CONTEMPORARY MANAGEMENT OF MALIGNANT PLEURAL EFFFUSION

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16/3/2018

Overview

- Problem statement
- Etiology
- Diagnosis
- Approach to treatment
- Treatment modalities
  - Repeated thoracocentesis
  - ICD insertion and pleurodesis
  - Indwelling Pleural Catheter
  - Surgical methods
  - Antitumour Therapy
- Conclusion

PROBLEM STATEMENT

- Malignant pleural effusion(MPE) is a common problem
- 15% of patients with cancer develop MPE during course of their disease
- One of the most common causes of exudative PE in developed countries and next to tuberculosis in developing countries like India when subjected to thoracocentesis
- In an Indian study 24% of exudative effusions were found to be malignant

Tandon et al, Lung India, Year 2015, Volume 32, Issue 4 [p. 326-330]

Why Its Recognition is Important?

- MPE predicts poor overall survival
- Median survival usually does not exceed 6 months from the diagnosis
- No strategy has shown to increase survival
- Management shifts from curative to palliative care
- Paramalignant effusions have more favourable prognosis and hence should be identified

Lucia et al Ann Thorac med 2017;12-3-10

ETIOLOGY

S.no.	Tumour	%
1	Ca Lung(Adenoca-m.c; SCC- l.c)	36
2	Breast Ca	25
3	Lymphoma(NHL>HL)	10
4	Ovarian Ca	5
5	Undiagnosed	7

Lung cancer, Ca breast and Lymphoma together account for ~75% of MPE

Fishman's pulmonary dis 5/e pg1181

Mechanisms of pleural effusion in malignancy

- Direct result
  - Pleural metastasis with increased permeability
  - Pleural mets with obstruction of pleural lymphatics
  - Medistinal lymph node involvement
  - Thoracic duct interruption
  - Bronchial obstruction
  - Pericardial involvement
- Indirect result
  - Hypoproteinemia
  - Pulm. Embolism
  - Postobstructive pneumonitis
  - Postradiation therapy

Light's pleural dis 6/e pg 156

DIAGNOSIS

- Imaging
  - CXR
  - Thoracic USG
  - Chest CT
- Thoracocentesis
- Percutaneus pleural biopsy
- Thoracoscopy
- VATS

Imaging

- Thoracic USG:
  - More sensitive and specific than CXR
  - Visualisation of pleural thickening and underlying mass
  - Pleural nodules >1 cm indicate malignancy(Sn-73%, Sp-100%)
  - Can identify unexapanded lung
- Chest CT
  - Pleural thickening >1cm and nodular and mediastinal thickening suggests malignancy
  - Should be performed if pleural fluid analysis does not reveal etiology of exudate

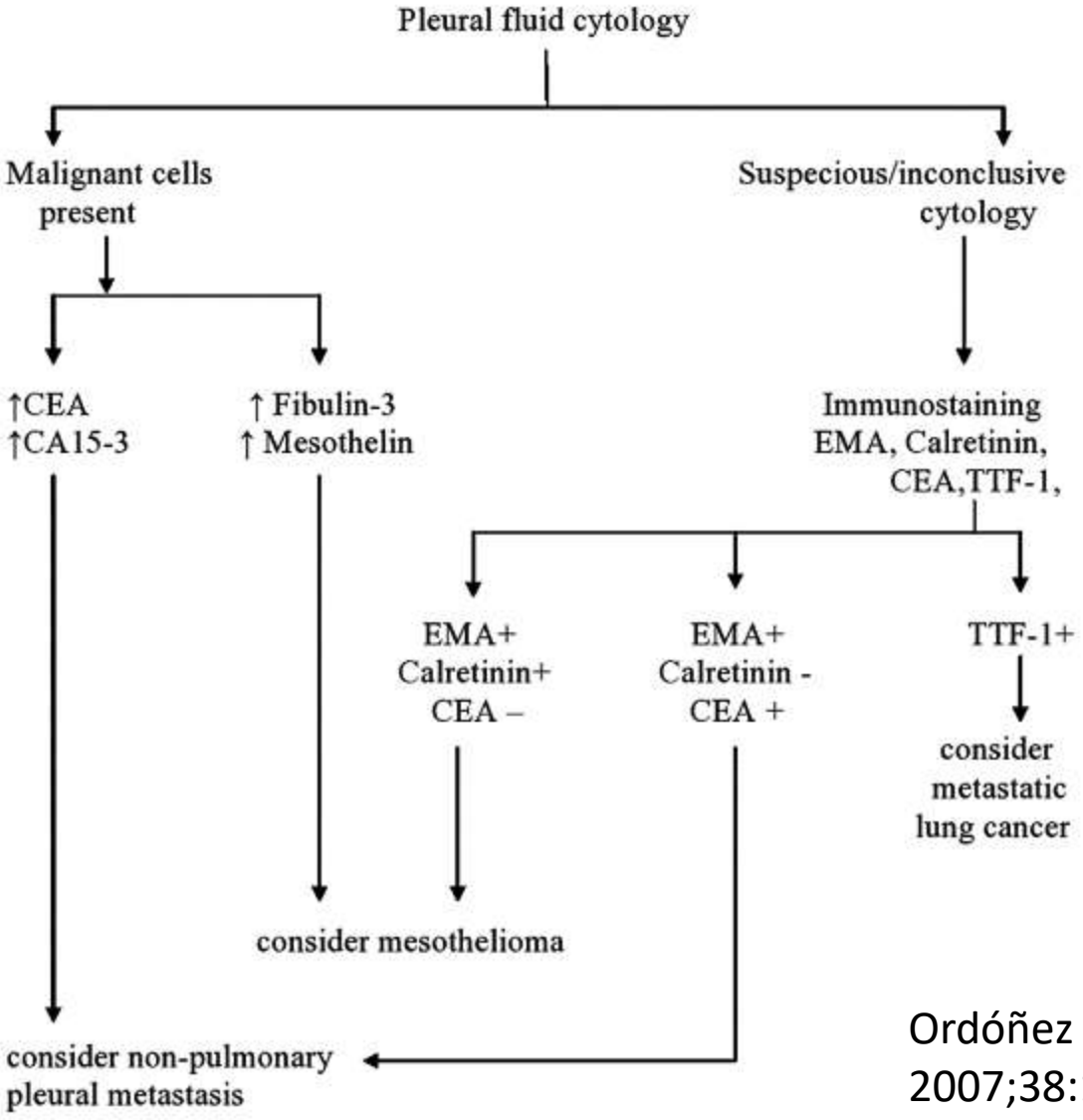
Qureshi NR, Thorax 2009;64: 139-43; Hallifax RJ, Thorax 2015; 70::192-3

