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REVIEW

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Surgery versus intrapleural fibrinolysis for management of complicated pleural infections: a systematic review and meta-analysis

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Abstract

Background Complicated pleural infection comprises of complex effusions and empyema. When tube thoracostomy is ineffective, treatment options include surgical drainage, deloculation and decortication or intrapleural fibrinolysis. We performed a systematic review and meta-analysis to examine which technique is superior in treating complicated pleural infections.

Methods PubMed, MEDLINE and EMBASE databases were searched for studies published between January 2000 to July 2023 comparing surgery and intrapleural fibrinolysis for treatment of complicated pleural infection. The primary outcome was treatment success. Secondary outcomes included hospital length of stay, chest drain duration and in-hospital mortality.

Results Surgical management of complicated pleural infections was more likely to be successful than intrapleural fibrinolysis (RR 1.18; 95% CI 1.02, 1.38). Surgical intervention group benefited from statistically significant shorter hospital length of stay (MD: 3.85; 95% CI 1.09, 6.62) and chest drain duration (MD: 3.42; 95% CI 1.36, 5.48). There was no observed difference between in-hospital mortality (RR: 1.00; 95% CI 0.99, 1.02).

Conclusion Surgical management of complicated pleural infections results in increased likelihood of treatment success, shorter chest drain duration and hospital length of stay in the adult population compared with intrapleural fibrinolysis. In-hospital mortality did not differ. Large cohort and randomized research need to be conducted to confirm these findings.

Keywords Complicated pleural infection, Empyema, Pleural effusion, Intrapleural fibrinolysis

Introduction

Complicated pleural infections, including complicated parapneumonic effusions and empyema, are characterised by the presence of purulent fluid within the pleural space [1]. They are associated with significant morbidity and mortality, with reported all-comer mortality rates exceeding 10% in the adult population [2–5]. Furthermore, the incidence of complicated pleural infections is increasing in all age groups, placing increasing burden on individuals and healthcare systems around the globe [6].

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The American Thoracic Society describes empyema in three stages: stage I being the exudative stage; stage II being the fibropurulent stage; and stage III being the organized stage (Table 1). For stage I empyema, intravenous antibiotics and chest drain insertion is a common and often adequate initial management strategy, with success rate around 80% [7]. Several options exist to treat more advanced stages of empyema, varying from intrapleural instillation of fibrinolytics, video-assisted thoracoscopic surgery and open decortication.

The rationale behind intrapleural fibrinolytic agent stems from observing decreased concentration tissue plasminogen activator and increased concentration of plasminogen activator inhibitor in the empyema fluid, resulting in overall decreased fibrinolytic activity [8]. By instilling intrapleural fibrinolytic agent, the aim of the treatment is to break down fibrin deposits, reduce fluid viscosity and facilitate drainage [9].

There is no consensus as to which treatment modality should be the next step in the management when antibiotic therapy and chest drain insertion fails, with proponents of early surgery suggesting that the surgical management leads to a better pleural space control, decreased risk of lung restriction and less requirement for an open decortication, while advocates of intrapleural fibrinolysis believe fibrinolysis can reduce the need for surgical intervention and is a reasonable initial management [10–12].

The aim of this systematic review and meta-analysis is to compare the outcomes between intrapleural fibrinolysis and the current gold standard surgical management in adult patients with complicated pleural infections.

Materials and methods

Literature search strategy

Literature search was conducted on PubMed, Ovid MEDLINE and EMBASE databases from 1st January 2000 to 5th July 2023. The search terms used were (empyema OR effusion) AND (fibrinol* OR surg*). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed.

Two authors (JC and BI) conducted independent literature search on selected databases to identify eligible studies. Screening of title, abstract and full manuscript were performed individually. Thirty-one full-text publications were independently reviewed for their eligibility. Discrepancies between authors' decisions were resolved through consensus or referral to third author (JK). Details are outlined in Fig. 1.

Eligibility criteria

The eligibility criteria for study inclusion were: (1) any retrospective or prospective investigative studies excluding case reports; (2) direct comparison between intrapleural fibrinolysis and thoracic surgery; (3) thoracic surgery defined video-assisted thoracoscopic surgery (VATS) or open decortication; (4) presentation of outcomes of stratified by intervention type; (5) publication date from January 2000 to search date; and (6) English language publication.

The primary surgical outcome of interest was treatment success. Secondary outcomes included hospital length of stay, post-operative chest drain duration and in-hospital mortality.

