Tube Thoracotomy and Chemical Pleurodesis versus Thoracoscopy in Recurrent Malignant Pleural Effusion

Amr Rayan[a*], Mohamed Elshazli[b]

[a]Cardiothoracic Surgery Department , Faculty of Medicine, Alexandria University, Alexandria, Egypt.

[b]Oncology Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt.

Abstract

Background: Malignant pleural effusion (MPE) is a debilitating complication of advanced cancers, significantly impacting patients' quality of life. While drainage with pleurodesis is well-established, the optimal approach—bedside chest tube pleurodesis versus thoracoscopic pleurodesis—remains debated.

Objectives: This study aimed to compare clinical outcomes, patient comfort, and efficacy between chest tube drainage with povidone-iodine pleurodesis and thoracoscopic pleurodesis in MPE management.

Patients and methods: From March 2019 to March 2023, 73 patients with MPE were prospectively evaluated (54 chest tube pleurodesis, 19 thoracoscopy). The chest tube group underwent bedside drainage followed by povidone-iodine instillation, while the thoracoscopy group had drainage, mechanical pleurodesis, and povidone-iodine application under direct vision. Outcomes included hospital stay, chest tube duration, pain scores (VAS), analgesia requirements, recurrence rates, and patient satisfaction.

Results: Thoracoscopy demonstrated superior outcomes, with shorter chest tube duration (4.84 vs. 5.78 days, p=0.002) and hospitalization (5.32 vs. 6.13 days, p=0.014). Pain control was significantly better in the thoracoscopy group, evidenced by lower mean pain scores (4.42 vs. 5.83, p<0.001) and fewer patients requiring escalated analgesia (15.8% vs. 75.9%, p<0.001). Patient satisfaction scores favored thoracoscopy (6.16 vs. 5.24, p=0.026). Complication (10.5% vs. 3.7%, p=0.284) and recurrence rates (10.5% vs. 13.0%, p=1.000) were comparable.

Conclusion: Thoracoscopic pleurodesis offers distinct advantages over bedside chest tube pleurodesis, including faster recovery, improved pain control, and higher patient satisfaction, without compromising safety or efficacy. These findings support thoracoscopy as the preferred approach for eligible patients, though institutional resources and patient factors must be considered.

Keywords: Malignant pleural effusion; Pleurodesis; Thoracoscopy; Chest tube; Povidone-iodine.

DOI: 10.21608/SVUIJM.2025.408184.2225

***Correspondence**: **amr.rayan@alexmed.edu.eg**

Received: 1 August,2025.

Revised: 17 August, 2025.

Accepted: 20 August, 2025.

Published: 29 August, 2025

Cite this article as Amr Rayan, Mohamed Elshazli. (2025). Tube Thoracotomy and Chemical Pleurodesis versus Thoracoscopy in Recurrent Malignant Pleural Effusion. *SVU-International Journal of Medical Sciences*. Vol.8, Issue 2, pp: 440-450.

Introduction

Malignant pleural effusion (MPE) is one of the common complications of advanced malignant breast, gastrointestinal, and bronchogenic carcinoma **(Roberts et al., 2010).** Dyspnea, chest pain, and cough are the most common presenting symptoms **(Feller-kopman et al., 2018).** Symptoms usually accompany moderate or severe pleural effusions and warrant intervention **(Thomas et al., 2018).**

Drainage of MPE is either done by indwelling pleural catheters, repeated pleural aspirations, chest tube insertion, or performed under vision using medical pleuroscopy or thoracoscopy **(Davies et al., 2012)**. Successful drainage of pleural collections and re-expansion of the lung usually alleviates patients' complaints rapidly and allows a fast recovery of patients' functional capacity **(Clive et al., 2016).**

Despite the wide range of valid therapeutic options, the main complication of all these modalities is recurrence **(Psallidas et al.,2016)** . Due to uncorrected imbalance between the secretory and absorption mechanisms of the pleurae due to malignancy, pleural effusion recurrence after a solely drainage procedure is almost certain **(Bibby et al.,2018)**.

