[1]	36 months‡	0.8 ± 1.3	1.3 ± 1.5	Mean ± SD	0.201

* Self-reported 10-point ordinal scale, with 1 being no pain

† Median of scores taken at Day 1 and Day 6 post-surgery

‡ Mean follow-up time of 36 months

Breathlessness was also reported by Chan et al, with a trend towards a higher mean Medical Research Council (MRC) dyspnoea score following thoracotomy (2.1 ± 2.0, mean ± SD) with VATS (0.9 ± 1.9, $p = 0.069$) after a mean follow-up period of 36 months.[1]

Length of hospital stay

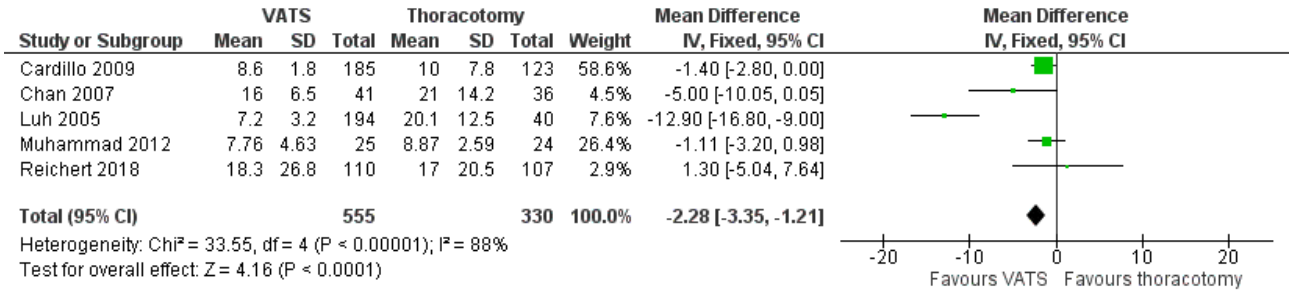
Length of hospital stay (LoS) was reported in all studies, but three studies reported median data (as shown in Table C5b) and hence were excluded from the meta-analysis.[3,6,8] Meta-analysis of the remaining five studies showed that the LoS was 2.3 days shorter (1.2 to 3.4 days) following VATS when compared with thoracotomy for the treatment of pleural infection in adults (Figure C5c).[1,2,4,5,7]

Table C5b: Comparison of length of post-operative hospital stay following VATS or thoracotomy for the treatment of pleural infection in adults

	Length of hospital stay (median days [range])		
Study	**VATS**	**Thoracotomy**	***p***
Marks 2012[6]	5 [4 - 8.5]	7 [5 - 14]	<0.0001
Semenkovich 2018[3]	12 [9 - 19]	15 [10 - 21]	NR
Towe 2019[8]	7 [5 - 11]	8 [6 - 13]	<0.0001

NR – not reported

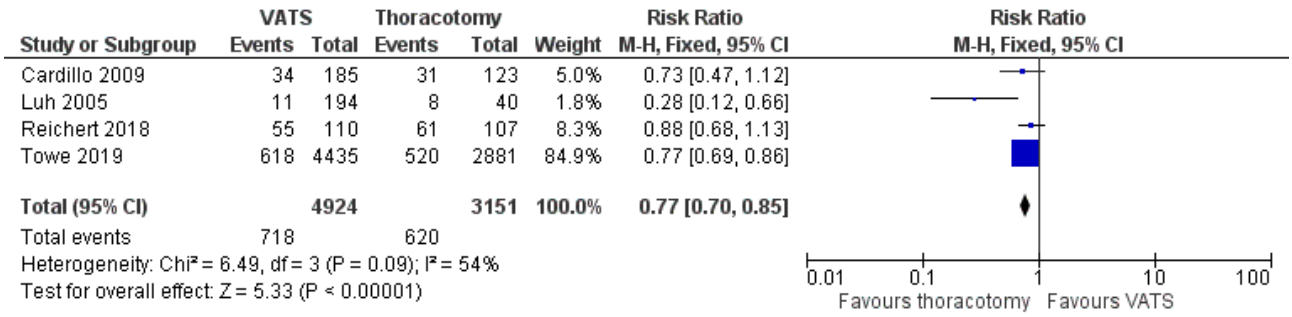
Figure C5c: Length of hospital stay (VATS versus thoracotomy)