Risk of bias

Quality assessment for non-randomised studies was performed independently by two authors (JC and JK) using the Newcastle–Ottawa Scale [13] (Table 2). This scale assesses selection, comparability and outcome for quality and risk of bias.

Statistical analysis

Continuous variables were presented as either mean and standard deviation or median with interquartile range. Categorical variables were presented as numbers and/or percentages. Meta-analysis was performed using raw data presented in each study and summarised in the form of risk ratios (RR) for binary outcomes and mean

Table 1 Stages of empyema, description, and commonly accepted treatment strategies

Empyema stage	Description	Treatment
I—Exudative	Sterile exudate, low in cellular count, accumulating in the pleural space	Antibiotics Intercostal drain
II—Fibropurulent	Frank pus and increase in white cells	Antibiotics Intercostal drain Fibrinolysis Decortication
III—Organized	Fibroblast proliferation. Formation of thick peel (rind) and potential lung entrapment. Pleural space accumulates very thick exudate with heavy sediment	Antibiotics Fibrinolysis Decortication

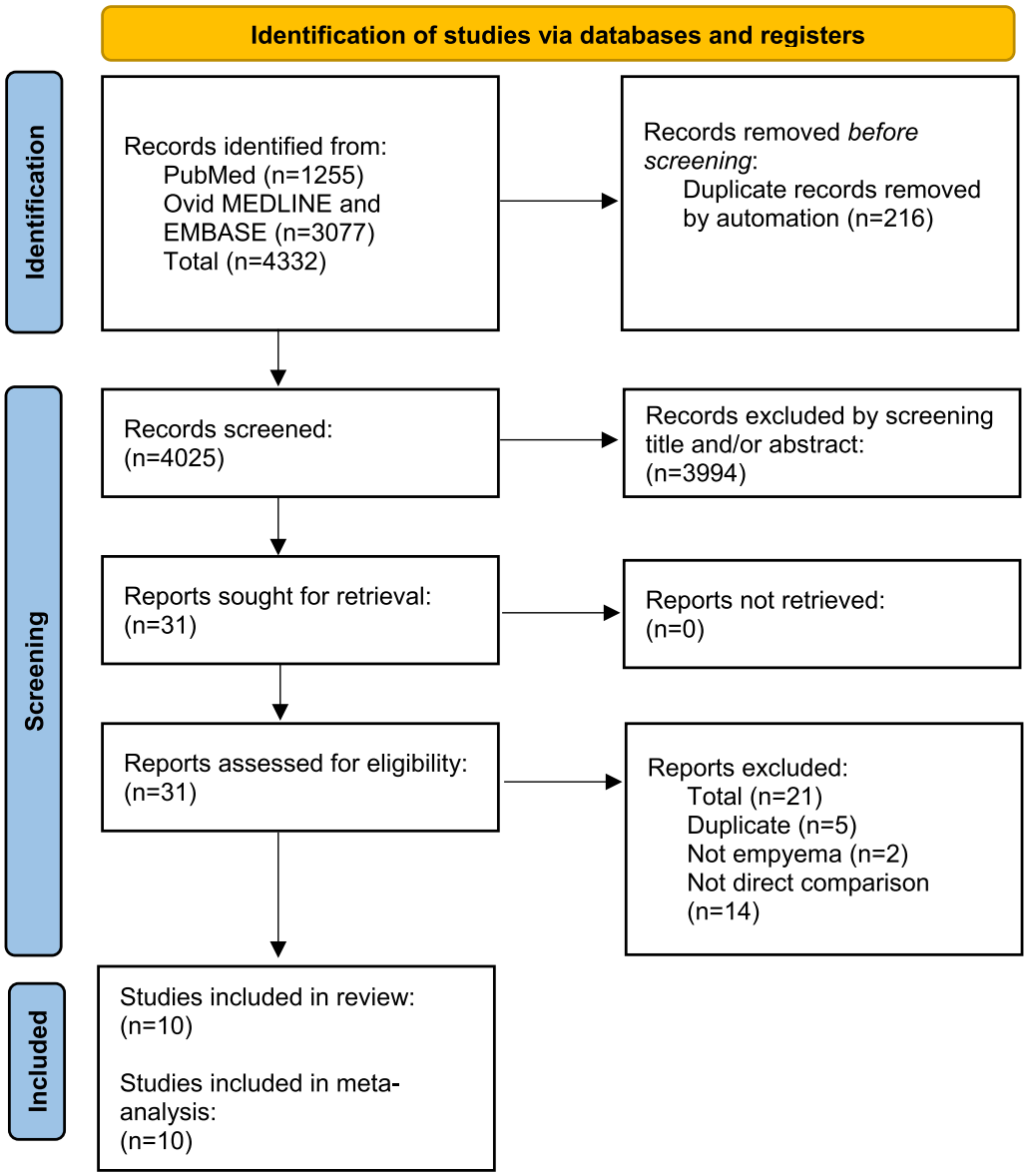

Fig. 1 PRISMA flowchart

difference (MD) for continuous outcomes. Outcomes of interest reported as median and interquartile range were converted to mean and standard deviation by the method outlined by Luo et al. [14], assuming a normal distribution for the cohort. The random effects model was used to assess effect estimates. Tau^2 (T^2) and I^2 values were used to assess heterogeneity. I^2 cut-off of 25%, 50% and 75% were used to indicate low, moderate, and high heterogeneity, respectively. Statistical significance was defined as $p < 0.05$. All statistical analysis was performed using Review Manager 5.4 (Cochrane Collaboration, Software Update, Oxford, UK).

Results

Study characteristics

The literature search returned 4,332 records for screening. After duplicates were removed, 4,025 records were screened based on title and abstract. Thirty-one studies underwent full text review and application of inclusion criteria, following which ten studies were deemed eligible for inclusion in this review [15–24]. Five studies were prospective [15, 18, 21, 23, 24] and remaining five studies [13, 14, 16, 17, 19] were retrospective in nature. All ten studies were included in the meta-analysis.

