Malignant Effusions

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Malignant Effusions

- Definition: Presence of malignant cells in the pleural space
- 75% are caused by neoplasms of
  - Lung
  - Breast
  - Ovary
  - Lymphoma
- Regardless of etiology overall median survival from diagnosis is 4 months

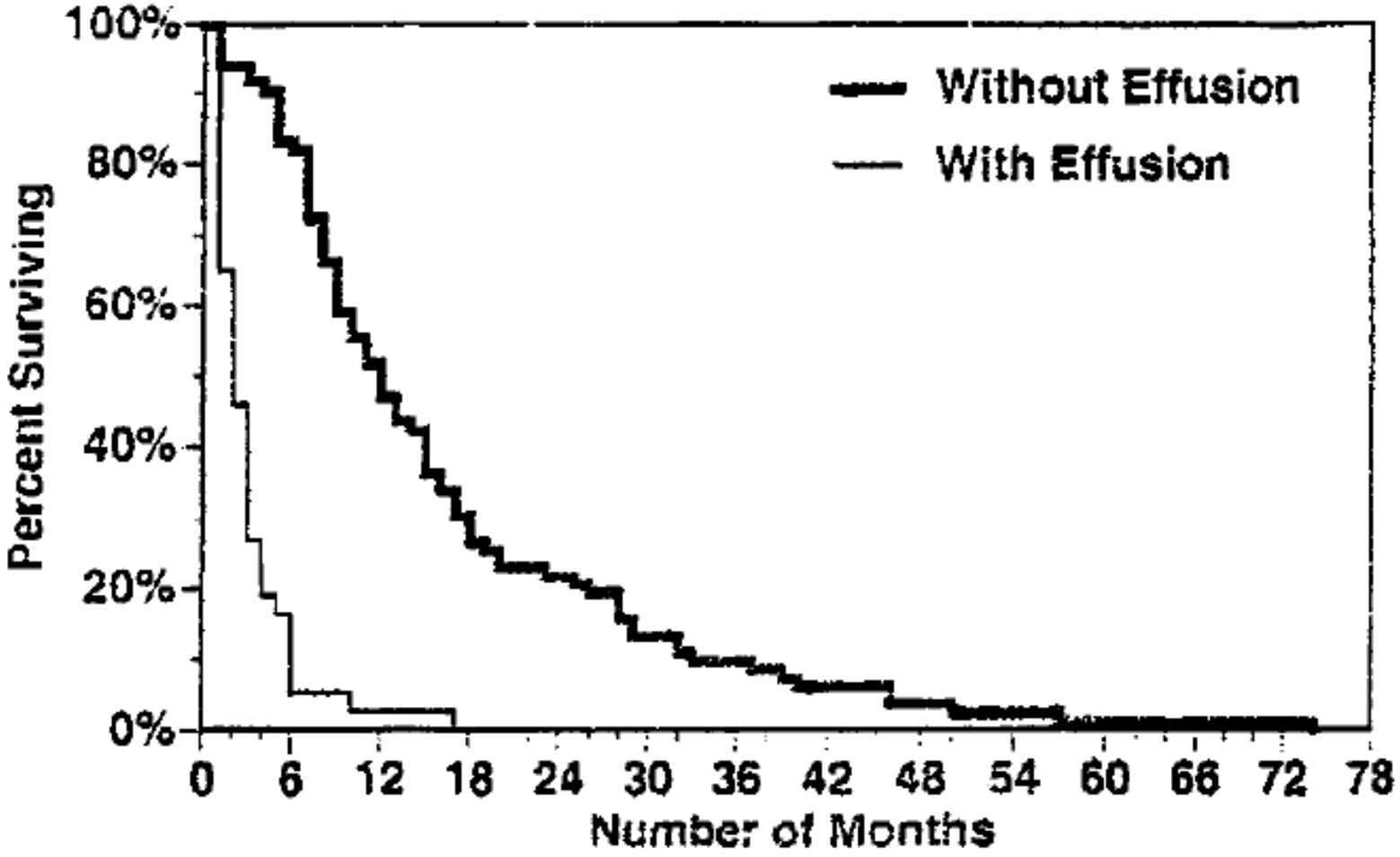


FIGURE 1. Kaplan-Meier survival rate by AJCC stage for patients with stage IIIB NSCLC.