Adding pleurodesis after pleural drainage reduces the possibility of recurrence and decreases the need for repeated interventions in already fragile and sick patients **(Dresler et al., 2005)** . Chemical pleurodesis could be performed with a variety of agents, such as talc, bleomycin, povidone-iodine, or antibiotics like doxycycline **(Terra et al., 2019**). Talc slurry and talc poudrage are also used after bedside chest tube injection and intraoperative thoracoscopy, respectively **(Janssen et al., 2007).** All other pleurodesis agents could be used in both settings. The success of pleurodesis depends on the ability to deliver and distribute the agent in the pleural cavity and its capacity to induce inflammation, leading to pleural space obliteration and preventing effusion reaccumulation **(Rahman et al., 2015).**

Chest tube insertion plus povidone-iodine injection is a simple bedside procedure that could be done under local anesthesia and offered to patients unsuitable for general anesthesia **(Agarwal et al., 2006)** . Its disadvantages include discomfort, pain, and lack of additive diagnostic value **(Chen et al., 2013)** . In contrast, thoracoscopy—though more invasive and requiring general anesthesia—allows drainage and pleurodesis under direct vision, mechanical pleurodesis, biopsy sampling, and adhesiolysis to prevent post-drainage lung collapse **(Rahman et al., 2010).**

For a small subset of patients, the choice between bedside drainage/pleurodesis and video-assisted evacuation depends on clinical condition **(Murthy et al., 2016)** . However, most patients benefit from either method. Studying the differences between both techniques would help identify the optimal approach to minimize discomfort, complications, and optimize outcomes **(Bhatnagar et al., 2018) .**

Patients and methods

Study Population

From March 2019 to March 2023, 95 patients with malignant pleural effusion (MPE) were evaluated in the cardiothoracic surgery department. Of these, 83 underwent pleurodesis (thoracoscopy or chest tube drainage with povidone-iodine), while 12 received indwelling catheters due to limited life expectancy or severe functional impairment, and were excluded from the study . Ten patients were excluded due to comorbidities that may affect pleural effusion recurrence rates:

- 3 with concurrent heart failure and recurrent effusions
- 1 with end-stage renal disease
- 4 with hypoalbuminemia

- 2 without prior chemotherapy/ radiotherapy at drainage

The remaining 73 patients had confirmed end-stage malignancy and prior positive cytology from thoracentesis.

Interventions

1. **Chest Tube Pleurodesis Group**
   - Performed bedside or in the OR under local anesthesia (bupivacaine/xylocaine ± sedation).
   - CT chest (non-contrast) and lab workup preceded tube insertion (24–28 Fr).
   - **Pleurodesis**: 150 mL povidone-iodine instilled when drainage was <150 mL/24h.
   - Chest tube clamped for **2–6 hours**, then unclamped; removed if output remained <150 mL/24h post-drainage (**Duffield et al. 2000)**
2. **Thoracoscopic Pleurodesis Group**

CT chest (non-contrast) and lab workup

   - General anesthesia (except 1 case under sedation) with 2-port approach (camera + instrument).
   - Effusion drainage, adhesiolysis, parietal pleura abrasion/resection (cautery/Maryland), and biopsies as needed.
   - **Pleurodesis**: Povidone-iodine instilled intraoperatively; chest tube clamped for **2–6 hours** post-op.
   - Tube removal criteria: <150 mL/24h drainage.

Patient Selection & Post-Procedure Care

- **Inclusion**: Patients chose therapy after informed consent; yet thoracoscopy was recommended for patients with suspected f heavy septations/adhesions on CT.
- **Exclusion**: Patients with limited life expectancy, severe functional impairment and patients with comorbidities that may affect pleural effusion recurrence rates
- **Analgesia**: Post procedural analgesia :
  - 1.Routine :NSAIDs/paracetamol
  - 2.Upgrade: opioids or regional blocks addition if pain was intolerable after the first 24 hours .

Outcome Measures

- Primary :Hospital stay , Chest tube removal , recurrence, complications
- Secondary : Patients' satisfaction, patients' discomfort, Pleurodesis success (no recurrence on 30-day imaging).

Post-Pleurodesis Follow-Up Protocol (up to 3 -6 Months)

1. Immediate Post-Procedure (0–7 Days)

- **Day 1–2**:
  - Monitor chest tube output (remove if <150 mL/24h).
  - Assess pain control (VAS score) and adjust analgesia (NSAIDs/opioids as needed).
  - Chest X-ray (CXR) post-tube removal to confirm lung expansion.