The total study population was 757 and cohort sizes ranged from 20 to 159. All included studies directly

Table 2 Newcastle–Ottawa Scale

Author, Year	Selection				Comparability		Outcomes			Total/9
	Representiveness of the cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study			Assessment of outcomes	Length of follow up	Adequacy of follow-up	
Ahmed (2016)	*	*	*	*		*	*	*	*	8
Dusemund (2013)		*	*	*		*	*	*	*	7
Ershadi (2022)	*	*	*	*	*	*	*	*	*	9
Federici (2021)	*	*	*	*		*	*	*	*	8
Kermenli (2021)	*	*	*	*		*	*	*	*	8
Metin (2010)		*	*	*	*	*	*	*	*	8
Muhammad (2012)		*	*	*		*	*	*	*	7
Samancilar (2018)	*	*	*	*			*	*	*	7
Suarez (2012)	*	*	*	*		*	*	*	*	8
Wilshire (2023)	*	*	*	*	*	*	*	*	*	9

compared intrapleural fibrinolysis with surgery (VATS and/or open decortication). 376 patients received intrapleural fibrinolysis and 381 patients underwent thoracic surgery. The baseline study characteristics are summarized in Tables 3 and 4.

Intrapleural fibrinolysis

Fibrinolytic agents used included alteplase [16], streptokinase [12, 14, 17–19], urokinase [13, 15, 20], and a combination of tissue plasminogen activator (tPA) and dornase alfa (DNase) [15, 21]. These agents were diluted in 30–250 ml of 0.9% NaCl and instilled via chest tube, where the tube was subsequently clamped for a period of between 1 to 6 h post instillation. The process was repeated up to twice per day, and the maximum duration of therapy was 14 days in one study [12]. Treatment duration was unspecified in two studies [16, 20]. Some studies prescribed a fixed duration of therapy, while others were guided by drain output of < 100 ml/24 h [17, 18].

Surgical technique

The most prevalent surgical technique was video-assisted thoracoscopic surgery (VATS) used in nine out of ten studies [13–21]. Only one study solely focused on thoracotomy and open decortication [12]. Three studies reported outcomes in both VATS and open approaches [13, 18, 20].

Cohort demographics

No statistically significant baseline patient demographic differences were demonstrated between the surgical and intrapleural fibrinolysis groups. Specifically, when comparing surgical group to the intrapleural fibrinolysis group, age (MD: − 1.54; 95% CI − 3.56, 0.47), female sex (RR: 0.86; 95% CI 0.39, 1.90), COPD (RR: 1.43; 95% CI 0.88, 2.34), smoking (RR: 1.10; 95% CI 0.59, 2.06), diabetes (RR: 1.25; 95% CI 0.80, 1.97) and detection of positive fluid culture (RR: 1.29; 95% CI 0.87, 1.92) did not differ significantly.