Complications

Post-operative complications were reported in six studies, which included prolonged air-leak, bleeding requiring transfusion or re-opening, wound dehiscence, pneumonia, prolonged ventilation and renal failure requiring dialysis.[2,4,5,7,8] One study reported no complications in both experimental arms (VATS or thoracotomy) and was excluded from the meta-analyses.[2] Of the remaining five studies, four reported on the number of participants who had experienced one, or more complication(s)[4,5,7,8] and two reported on individual complications[1,8]. Meta-analysis showed that the number of participants expected to experience one, or more complication(s) was slightly lower following VATS (152 per 1000 patients (138 to 167) compared with 197 per 1000 following thoracotomy (Figure C5d).

Figure C5d: Complications (VATS versus thoracotomy)



Meta-analysis of individual complications (air leak and need for ventilatory support) also showed a slight increase following thoracotomy (Figure C5e) and a summary of the data is shown in Table C5c.

Figure C5e: Individual complications (VATS versus thoracotomy)

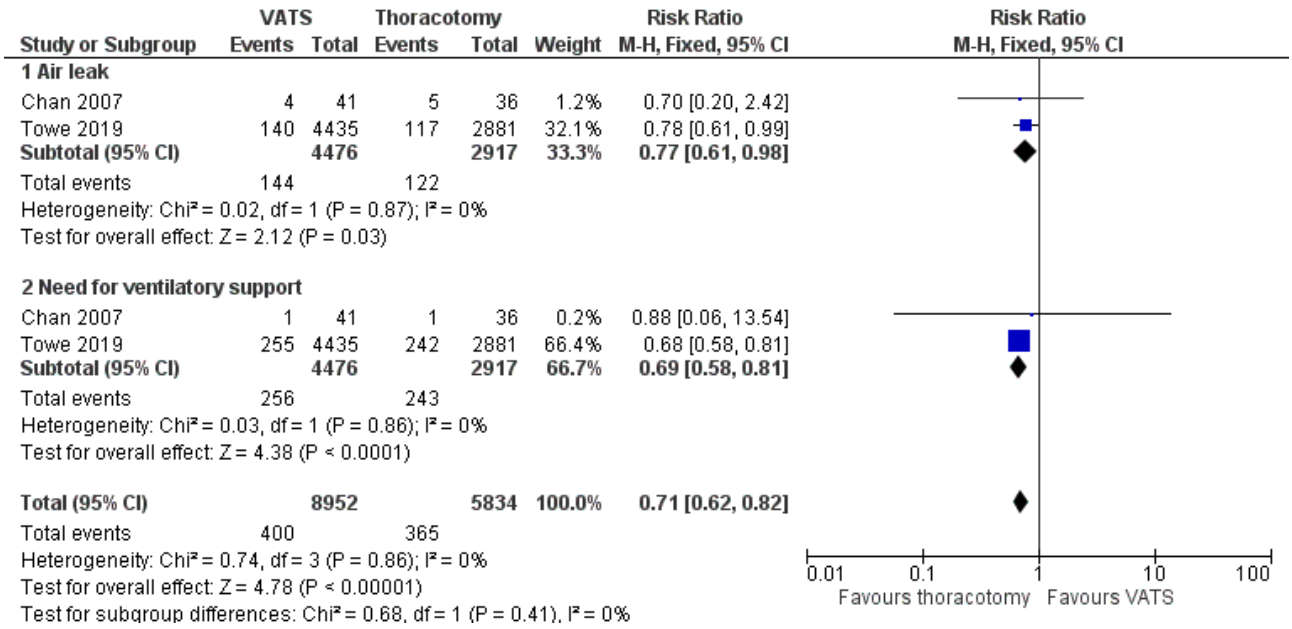


Table C5c: Comparison of rate of individual complications following VATS or thoracotomy for the treatment of pleural infection in adults

Complication	No. studies	**Anticipated risk of complication** (per 1000 patients) VATS	Thoracotomy
Air leak*	2	32 (26 to 41)	42
Need for ventilatory support	2	57 (48 to 67)	83

* Chan et al >7 days duration[1] and Towe et al >5 days duration[8]