Pathogenesis

- Established by
  - Direct extension
  - Embolization to visceral pleura via pulmonary vasculature
  - Hematogenous mets to parietal pleura
- Once established
  - Obstruction of lymphatics
  - Chemokines increasing vascular and pleural permeability
- Lymphomas
  - Hodgkin's Disease: Thoracic duct obstruction
  - Non Hodgkin's Disease: Pleural infiltration

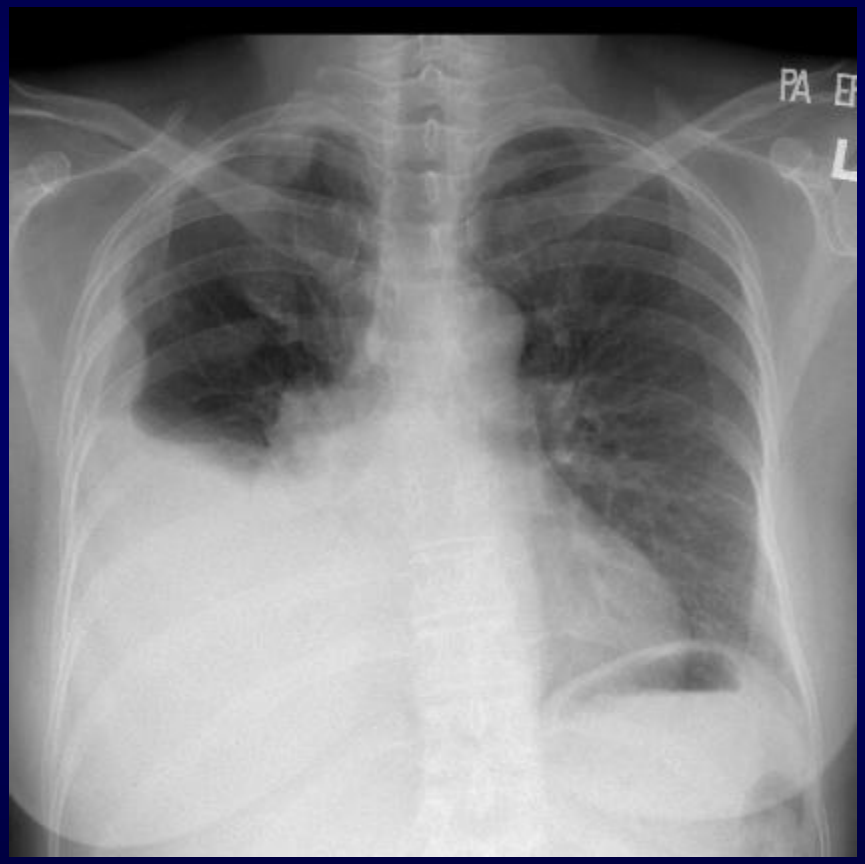
Paramalignant Effusions

- Local Effects
  - Blocked lymphatics
  - Endobronchial obstruction with atelectasis
  - Trapped lung
  - Chylothorax
  - SVC syndrome
  - Pericardial effusion
- Systemic Effects
  - Pulmonary embolism
  - Hypoalbuminemia
- Complications of therapy
  - Radiation induced pleuritis
  - Chemotherapy: Cyclophosphamide, mitomycin, methotrexate

The detection of an effusion coincident with a newly diagnosed cancer does not establish a malignant pleural effusion because 50% are non malignant.

Radiological diagnosis

- Circumferential lobulated pleural thickening
- Crowding of ribs
- Elevated hemidiaphragm
- Ipsilateral mediastinal shift



Advanced diagnostic imaging

- CT scans
  - Circumferential pleural thickening
  - Pleural nodules
  - Parietal pleural thickness > 10mm
  - Mediastinal pleural involvement
  - Evidence of primary tumour
  - Sensitivity 88-100% Specificity 22-56%
- PET-FDG combined with CT
  - Sensitivity 95%, specificity 80%, PPV 91%, NPV 89%

Pleural fluid analysis

- Transudative in 3 to 10% of malignant effusions because of imperfect application of diagnostic rules and co-morbid conditions such as CCF and cirrhosis
- Role of biomarkers?