Clinical outcomes

Surgical management of complicated pleural infections was more likely to be successful than intrapleural fibrinolysis (RR 1.18; 95% CI 1.05, 1.32) (Fig. 2). Patients who received surgical intervention benefited from statistically significant shorter hospital length of stay (MD: 3.85 days; 95% CI 1.09, 6.62 days) (Fig. 3) and chest drain duration (MD: 3.42 days; 95% CI 1.36, 5.48 days) (Fig. 4). There was no observed difference between in-hospital mortality (RR: 1.00; 95% CI 0.99, 1.02).

Sensitivity analysis was performed using the leave-one-out analysis method. Treatment success remained statistically significant. Treatment success remained statistically significant in favour of surgical approach (RR: 1.18; 95% CI 1.02, 1.38) when the largest study reporting treatment success was removed [18]. Similarly, hospital length of stay remained significantly shorter in the surgical group (MD: 4.33 days; 95% CI 1.28, 7.39 days). No statistically significant differences were observed in chest drain duration (MD: 3.75 days; 95% CI 0.76, 6.73) and in-hospital mortality (RR: 1.01; 95% CI 0.98, 1.04).

Comment

To the authors' knowledge, this is the first systematic review and meta-analysis to directly compare outcomes of intrapleural fibrinolysis against the gold standard surgical management in the treatment of complicated pleural infections. Our meta-analysis demonstrated that surgery was more likely to be successful, lead to shorter chest drain duration and hospital length of stay in cohorts matched for potentially confounding factors including age, sex, smoking status, diabetes and positive pleural fluid culture.

Table 3 Summary of Study Characteristics

Author, year	Study period	Location	Study design	Study participants	Follow-up duration
Ahmed, 2016	NR	Pakistan	P	78	In-hospital stay
Dusemund, 2013	Jan 2001 – Dec 2008	Switzerland	R	78	In-hospital stay
Ershadi, 2022	Jan 2018 – Jan 2021	Iran	R	46	In-hospital stay
Federici, 2021	Jan 2014 – Jan 2018	Switzerland	P	159	In-hospital stay
Kermenli, 2021	Mar 2015 – Aug 2020	Turkey	R	49	NR
Metin, 2010	Jan 1995 – Dec 2007	Turkey	R	67	NR
Muhammad, 2012	Jan 2008 – June 2010	Egypt	P	69	6 months
Samancilar, 2018	Jan 2005 – Dec 2014	Turkey	R	78	In-hospital stay
Suarez, 2012	2001 – 2007	Spain	P	113	1 year
Wilshire, 2023	Mar 2019 – Dec 2021	USA	Prospective RCT	20	90 days

NR: Not Reported; P: Prospective; R: Retrospective; RCT: Randomised Controlled Trial