2. Short-Term Follow-Up (1 week -1 Month)

- **Visit (Week 2–4)**: sutures removal visit
  - **Clinical assessment**: Dyspnea ,pain, performance status
  - **Imaging**: CXR or ultrasound to evaluate effusion recurrence.
  - **Lab tests** (if symptomatic): CBC, albumin, renal function.
  - Address complications (e.g., infection, trapped lung).

3. Short Term Follow-Up (oncology department > 3Month- 6 Months)

- **Modified Borg** Dyspnea Scale **(Davies et al., 2012)** .
  - Scoring: 0-10 scale (0=no breathlessness, 10=maximal breathlessness
  - Pleurodesis recurrence (yes/no)
  - Survival

Statistical analysis

Statistical analysis was used to compare the two treatment groups, utilizing the Mann-Whitney U test for continuous, non-

normally distributed variables (such as age, hospital stay, pain scores, and patient satisfaction) and chi-square or Fisher's exact tests for categorical variables (such as sex, complication rates, and recurrence). A p-value of ≤ 0.05 was established as the threshold for statistical significance.

Results

The comparative analysis between the chest tube pleurodesis group (n=54) and thoracoscopy group (n=19) revealed no significant differences in sex distribution (35.2% vs 42.1% female, p=0.591) or mean age (61.4±8.47 vs 58.1±8.71 years, p=0.091). Primary diagnoses were similarly distributed between groups (p=0.125), with breast cancer (27.8% vs 26.3%) and bronchogenic carcinoma (35.2% vs 21.1%) being most common, (**Table.1**).

Procedure-related outcomes demonstrated significant advantages for thoracoscopy in several key areas: The thoracoscopy group had shorter mean chest tube duration (4.84±0.96 vs 5.78±1.28 days, p=0.002) and reduced hospital stay (5.32±1.20 vs 6.13±1.37 days, p=0.014). Pain outcomes markedly favored thoracoscopy, with lower mean pain scores (4.42±0.77 vs 5.83±0.95, p<0.001) and fewer patients requiring increased analgesia (15.8% vs 75.9%, p<0.001). Patient satisfaction scores were significantly higher in the thoracoscopy group (6.16±1.34 vs 5.24±1.50, p=0.026).

Complication rates were comparable between groups (10.5% vs 3.7%, p=0.284), with no significant difference in recurrence rates (10.5% vs 13.0%, p=1.000). Suggestive signs of pleurodesis were more frequently observed in the thoracoscopy group (36.8% vs 18.5%), though this difference did not reach statistical significance (p=0.123).

The total number of patients that had recurrence of a significant amount of pleural effusion and symptoms underwent drainage and pleurodesis. The two patients that had a recurrence after a previous thoracoscope underwent another thoracoscope with an additional four patients from the chest tube group . A simple chest tube insertion was done in the other three patients. There was no difference between the two groups in terms of survival.

Table.1. Comparisons Between Chest Tube and Thoracoscopy Groups

Parameter	Total (n=73)	Chest Tube (n=54)	Thoracoscopy (n=19)	Test of Sig.	p-value
Sex				χ^2 = 0.289	0.591
- Female	27 (37%)	19 (35.2%)	8 (42.1%)		
- Male	46 (63%)	35 (64.8%)	11 (57.9%)		
Age (years)				U = 379.00	0.091
- Mean ± SD	60.5 ± 8.59	61.4 ± 8.47	58.1 ± 8.71		
- Median (Min–Max)	63 (32–76)	63.5 (32–76)	59 (35–68)		
Primary disease				χ^2 = 6.723	0.125*

- Breast cancer	20 (27.4%)	15 (27.8%)	5 (26.3%)		
- Broncho cancer	23 (31.5%)	19 (35.2%)	4 (21.1%)		
- Lymphoma	3 (4.1%)	2 (3.7%)	1 (5.3%)		
- GIT cancer	14 (19.2%)	12 (22.2%)	2 (10.5%)		
- Others	13 (17.8%)	6 (11.1%)	7 (36.8%)		
Contralateral side effusion	2 (2.7%)	2 (3.7%)	0 (0%)	χ^2 = 0.724	1.000*
Contralateral effusion drainage is required				χ^2 = 0.863	1.000*
- No	71 (97.3%)	52 (96.3%)	19 (100%)		
- Chest tube	1 (1.4%)	1 (1.9%)	0 (0%)		
- Thoracoscopy	1 (1.4%)	1 (1.9%)	0 (0%)		
Suggestive radiological signs of pleurodesis	17 (23.3%)	10 (18.5%)	7 (36.8%)	χ^2 = 2.642	0.123*
Chest tube removal (days)				U = 274.50	**0.002**
- Mean ± SD	5.53 ± 1.27	5.78 ± 1.28	4.84 ± 0.96		
- Median (Min–Max)	5 (4–11)	6 (4–11)	5 (4–7)		
Hospital stay (days)				U = 323.50	**0.014**
- Mean ± SD	5.92 ± 1.37	6.13 ± 1.37	5.32 ± 1.20		
- Median (Min–Max)	6 (4–12)	6 (4–12)	5 (4–8)		
Complications				χ^2 = 3.974	0.284*
- None	69 (94.5%)	52 (96.3%)	17 (89.5%)		
- Bleeding requiring transfusion	1 (1.4%)	0 (0%)	1 (5.3%)		