Diagnostic accuracy of tumour markers for malignant pleural effusion: a meta-analysis

Q-L Liang, H-Z Shi, X-J Qin, X-D Liang, J Jiang, H-B Yang

Table 1 Pooled results of diagnostic accuracy of each tumour marker in malignant pleural effusions (MPE)

	CA 125	CA 15-3	CA 19-9	CYFRA 21-1
Number of studies	10	11	7	18
Number of patients with MPE/non-MPE	512/801	819/966	598/488	1152/1122
Sensitivity (95% CI)	0.48 (0.44 to 0.53)	0.51 (0.47 to 0.54)	0.25 (0.21 to 0.28)	0.55 (0.52 to 0.58)
Heterogeneity* (p)	212.65 (<0.001)	76.46 (<0.001)	99.32 (<0.001)	246.24 (<0.001)

Pleural fluid cytology

- Diagnostic yield about 65%
- Does not increase with volume of fluid but with repeated thoracentesis

Pleural biopsy

- Closed pleural biopsy: Leads to a diagnosis in only 7 % of patients with pre-existing negative cytology
- CT-guided sensitivity 87%, specificity 100%, PPV 100%, NPV 80 %
- (Needs at least 5 mm thickening of pleura)

Thoracoscopy

- Sensitivity 90-100%
- However, less effective in providing a specific diagnosis for non-malignant pleural disease
- Leads to a diagnosis with unexplained exudative pleural effusions in only 50%
- Refer patients if
  - Symptoms > 1 month
  - Absence of fever
  - Hemorrhagic effusion
  - Radiological findings of malignancy

Ferrer J et al. Chest 2005; 127(3): 1017

ORIGINAL ARTICLE

Prospective evaluation of flex-rigid pleuroscopy for indeterminate pleural effusion: Accuracy, safety and outcome

PYNG LEE,[1] ANNE HSU,[1] CONSTANCE LO[1] AND HENRI G. COLT[2]

[1]*Department of Respiratory and Critical Care Medicine, Singapore General Hospital, Singapore, and* [2]*Pulmonary and Critical Care Medicine, University of California, Irvine Medical Center, Orange, California, USA*

Diagnostic accuracy of flex-rigid pleuroscopy (%)	96
Sensitivity	94
Specificity	100
Negative predictive value	88

Prospective evaluation of flex-rigid pleuroscopy for indeterminate pleural effusion: Accuracy, safety and outcome