Table 4 Summary of baseline patient characteristics

Author, year	Surgery vs fibrinolysis (n)	Surgical technique	Fibrinolysis technique	Cohort demographics (surgery vs fibrinolysis)	Definition of treatment success
Ahmed, 2016	43 vs 35	Open	Agent(s): Streptokinase Dose: 250,000 units Dilution: 100 ml 0.9% NaCl Chest drain clamp time: 4 h Duration: Daily for up to 14 days	Age: 55.53 (8.82) vs 56.42 (8.21), p = 0.89 BMI: 25.8 (4.56) vs 24.8 (3.9), p = 0.29 Female %: 11.6 vs 17.1 COPD: NR Smoker: 16 vs 12, p = 0.79 Diabetes: 14 vs 9, p = 0.51 Positive pleural fluid culture: 39 vs 33, p = 0.69	Fibrinolysis - Daily drainage < 50 ml or resolution of pleural collection on chest radiography Surgery - No air leak and daily drainage < 50 ml post complete decortication to obtain maximum lung expansion
Dusemund, 2013	30 vs 48	VATS ± Open	Agent(s): Urokinase Dose: 100,000 units Dilution: 100 ml 0.9% NaCl Chest drain clamp time: 4 h Duration: NR; repeated up to 5 times	Age: NR BMI: NR Female %: 42.3 vs 57.7 COPD: NR Smoker: 33 vs 16 Diabetes: 11 vs 2 Positive pleural fluid culture: 17 vs 31	N/A
Ershadi, 2022	28 vs 18	VATS	Agent(s): Streptokinase Dose: 250,000 units Dilution: 100 ml 0.9% NaCl Chest drain clamp time: 4 h Duration: 4 consecutive days	Age: 45.6 (10.6) vs 47.1 (11.3), p = 0.666 BMI: NR Female %: 21.4 vs 22.2, p = 0.949 COPD: 2 vs 1 Smoker: NR Diabetes: 4 vs 3 Positive pleural fluid culture: 13 vs 9	- Sufficient pulmonary expansion thus not requiring decortication via thoracotomy
Federici, 2021	66 vs 93	VATS	Agent(s): Urokinase (until 2016)→ tPA + DNase Dose: 250,000 units→ 10 + 5 mg Dilution: 30 ml 0.9% NaCl Chest drain clamp time: 3 h Duration: BD for 5 days→BD for 5 days	Age: 56 [16] vs 62 [17], p = 0.048 BMI: Female %: 30.3 vs 31.2, p = 0.906 COPD: 8 vs 7, p = 0.705 Smoker: NR Diabetes: 6 vs 14 p = 0.057 Positive pleural fluid culture: 28 vs 24	- Daily drainage < 200 ml - Cessation of air-leak - Resolution of infection / sepsis - Resolution of pleural loculations
Kermenli, 2021	28 vs 21	VATS	Agent(s): Alteplase Dose: 10 mg Dilution: 100 ml 0.9% NaCl Chest drain clamp time: 1 h Duration: BD; treatment duration not specified	Age: Combined: 50.6 (17.8), p = 0.294 BMI: NR Female %: NR separately COPD: 5 vs 1 Smoker: NR Diabetes: 4 vs 4 Positive pleural fluid culture: 5 vs 6	- Lung expansion - Cessation of air-leak - Serous drain output - Daily drainage < 200 ml
Metin, 2010	44 vs 23	VATS	Agent(s): Streptokinase Dose: 250,000 units Dilution: 250 ml 0.9% NaCl Chest drain clamp time: 4–6 h Duration: Daily, until drainage < 100 ml/24 h and serous	Age: 49 [15] vs 55 [16] BMI: NR Female %: 40.9 vs 26.1 COPD: NR Smoker: NR Diabetes: NR Positive pleural fluid culture: 31 vs 13	- Daily drainage < 100 ml - Serous drain output - > 50% pleural fluid drainage - Adequate lung expansion - Control of sepsis

Table 4 (continued)

Author, year	Surgery vs fibrinolysis (n)	Surgical technique	Fibrinolysis technique	Cohort demographics (surgery vs fibrinolysis)	Definition of treatment success
Muhammad, 2012	49 vs 20	VATS and Open	Agent(s): Streptokinase Dose: 250,000 units Dilution: 100 ml 0.9% NaCl Chest drain clamp time: 4 h Duration: Daily for 7 days or until < 100 ml/24 h	Age: 32.0 (8.86) vs 32.3 (9.62) BMI: NR Female %: 25.49 vs 25 COPD: NR Smoker: NR Diabetes: NR Positive pleural fluid culture: NR	Fibrinolysis - Daily drainage < 100 ml - Radiologic resolution of pleural collection Surgery - Complete lung re-expansion (lungs touching lateral wall and diaphragm) - Cessation of air leak - Daily drainage < 100 ml
Samancilar, 2018	54 vs 24	VATS	Agent(s): Streptokinase Dose: 250,000 units Dilution: NR Chest drain clamp time: NR Duration: Daily for 5 days	Age: 44.48 (16.77) vs 45.75 (13.17), p = 0.744 BMI: NR Female %: 24.07 vs 20.83, p = 0.754 COPD: 10 vs 5 Smoker: NR Diabetes: 5 vs 0 Positive pleural fluid culture: NR	N/A
Suarez, 2012	29 vs 84	VATS ± Open	Agent(s): Urokinase Dose: 100,000 units Dilution: NR Chest drain clamp time: NR Duration: TDS for 48 h	Age: 53.2 (13.4) vs 51.7 (12.5) BMI: NR Female %: 24.1 VS 20.2 COPD: 7 vs 12 Smoker: 16 vs 45 Diabetes: 3 vs 14 Positive pleural fluid culture: NR	N/A
Wilshire, 2023	10 vs 10	VATS	Agent(s): tPA and DNase Dose: 10 mg and 5 mg Dilution: NR Chest drain clamp time: 1 h Duration: BD for total of 4 to 6 doses	Age: 59.2 (17.2) vs 52.4 (18.1) BMI: 27 [24–29] vs 24 [22–33] Female %: 20 vs 30 COPD: 1 vs 1 Smoker: NR Diabetes: 1 vs 1 Positive pleural fluid culture: 7 vs 4	- Resolution of infection (fever, leucocytosis and persistent pleural collection > 48 h post intervention)