Evidence statements

Post-operative mortality and the need for repeat intervention are similar following video-assisted thoracoscopic surgery (VATS) or thoracotomy for pleural infection (**Very low**)

Immediate post-operative pain appears to be less following video-assisted thoracoscopic surgery (VATS) than thoracotomy for pleural infection (**Ungraded**)

Length of hospital stay appears to be shorter following video-assisted thoracoscopic surgery (VATS) than thoracotomy for pleural infection (**Very low**)

Video-assisted thoracoscopic surgery (VATS) access appears to cause fewer post-operative complications than thoracotomy for pleural infection (**Very low**)

Recommendation

- Video-assisted thoracoscopic surgery (VATS) access should be considered over thoracotomy for adults in the surgical management of pleural infection (**Conditional**)

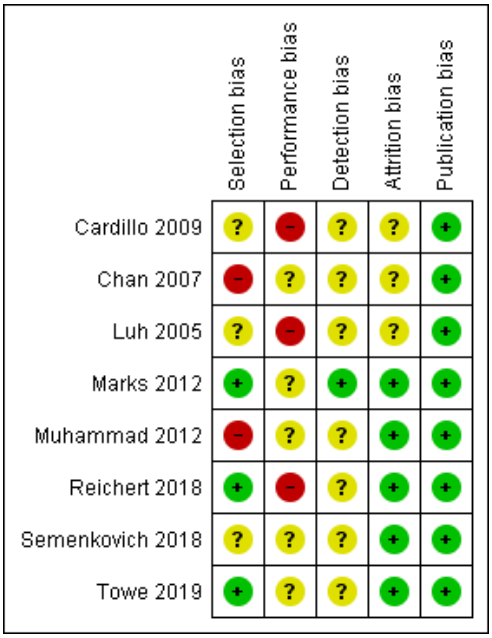
Good Practice Point

- ✓ When selecting a surgical access for the treatment of pleural infection in adults it is important to ensure the technique can facilitate optimal clearance of infected material and achieve lung re-expansion where appropriate

Research Recommendation

- Further research is needed into determining the optimal surgical management of advanced stage empyema with trapped lung

Risk of bias summary



GRADE analyses

For adults with pleural infection, which surgical approach provides the best clinical outcomes?

Population: Adults (18+) with pleural infection

Intervention: Video-assisted thoracoscopic surgery (VATS)

Comparator: Thoracotomy

Outcome	Number of participants (studies)	Relative effect (95% CI)	Anticipated absolute effects		Quality of the Evidence (GRADE)
			Thoracotomy	VATS	
Mortality	10607 (5 studies)	RR 0.75 (0.62 to 0.91)	**47 per 1000**	**35 per 1000** (29 to 42)	⨁◯◯◯ **VERY LOW** [a,b,c]
Repeat intervention	10450 (5 studies)	RR 0.78 (0.63 to 0.95)	**39 per 1000**	**31 per 1000** (25 to 37)	⨁◯◯◯ **VERY LOW** [a,c]
Complications – combined	8075 (4 studies)	RR 0.77 (0.70 to 0.85)	**197 per 1000**	**152 per 1000** (138 to 167)	⨁◯◯◯ **VERY LOW** [a,c]
Complications – air leak	7393 (2 studies)	RR 0.77 (0.61 to 0.98)	**42 per 1000**	**32 per 1000** (26 to 41)	⨁◯◯◯ **VERY LOW** [a,c]
Complications – need for ventilator support	7393 (2 studies)	RR 0.69 (0.58 to 0.81)	**83 per 1000**	**57 per 1000** (48 to 67)	⨁◯◯◯ **VERY LOW** [a,c]

CI: Confidence interval

Explanations

a. High risk of bias across the studies
b. Serious inconsistency across the studies
c. Some imprecision, CIs cross one MID

For adults with pleural infection, which surgical approach provides the best clinical outcomes?