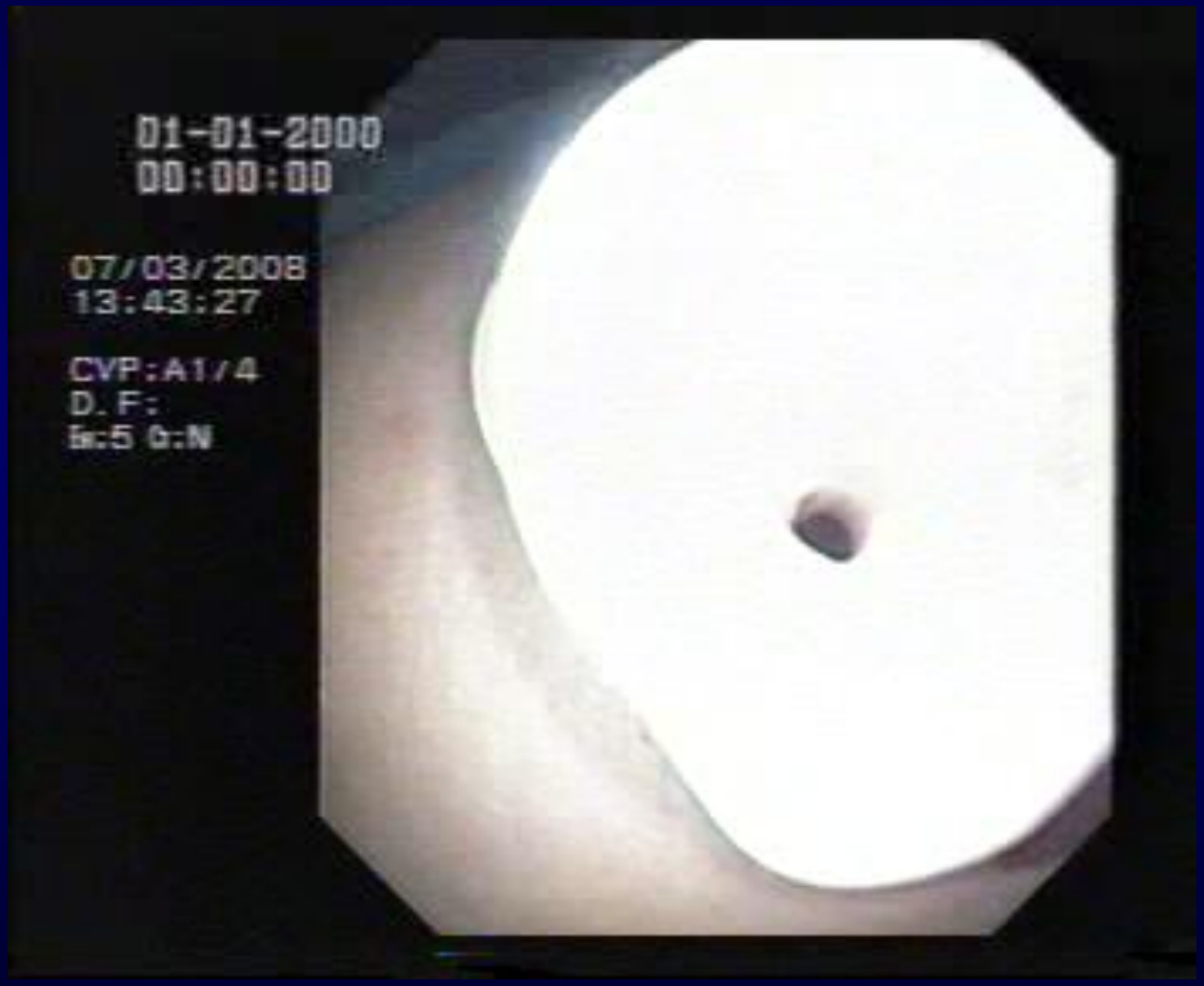
PYNG LEE,[1] ANNE HSU,[1] CONSTANCE LO[1] AND HENRI G. COLT[2]

[1]*Department of Respiratory and Critical Care Medicine, Singapore General Hospital, Singapore, and* [2]*Pulmonary and Critical Care Medicine, University of California, Irvine Medical Center, Orange,*

Table 3 Indicators of the safety and accuracy of pleuroscopy

Variables	Values
Procedure	
Median time to pleuroscopy (days)	3 (range, 2–4)
Median dose of midazolam (mg)	2 (range, 2–3)
Median duration of procedure (min)	30 (range, 30–40)
Median pain score (VAS)	2 (range, 2–3)
Complications	
Major	0
Minor	
Fever	8 (16%)
Perioperative pain requiring additional IM analgesia (VAS 5, range 4–6)	5 (10%)
Mortality at 30 days	0%

Medical thoracoscopy/Pleuroscopy



Management of Malignant Pleural Effusions

- Paradigm is palliative and does not improve survival.
- Most physicians wait for symptoms or functional limitations before intervening
- Early intervention to prevent complications
  - Lung entrapment
  - Loculations

If symptoms do not improve with large volume thoracentesis, alternative causes of dyspnoea should be identified.