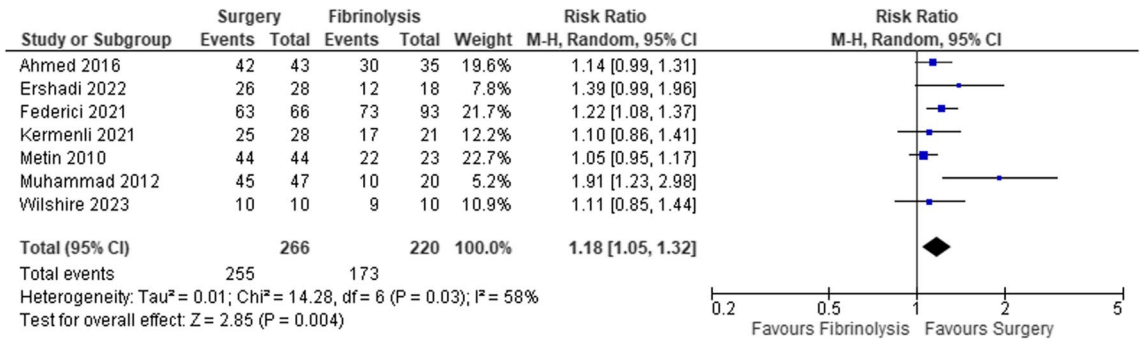

Fig. 2 Forest plot displaying relative risk (RR) of treatment success between surgical management and intrapleural fibrinolysis

Standard initial medical management, comprising of antibiotics and chest tube drainage, is reported to fail in approximately 30% of patients [25]. It should be noted that while intrapleural fibrinolysis may beneficially avoid surgery in a select group of patients, its failure means delayed surgical referral and treatment leading to further deterioration of patients. Further, it can increase the complexity of the operation by increasing the likelihood of conversion to open surgery and bleeding, given studies have reported approximately 4% clinically significant

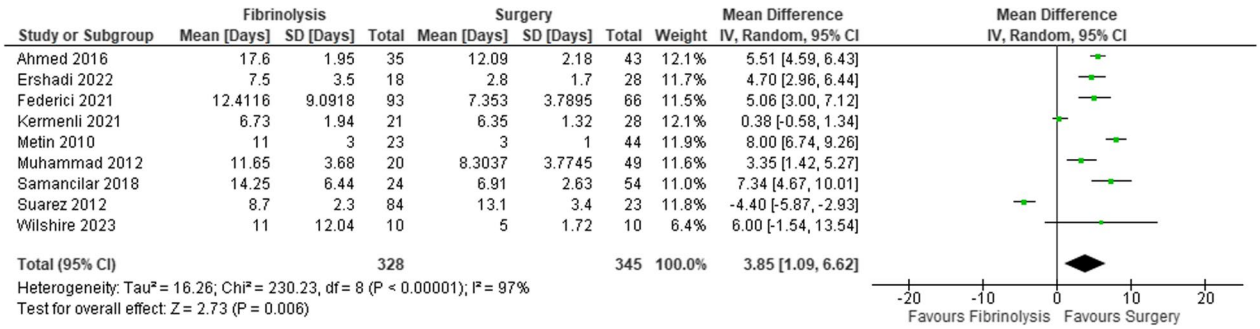

Fig. 3 Forest plot displaying mean difference (MD) of hospital length of stay between surgical management and intrapleural fibrinolysis, displayed in days