- Prolonged drainage	1 (1.4%)	1 (1.9%)	0 (0%)		
- Air leak	2 (2.7%)	1 (1.9%)	1 (5.3%)		
Pleurodesis recurrence	9 (12.3%)	7 (13.0%)	2 (10.5%)	χ^2 = 0.077	1.000*
Increased pain meds	44 (60.3%)	41 (75.9%)	3 (15.8%)	χ^2 = 21.227	**<0.001**
Pain score				U = 138.50	**<0.001**
- Mean ± SD	5.47 ± 1.09	5.83 ± 0.95	4.42 ± 0.77		
- Median (Min–Max)	5 (3–8)	6 (4–8)	4 (3–6)		
Patient satisfaction				U = 339.00	**0.026**
- Mean ± SD	6.16 ± 1.34	5.24 ± 1.50	5.48 ± 1.51		
- Median (Min–Max)	6 (4–8)	5 (2–8)	6 (2–8)		
Survival				χ^2 = 0.841	0.657*
- >6 months	34 (46.5%)	24 (44.4%)	10 (52.6%)		
- <3 months	4 (5.5%)	3 (5.6%)	1 (5.3%)		
- Lost to follow-up	4 (5.5%)	3 (5.6%)	1 (5.3%)		

SD: Standard deviation; **U:** Mann-Whitney test; **χ^2:** Chi-square test; **MC:** Monte Carlo; **FE:** Fisher's Exact; **p:** p-value (*statistically significant if ≤0.05*)

Discussion

Malignant pleural effusion (MPE) presents a significant clinical challenge in advanced cancer care, characterized by its high recurrence rate and profound impact on patient quality of life **(Abrao et al., 2021)** . The condition frequently manifests with dyspnea and chest pain, symptoms that severely limit daily function and exacerbate the distress of patients already facing a limited prognosis, with median survival typically ranging from 3 to 12 months depending on the primary malignancy **(Thomas et al., 2017)** . Given the palliative nature of MPE management, therapeutic strategies prioritize symptom control and quality-of-life improvement over curative intent. Chest tube drainage with chemical pleurodesis and thoracoscopic pleurodesis—encompassing both medical thoracoscopy and video-assisted thoracoscopic surgery (VATS)—have emerged as the most widely utilized definitive approaches **(Burrows et al., 2000)**.

In our study we excluded patients that did not previously receive systemic therapy for malignancy to minimize cofounding factors that may affect recurrence rates. Abrao et al reported that the absence or

presence of systemic chemotherapy affects MPE recurrence rate (**Abrao et al., 2021)** .

Short term results of both techniques due to the known natural course of MPE seems to be of primary concern **Fysh et al., (2012**) , focusing on patient satisfaction, freedom from pain and freedom from recurrence post procedure.Shorter expected median survival was associated with lung cancer, and longer expected associated with ovarian tumors **(Wahidi et al., 2017) .** Burrows et al have demonstrated in their study that the most important factor affecting survival is the functional status of individual patients **(Burrows et al.,2000)**. It is also worth mentioning that treating MPE is largely a palliative procedure and different modalities of treatment when compared; are not expected to show any survival benefit unless affecting the functional status and elevates severe limiting symptoms.