TABLE 4. **Causes of Dyspnea in Patients With Malignant Pleural Effusions**

- Pleural
  - Malignant effusions
  - Effusions caused by
    - Drugs
    - Pneumonia
    - Heart failure
    - Pulmonary embolism
- Pulmonary parenchyma
  - Lymphangitic cancer
  - Chemotherapy-induced pneumonitis or fibrosis
  - Radiation fibrosis or pneumonitis
  - Extensive tumor mass with lung restriction
- Airways
  - Airway obstruction by tumor
  - Bilateral vocal cord paralysis from recurrent laryngeal nerve praxis
- Cardiac and pericardial
  - Chronic heart failure
  - Pericardial effusion
  - Constrictive pericarditis
  - Restrictive cardiomyopathy due to tumor infiltration
- Vascular
  - Pulmonary thromboemboli
  - Tumor emboli
- Other
  - Deconditioning
  - Poor nutrition
  - Cancer-related cachexia
  - Myopathy
  - Chest wall invasion by tumor
  - Progression of underlying lung disease (eg, emphysema)

Therapeutic Thoracentesis

- Although symptoms can improve after thoracentesis 98-100% of patients with malignant effusions re-accumulate within 30 days
- Repeated thoracentesis reserved for
  - Slow re-accumulation
  - Chemo responsive cancers eg. Lymphoma, breast
  - Patient unlikely to survive beyond 1-3 months
  - Patient cannot tolerate more interventional procedures

TABLE 3. **Questions to Guide Selection of Patients for Pleurodesis**

Is the underlying tumor and resulting malignant pleural effusion responsive to chemotherapy or radiotherapy?
Are the patient's respiratory symptoms caused by the effusion?
Does the patient's dyspnea improve after therapeutic thoracentesis?
Do alternative causes of dyspnea exist that will not respond to pleurodesis?
Does the patient's life expectancy warrant pleurodesis (eg, is it longer than 2-3 months)?
Will pleurodesis resolve the effusion and sufficiently improve the patient's symptoms?
Does the lung expand to the chest wall after therapeutic thoracentesis?
Do imaging studies suggest multiloculated effusions and thick visceral pleural membranes suggestive of a trapped lung?
Will the amount of intrapleural tumor prevent an effective pleurodesis?
Do imaging studies detect large tumor masses along pleural surfaces?

Pleurodesis

- Despite careful patient selection at expert centres 32% of patients do not survive 30 days after pleurodesis.
- Performance status most value in estimating post pleurodesis survival

Who Gains Most? A 10-Year Experience With 611 Thoracoscopic Talc Pleurodeses

Volker Steger, MD, Ute Mika, Heikki Toomes, MD, Tobias Walker, MD, Corinna Engel, Thomas Kyriss, MD, Gerhard Ziemer, MD, and Godehard Friedel, MD

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Table 4. Analysis of Risk Factors for a Nonsuccessful Pleurodesis

		Full Model	
Variable	N	*p* Value	OR
Chest tube duration (≤10 days)	431	<0.0001	3.0
Previous thoracic irradiation	104	0.0155	1.9
Disease	506	0.0984	0.9
Karnofsky index (≤60%)	151	0.1187	1.4
BMI (<25 kg/m^2)	356	0.4242	1.2
Age in classes		0.9250	1.0

TABLE 5. **Available and Investigational Sclerosing Agents for Pleurodesis**

Agent	Reported success rates* (%)
Mineral	
Talc	70-100[115,144,151-157]
Antibiotic	
Doxycycline	60-81[158-160]
Quinacrine	64-100[161-165]
Antiseptic	
Iodopovidone	64-96[166-170]
Silver nitrate	96[153]
Anticancer drug	
Bleomycin	64-84[148,156,171,172]
Mitoxantrone	76-88[173-175]
Cisplatin	65-83[176,177]
Bacterial product or component	
Corynebacterium parvum	65-92[178-182]
Staphylococcus aureus superantigen	100[183]
OK432	53-79[176,184,185]
Cytokine	
Interferon alpha-2β	62-100[171,186,187]