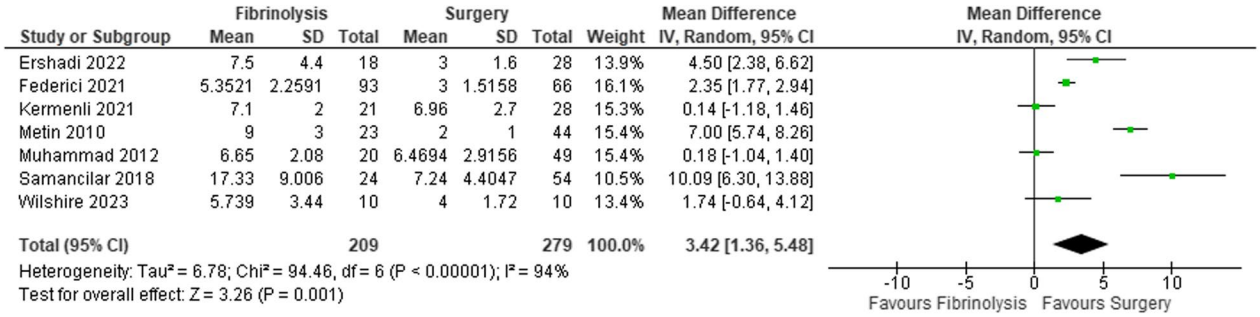

Fig. 4 Forest plot displaying mean difference (MD) of chest drain duration between surgical management and intrapleural fibrinolysis, displayed in days

bleeding risk where majority of those affected required an active intervention such surgical exploration (25%), additional chest drain (6%) or administration of blood products (53%) [26]. Evidently, serious complications can arise within the intrapleural fibrinolysis group and in-hospital mortality did not differ between the two comparable cohorts. Thus, our analysis supports the notion that patients with complicated pleural infections should be promptly referred to thoracic surgeons for review and determination of surgical candidacy to avoid any delay in treatment with view to determining the best treatment strategy within the multidisciplinary setting involving surgeons and respiratory physicians.

This study has several limitations. The results of current meta-analysis are moderate- to highly heterogenous. The cause of the heterogeneity is likely multifactorial, reflecting the small pooled cohort size, inconsistencies in the treatment regimens particularly in the fibrinolysis arm and inherent ambiguity in defining what is "treatment success". Sensitivity analysis performed to circumvent this issue showed that the primary outcome of treatment success as well as the important measure of hospital length of stay remained statistically significant in favour of surgical decortication. Difference in chest drain duration was no longer statistically significant and in-hospital mortality remained statistically indifferent. Selection bias is also particularly relevant in current meta-analysis as in many studies patient assignment to treatment were not randomized. This could mean that those who were referred and treated for surgery may have had a better physiological baseline to tolerate such invasive procedure. For example, the fibrinolysis cohort in the study by Federici et al. [18] were statistically significantly older, and almost significantly more likely to be diabetic whereas Dusemund et al. [16] observed that those in the surgical group were more frequent smokers and diabetic. These baseline differences may serve as a major confounder in the analysis.

Further, owing to the small number of studies that were eligible for this systematic review and meta-analysis, we were unable to examine several potentially insightful outcomes such as morbidity, time until return to work, opioid use and quality of life after discharge from the hospital. These deficiencies highlight the need for future high-powered trials which compare the two treatment strategies.

Conclusion

Our analysis demonstrates that surgical management of complicated pleural infections is more likely to be successful and result in shorter chest drain duration and hospital length of stay in the adult population. In-hospital mortality did not differ. Larger randomised controlled trials and research reporting on short and long-term outcomes, economic burden and other important measures of morbidity are required to confirm the current findings and to determine optimal treatment for complicated pleural infections.