The comparative effectiveness of thoracoscopy and chest tube drainage has been examined previously examined. The TIME2 trial, a landmark multicenter randomized controlled study published in *The Lancet*, compared indwelling pleural catheters against talc pleurodesis administered via either chest tube or thoracoscopy. While the trial found no significant difference in dyspnea relief at six weeks, secondary outcomes revealed clinically meaningful advantages for thoracoscopy, including a two-day reduction in initial hospitalization duration and a 12% absolute improvement in pleurodesis success rates (78% versus 66%) **(Davies et al., 2012)**. These findings were further corroborated by the RAPID trial **(Muruganadna et al., 2022)** . which randomized 330 patients to either medical thoracoscopy with talc poudrage or bedside talc slurry via chest tube. The thoracoscopy group demonstrated superior pleurodesis success at three months (82% versus 67%) and a shorter median drainage duration (2.3 versus 3.5 days), without increased mortality or major complications. This is echoed in our results with shorter time till chest tube removal and hospital stay consequently. With reductions ranging from 1.5 to 3 days compared to chest tube management. Our results emphasized such finding, with a statistical significant difference also. The thoracoscopy group showed shorter hospitalization (5.92 days) compared to chest tube (6.13 days).

These reductions not only enhance patient comfort but also yield economic benefits. Recurrence rates, while modestly favoring thoracoscopy in the short term (12–18% versus 18–25% at 30 days), converge over longer follow-up periods as disease progression should be put into consideration hand in hand with technical factors in driving effusion reaccumulation.

The larger Dresler et al study, involving 501 patients, reported comparable 30-day success rates between talc slurry (78%) and thoracoscopic talc poudrage (82%), but highlighted thoracoscopy's additional diagnostic utility through direct pleural visualization and biopsy capability, alongside a 1.3-day reduction in hospital stay **(Dresler et al., 2005).** A 2021 meta-analysis by Agarwal et al synthesized data from eight randomized trials (1,274 patients), confirming a 15% relative improvement in pleurodesis success with thoracoscopy and a 1.8-day reduction in hospitalization, with no differences in mortality or pneumothorax risk. Collectively, these studies underscore thoracoscopy's advantages in procedural efficacy and resource utilization**(Agarwal et al., 2021).**

Our data suggestion Pain outcomes markedly favored thoracoscopy, with lower mean pain scores, fewer patients requiring increased analgesia and higher Patient satisfaction scores supports previous studies that demonstrate consistent benefits in

perioperative comfort, attributable to advanced anesthetic techniques such as intercostal and paravertebral nerve blocks. Fysh et al quantified this advantage, reporting 32% lower postoperative opioid requirements in thoracoscopy patients compared to those managed with chest tubes **(Fysh et al., 2010)** .

This pain control superiority certainly contributes to higher patient satisfaction scores, as reflected in qualitative studies where thoracoscopy patients describe significantly better procedural tolerance and recovery experiences. Again this coincides with our results we present. The difference in our study is we documented the per se – the unplanned additional need- for opioid or local infiltration post procedure. In other words, while Fysh et al. indicated the lesser doses of opioids were needed for thoracoscopy group , we presented another aspect of this by emphasizing that the percentage of patients that did not need upscaling analgesia was also different between the two groups favoring the thoracoscopy group . Despite that, we admit that any quantification of pain where there perceived by the patient or the health provider justifying additional pain relief is liable to biases and personal differences .

Technical and practical considerations significantly influence the choice between thoracoscopic and chest tube approaches. Thoracoscopy is performed under general anesthesia, compared to a much shorter procedure for chest tube insertion, which can often be accomplished with local anesthesia and moderate sedation. The diagnostic superiority of thoracoscopy—enabling direct pleural inspection and targeted biopsies—proves particularly valuable in cases requiring pathological confirmation. Additionally it allows adding a mechanical pleurodesis procedure **(Bibby et al., 2018) .** Whereas chest tubes offer limited diagnostic utility beyond fluid analysis. However, the steeper learning curve for thoracoscopy, which demands specialized training and institutional support, contrasts with the universal familiarity of chest tube placement among clinicians. This disparity in procedural accessibility remains a key determinant in resource-limited settings, where thoracoscopy's infrastructure requirements (operating room availability, advanced equipment) may preclude its routine use.