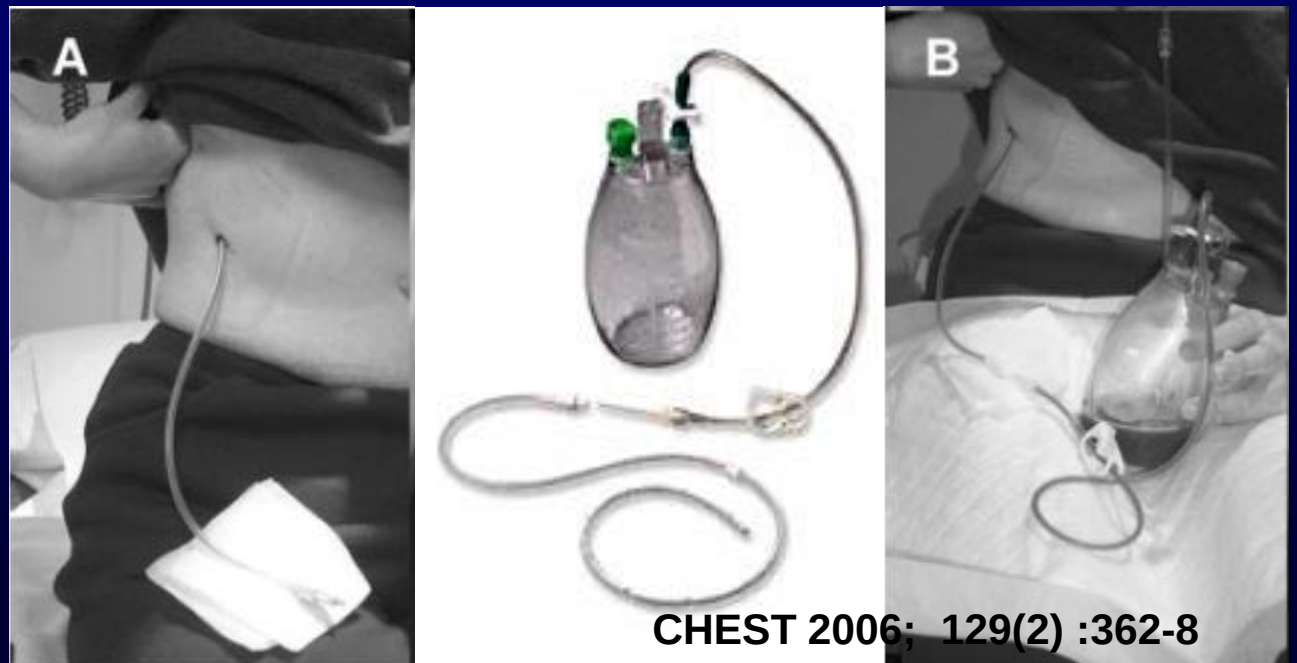
*Success rates variably reported as rate immediately after pleurodesis or rate obtained at different time points after pleurodesis.

Thoracoscopic vs chest catheter pleurodesis

- Cochrane systematic review reported slightly better outcomes with thoracoscopy (Relative risk of non recurrence 1.19)
- Not supported in RCT (Dresler CM et al. Chest 2005) except in subgroups: Lung and Breast cancer
- Benefit of thoracoscopy is adhesiolysis

Long-term pleural catheters

- Immediate relief of dyspnoea in 94-100%
- Spontaneous pleurodesis occurring in 40-58% after 2-6 weeks of drainage
- Modality of choice for trapped lungs



CHEST 2006; 129(2) :362-8

Single-Center Experience With 250 Tunnelled Pleural Catheter Insertions for Malignant Pleural Effusion*

Alain Tremblay, MD, FCCP; and Gaëtane Michaud, MD, FCCP

Table 2—*Frequency of Complications Post-TPC Placement

Complication	Cases	
	No.	%
Unsuccessful insertion	10	4.0
Symptomatic loculation	21	8.4
Asymptomatic loculation	10	4.0
Empyema	8	3.2
PTX/SQ Air/BPF	6	2.4
Cellulitis	4	1.6
Recurrent fluid	4	1.6
Dislodged	3	1.2
Bleeding	2	0.8
Tumor seeding	1	0.4
Pain requiring removal	1	0.4
Extrapleural catheter	1	0.4

*PTX = pneumothorax; SQ = subcutaneous; BPF = bronchopleural fistula.

Surgical techniques

- Pleuro-peritoneal shunts
  - Alternative for trapped lungs
  - Attractive in chylous effusions
  - Complication rate 15% (infection, shunt occlusion, skin erosion)
- Surgical decortication and pleurodesis

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