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Author contributions
J.C. conducted the literature search, data analysis, Figs. 1–4 and wrote the manuscript. J.K. conducted the literature search and data analysis. B.I. conducted the literature search and prepared Table 1. S.C. extracted data from research papers and prepared Tables 3 and 4. C.F. provided expert opinion and guidance on the topic. All authors reviewed the manuscript.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Shin JA, Chang YS, Kim TH, Haam SJ, Kim HJ, Ahn CM, et al. Surgical decortication as the first-line treatment for pleural empyema. J Thorac Cardiovasc Surg. 2013;145(4):933-9 e1.
2. Ferguson AD, Prescott RJ, Selkon JB, Watson D, Swinburn CR. The clinical course and management of thoracic empyema. QJM. 1996;89(4):285–9.
3. Farjah F, Symons RG, Krishnadasan B, Wood DE, Flum DR. Management of pleural space infections: a population-based analysis. J Thorac Cardiovasc Surg. 2007;133(2):346–51.
4. Davies CW, Kearney SE, Gleeson FV, Davies RJ. Predictors of outcome and long-term survival in patients with pleural infection. Am J Respir Crit Care Med. 1999;160(5 Pt 1):1682–7.
5. Maskell NA, Davies CW, Nunn AJ, Hedley EL, Gleeson FV, Miller R, et al. U.K. Controlled trial of intrapleural streptokinase for pleural infection. N Engl J Med. 2005;352(9):865–74.
6. Rosenstengel A. Pleural infection-current diagnosis and management. J Thorac Dis. 2012;4(2):186–93.
7. Berger HA, Morganroth ML. Immediate drainage is not required for all patients with complicated parapneumonic effusions. Chest. 1990;97(3):731–5.
8. Aleman C, Alegre J, Monasterio J, Segura RM, Armadans L, Angles A, et al. Association between inflammatory mediators and the fibrinolysis system in infectious pleural effusions. Clin Sci (Lond). 2003;105(5):601–7.
9. Tuncozgur B, Ustunsoy H, Sivrikoz MC, Dikensoy O, Topal M, Sanli M, et al. Intrapleural urokinase in the management of parapneumonic empyema: a randomised controlled trial. Int J Clin Pract. 2001;55(10):658–60.
10. Bouros D, Antoniou KM, Chalkiadakis G, Drositis J, Petrakis I, Siafakas N. The role of video-assisted thoracoscopic surgery in the treatment of parapneumonic empyema after the failure of fibrinolytics. Surg Endosc. 2002;16(1):151–4.
11. 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):1427–32.
12. Rahman NM, Maskell NA, West A, Teoh R, Arnold A, Mackinlay C, et al. Intrapleural use of tissue plasminogen activator and DNase in pleural infection. N Engl J Med. 2011;365(6):518–26.
13. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa: University of Ottawa; 2000.
14. Luo D, Wan W, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. Stat Methods Med Res. 2018;27(6):1785–805.
15. Ahmed S, Azam H, Basheer I. Is open decortication superior to fibrinolytic therapy as a first line treatment in the management of pleural empyema? Pak J Med Sci. 2016;32(2):329–32.
16. Dusemund F, Weber MD, Nagel W, Schneider T, Brutsche MH, Schoch OD. Characteristics of medically and surgically treated empyema patients: a retrospective cohort study. Respiration. 2013;86(4):288–94.
17. Ershadi R, Vahedi M, Rafieian S. Efficacy of video-assisted thoracoscopic surgery versus intrapleural streptokinase for treatment of parapneumonic empyema with multiloculation and septation. Kardiochir Torakochirurgia Pol. 2022;19(2):86–9.
18. Federici S, Bedat B, Hayau J, Gonzalez M, Triponez F, Krueger T, et al. Outcome of parapneumonic empyema managed surgically or by fibrinolysis: a multicenter study. J Thorac Dis. 2021;13(11):6381–9.
19. Kermenli T, Azar C. Can intrapleural alteplase treatment be an alternative to videothoracoscopic deloculation and decortication in pleural empyema? Wideochir Inne Tech Maloinwazyjne. 2021;16(3):580–6.
20. Metin M, Yeginsu A, Sayar A, Alzafer S, Solak O, Ozgul A, et al. Treatment of multiloculated empyema thoracis using minimally invasive methods. Singapore Med J. 2010;51(3):242–6.
21. Muhammad MI. Management of complicated parapneumonic effusion and empyema using different treatment modalities. Asian Cardiovasc Thorac Ann. 2012;20(2):177–81.
22. Samancilar O, Akcam TI, Kaya SO, Ozturk O, Akcay O, Ceylan KC. The efficacy of VATS and intrapleural fibrinolytic therapy in parapneumonic empyema treatment. Ann Thorac Cardiovasc Surg. 2018;24(1):19–24.
23. Rodriguez Suarez P, Freixinet Gilart J, Hernandez Perez JM, Hussein Serhal M, Lopez Artalejo A. Treatment of complicated parapneumonic pleural effusion and pleural parapneumonic empyema. Med Sci Monit. 2012;18(7):443–9.
24. Wilshire CL, Jackson AS, Vallieres E, Bograd AJ, Louie BE, Aye RW, et al. Effect of intrapleural fibrinolytic therapy vs surgery for complicated pleural infections: a randomized clinical trial. JAMA Netw Open. 2023;6(4):e237799.
25. Subotic D, Lardinois D, Hojski A. Minimally invasive thoracic surgery for empyema. Breathe (Sheff). 2018;14(4):302–10.
26. Akulian J, Bedawi EO, Abbas H, Argento C, Arnold DT, Balwan A, et al. Bleeding risk with combination intrapleural fibrinolytic and enzyme therapy in pleural infection: an international, multicentre, retrospective cohort study. Chest. 2022;162(6):1384–92.

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