Population: Adults (18+) with pleural infection

Intervention: Video-assisted thoracoscopic surgery (VATS)

Comparator: Thoracotomy

Outcome	Number of participants (studies)	Estimate of effect	Quality of the Evidence (GRADE)
Length of hospital stay	885 (5 studies)	2.28 days lower (1.21 lower to 3.35 lower) in the intervention group	⨁◯◯◯ **VERY LOW** [a,b]

Explanations

a. High risk of bias across the studies

b. Some inconsistency across the studies

Recommendation Table

Question Details

POPULATION:	Adults aged 18+ with pleural infection
INTERVENTION:	Video-assisted thoracoscopic surgery (VATS)
COMPARISON:	Thoracotomy
OUTCOMES:	Mortality; need for repeat intervention; quality of life; patient symptoms; length of hospital stay; complications

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	**Probably yes**	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour the intervention or the comparison	**Probably favours the intervention**	Favours the intervention	Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
☐	☐	☐	☒	☐

CONCLUSIONS

Recommendation

Video-assisted thoracoscopic surgery (VATS) access should be considered over thoracotomy for adults in the surgical management of pleural infection

Justification

Post-operative mortality and the need for repeat intervention are similar following video-assisted thoracoscopic surgery (VATS) or thoracotomy for pleural infection (**Very low**)

Immediate post-operative pain appears to be less following video-assisted thoracoscopic surgery (VATS) than thoracotomy for pleural infection (**Ungraded**)

Length of hospital stay appears to be shorter following video-assisted thoracoscopic surgery (VATS) than thoracotomy for pleural infection (**Very low**)

Video-assisted thoracoscopic surgery (VATS) access appears to cause fewer post-operative complications than thoracotomy for pleural infection (**Very low**)

Subgroup considerations

Subgroups were not considered

Research priorities

Further research is needed into determining the optimal surgical management of advanced stage empyema with trapped lung

References

1. Chan DT, Sihoe AD, Chan S, et al. Surgical treatment for empyema thoracis: is video-assisted thoracic surgery "better" than thoracotomy? *Annals of Thoracic Surgery.* 2007;84(1):225-231.
2. Muhammad MI. Management of complicated parapneumonic effusion and empyema using different treatment modalities. *Asian Cardiovascular & Thoracic Annals.* 2012;20(2):177-181.
3. Semenkovich TR, Olsen MA, Puri V, Meyers BF, Kozower BD. Current state of empyema management. *Annals of Thoracic Surgery.* 2018;105(6):1589-1596.
4. Cardillo G, Carleo F, Carbone L, et al. Chronic postpneumonic pleural empyema: comparative merits of thoracoscopic versus open decortication. *European Journal of Cardio-Thoracic Surgery.* 2009;36(5):914-918.
5. Luh SP, Chou MC, Wang LS, Chen JY, Tsai TP. Video-assisted thoracoscopic surgery in the treatment of complicated parapneumonic effusions or empyemas: outcome of 234 patients. *Chest.* 2005;127(4):1427-1432.
6. Marks DJ, Fisk MD, Koo CY, et al. Thoracic empyema: a 12-year study from a UK tertiary cardiothoracic referral centre. *PLoS ONE [Electronic Resource].* 2012;7(1):e30074.
7. Reichert M, Posentrup B, Hecker A, et al. Thoracotomy versus video-assisted thoracoscopic surgery (VATS) in stage III empyema-an analysis of 217 consecutive patients. *Surgical Endoscopy.* 2018;32(6):2664-2675.
8. Towe CW, Carr SR, Donahue JM, et al. Morbidity and 30-day mortality after decortication for parapneumonic empyema and pleural effusion among patients in the Society of Thoracic Surgeons' General Thoracic Surgery Database. *Journal of Thoracic and Cardiovascular Surgery.* 2019;157(3):1288-1297.e1284.

Question Protocol

Field	Content
Review Question	For adults with pleural infection, which surgical approach provides the best clinical outcomes?
Type of review question	Intervention review
Objective of the review	To determine whether open or video assisted thoracoscopic surgery is better at improving outcomes in patients undergoing surgery for pleural infection.
Eligibility criteria – population / disease / condition / issue / domain	Adults (18+) with pleural infection undergoing surgery
Eligibility criteria – intervention(s)	Thoracotomy
Eligibility criteria – comparators(s)	Video Assisted Thoracoscopic Surgery
Outcomes and prioritisation	Mortality Need for repeat intervention Quality of life Patient symptoms including pain Length of hospital stay Complications
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	VATS and open thoracotomy are associated with differing lengths of stay and complications. Is one better than the other at improving outcomes in surgery for pleural infection?