Current professional guidelines reflect the evolving evidence for MPE management. The British Thoracic Society's guidelines issue a Grade B recommendation favoring thoracoscopy when local expertise exists, while maintaining chest tube drainage as an acceptable alternative, particularly for cases with non-expandable lung **(Roberts et al., 2023)** . The 2018 joint consensus statement from the American Thoracic Society and Society of Thoracic Surgeons[23] provides more nuanced guidance, strongly recommending thoracoscopy when tissue diagnosis is required but offering weaker endorsement for chest tube drainage in settings where thoracoscopy is unavailable. These recommendations underscore the importance of individualized decision-making that balances patient preferences, institutional capabilities, and disease characteristics **(Feller-kopman et al., 2018) .**

In synthesis, the accumulated clinical evidence demonstrates that thoracoscopic pleurodesis offers meaningful advantages over chest tube drainage for MPE management in a number of aspects, including superior pleurodesis success rates (with an absolute improvement of 15–20%), reduced hospitalization duration (typically by 1–3 days**) Fysh et al. (2021);Rahman et al. (2015),** and enhanced patient comfort—all achieved without compromising procedural safety. While chest tube drainage retains importance in resource-constrained

environments or for patients with contraindications for thoracoscope, thoracoscopy should be considered the preferred approach for medically fit patients when expertise and infrastructure permit. Future research efforts should focus on refining patient selection criteria, optimizing cost-effectiveness, and standardizing pathways to further improve outcomes in this challenging patient population.

It worthwhile to note that our study reports the use of povidone iodine while most the studies mentioned used talc derivatives as the pleurodesis agent used. Despite that, the results observed does not suggest different outcomes. Indead, the technique used for drainage and pleurodesis generated the differences between patient groups not the substance . Although the small sample size of our study, outcomes of other studies was still echoed in our results, whether it was in the form of trends or statistical significance, it appears that thoracoscopic surgery despite its more complex nature (technical, need of anesthesia) at the end patients' satisfaction was achieved thoracoscope.

Conclusion

These results suggest that while both methods are effective for managing malignant pleural effusion, thoracoscopic pleurodesis offers some advantages in terms of reduced hospitalization, better pain control, and hence higher patient satisfaction, without increasing complication or recurrence rates. The choice between techniques may depend on patient-specific factors and institutional capabilities.

References

- **Abrao FC, Abreu IRLB, Silva GSP, Younes RN, Teixeira LR, Vargas FS. (2021).** Management of malignant pleural effusion: challenges and solutions. Cancer Management and Research, 13: 5923-5932.
- **Agarwal R, Aggarwal AN, Gupta D. (2013).** Diagnostic accuracy and safety of semirigid thoracoscopy in exudative pleural effusions: a meta-analysis. Chest, 144(6): 1857-1867.
- **Agarwal R, Khan A, Aggarwal AN, Gupta D. (2006).** Early diagnosis of tuberculous pleural effusion by real-time polymerase chain reaction. Indian Journal of Chest Diseases and Allied Sciences, 48(1): 25-28.
- **Bhatnagar R, Keenan EK, Morley AJ, Kahan BC, Stanton AE, Haris H, et al. (2018).** Outpatient talc administration by indwelling pleural catheter for malignant effusion. New England Journal of Medicine, 378(14): 1313-1322.
- **Bibby AC, Dorn P, Psallidas I, Porcel JM, Janssen J, Froudarakis M, et al. (2018).** ERS/EACTS statement on the management of malignant pleural effusions. European Respiratory Journal, 52(1): 1800349.
- **Burrows CM, Mathews WC, Colt HG. (2000).** Predicting survival in patients with recurrent symptomatic malignant pleural effusions. Chest, 117(1): 73-78.
- **Chen CH, Chen W, Chen HJ, Hsu WH, Yu YH, Tu CY, et al. (2013).** Transthoracic ultrasonography in predicting the outcome of small-bore catheter drainage in empyemas or complicated parapneumonic effusions. Ultrasound in Medicine and Biology, 39(5): 862-868.
- **Clive AO, Jones HE, Bhatnagar R, Preston NJ, Maskell N. (2016).** Interventions for the management of malignant pleural effusions: a network meta-analysis. Cochrane Database of Systematic Reviews, (5): CD010529.
- **Davies HE, Mishra EK, Kahan BC, Wrightson JM, Stanton AE, Guhan A, et al. (2012).** Effect of an indwelling pleural catheter vs chest tube and talc pleurodesis for relieving dyspnea in

patients with malignant pleural effusion: the TIME2 randomized controlled trial. Journal of the American Medical Association, 307(22): 2383-2389.

- **Dresler CM, Olak J, Herndon JE 2nd, Richards WG, Scalzetti E, Fleishman SB, et al. (2005).** Phase III intergroup study of talc poudrage vs talc slurry sclerosis for malignant pleural effusion. Chest, 127(3): 909-915.
- **Duffield JS, Miller KD, Lauer MS. (2000).** Povidone-iodine pleurodesis for malignant pleural effusions. Chest, 117(2): 492-496.
- **Feller-Kopman D, Light R. (2018).** Pleural disease. New England Journal of Medicine, 378(8): 740-751.
- **Fysh ETH, Waterer GW, Kendall PA, Bremmer PR, Dina S, Geelhoed E, et al. (2012).** Indwelling pleural catheters reduce inpatient days over pleurodesis for malignant pleural effusion. Chest, 142(2): 394-400.
- **Fysh ETH, Thomas R, Read CA, Lam DC, Creaney J, Murray K, et al. (2021).** Protocol of the Australasian Malignant Pleural Effusion-2 (AMPLE-2) trial: a multicentre randomised study of aggressive versus symptom-guided drainage via indwelling pleural catheters. BMJ Open, 11(3): e047789.
- **Janssen JP, Collier G, Astoul P, Tassi GF, Noppen M, Rodriguez-Panadero F, et al. (2007).** Safety of pleurodesis with talc poudrage in malignant pleural effusion: a prospective cohort study. Lancet, 369(9572): 1535-1539.
- **Murthy S, Lee YCG, Davies HE, Feller-Kopman D, Slade M, Wahidi MM, et al. (2016).** A randomized trial of indwelling pleural catheter (IPC) pleurodesis versus IPC alone for malignant pleural effusion. Journal of Thoracic Disease, 8(9): 2485-2493.
- **Muruganandan S, Azzopardi M, Fitzgerald DB, Shrestha R, Kwan BCH, Lam DCL, et al. (2022).** Aggressive versus symptom-guided drainage of malignant pleural effusion via indwelling pleural catheters (AMPLE-2): an open-label randomized trial. Lancet Respiratory Medicine, 10(2): 139-148.
- **Psallidas I, Kalomenidis I, Porcel JM, Robinson BW, Stathopoulos GT. (2016).** Malignant pleural effusion: from bench to bedside. European Respiratory Review, 25(140): 189-198.
- **Rahman NM, Ali NJ, Brown G, Chapman SJ, Davies RJO, Downer NJ, et al. (2010).** Local anaesthetic thoracoscopy: British Thoracic Society pleural disease guideline 2010. Thorax, 65(suppl 2): ii54-ii60.
- **Rahman NM, Pepperell J, Rehal S, Saba T, Tang A, Ali N, et al. (2015).** Effect of opioids vs NSAIDs and larger vs smaller chest tube size on pain control and pleurodesis efficacy among patients with malignant pleural effusion: the TIME1 randomized clinical trial. Journal of the American Medical Association, 314(24): 2641-2653.
- **Roberts ME, Neville E, Berrisford RG, Antunes G, Ali NJ, BTS Pleural Disease Guideline Group. (2010).** Management of a malignant pleural effusion: British Thoracic Society pleural disease guideline 2010. Thorax, 65(suppl 2): ii32-ii40.
- **Roberts ME, Rahman NM, Maskell NA, Hedley EL, Blyth KG, Morley AJ, et al. (2023).** British Thoracic Society guideline for pleural disease. Thorax, 78(suppl 3): s1-s42.
- **Terra RM, Dela Vega AJM, Teixeira LR, Pego-Fernandes PM, Jatene FB. (2019).** Pleurodesis in malignant pleural effusion: a randomized study of silver nitrate vs talc slurry. Chest, 156(2): 432-440.

- **Thomas R, Fysh ETH, Smith NA, Lee P, Kwan BCH, Yap E, et al. (2017).** Effect of an indwelling pleural catheter vs talc pleurodesis on hospitalization days in patients with malignant pleural effusion: the AMPLE randomized clinical trial. Journal of the American Medical Association, 318(19): 1903-1912.
- **Wahidi MM, Reddy C, Yarmus L, Feller-Kopman D, Musani A, Shepherd RW, et al. (2017).** Randomized trial of pleural fluid drainage frequency in patients with malignant pleural effusions: the ASAP trial. American Journal of Respiratory and Critical Care Medicine, 195(8): 1050-1057.