Thoracocentesis

- USG guidance
- 60 ml of pleural fluid provides greater diagnostic yield than smaller amount(sensitivity~60% in adenoca, only 30% in mesothelioma)
- 2nd cytology increases sensitivity by 27%, if initial tap was therapeutic(freshly exfoliated cells)
- Further tap doesn't increase yield
- Pl. fluid can be used for IHC and flow cytometry if primary is unknown

Swiderek J, Chest 2010; 137:68-73
Hooper C, BTS pleural dis guidelines, thorax 2010; 65suppl 2:ii4-17
Singh N, Diagn Cytopathol. 2017 Mar;45(3):195-201

Biomarkers in MPE



Ordóñez NG;Hum Pathol 2007;38:1-16

Pleural biopsy

- Undiagnosed exudative pleural effusion when clinical or radiological findings are unable to diagnose the etiology
- Closed pleural biopsy
  - Preferred in resource limited settings
  - Poor yield because of patchy invasion of pleura by tumour(~ 60%), no significant increase in yield even if combined with PF aspiration
  - Performs better if done under imaging guidance(yield 70-80%)
  - Simple, safe and low cost procedure

Tomlinson JR, Semin respir med 1987;9:30-60
Pereyra MF Can Respir J 2013;20:362-6
Benamore RE, Clin Radiol 2006;61:700-5

Thoracoscopy

- Very good yield, sensitivity 91-95%
- Diagnostic accuracy increases further if point of care USG is used
- Advantages
  - Under direct visualisation
  - Multiple biopsies possible
  - Large volume drainage of PE
  - Pleurodesis can be done

J Bronchology Interv Pulmonol. 2015 Apr;22(2):121-9
Rahmann NM, Thorax 2010;65 suppl2:ii54-60

Thoracoscopy

Results of the retrospective study done at PGI on 348 patients over 10 years

	Closed-Blind Pleural Biopsy (n = 84)	Thoracoscopy Without Point-of-Care Ultrasonography (n = 171)	Thoracoscopy With Point-of-Care Ultrasonography (n = 77)	Total Thoracoscopy (n = 248)	P*
Procedural yield	71 (84.5)	155 (90.6)	76 (98.7)	231 (93.2)	0.02
Failed procedure (biopsy not taken)	0	16 (9.4)	1 (1.3)	17 (6.8)	
Adhesions	0	14	1	15	
Bleeding	0	1	0	1	
Excessive cough	0	1	0	1	
Nonrepresentative biopsy	13 (15.5)	0	0	0	

J Bronchology Interv Pulmonol. 2015 Apr;22(2):121-9

Thoracoscopy

- Disadvantages
  - Hospitalisation required
  - Many contraindications: highly loculated PE, CV instability, P-HTN, hypoxemia
  - Risk of tumour invasion through tract(9-16%)
  - Procedure is safe with mortality 0.37% and complication rate 5.6% most common being empyema

Rahman NM, Thorax 2010;65 suppl2:ii54-60
Lee C, Lung Cancer 2009;66:150-6
J Bronchology Interv Pulmonol. 2015 Apr;22(2):121-9

Thoracoscopy in mesothelioma

- Thoracoscopic biopsy has a high diagnostic yield for mesothelioma, approaching 100% in some series, while the yield for pleural fluid cytology alone is 25% and that for combined pleural fluid cytology and closed pleural biopsy is 40%

Hooper C; BTS guidelines 2010; thorax 2010;65 suppl2;ii4-17

Video Assisted Thoracic Surgery(VATS)

- Gold Standard for diagnosis of MPE
- Requires general anaesthesia
- Diagnostic yield more than 95%
- Useful when cytology and pleural biopsy negative and when additional procedure needs to be performed e.g. pleurectomy, decortication.
- Complication risk <1%

Hooper C; BTS guidelines 2010; thorax 2010;65 suppl2;ii4-17

Approach to Treatment

- PROGNOSIS: Median survival-3 to 12 months
- Depends on various factors like
  - Age
  - Performance status(Karnofsky<30- 1.1 months
    Karnofsky>70- 13.2 months)
  - Tumour type: Mesothelioma has better prognosis, lymphoma and breast Ca respond to chemotherapy and have prolonged survival as compared to NSCLC
  - A pleural effusion in the setting of lung cancer usually excludes operability
  - Comorbidities

Heffner JE,*Chest. 2000;117:79–86*
Fishman's pulmonary dis 5/e pg1183

Prognosis

- Tumour stage (e.g. mesothelioma: pt. with only ipsilateral involvement of the pleura and lung survive the longest, distant hematogenous metastases have the shortest survival)
- Epithelial type mesothelioma has a median survival twice that of the sarcomatous type
- PF composition: low pH(<7.30), low glucose(<60) a/w poor survival

Heffner JE,*Chest. 2000;117:79–86*

LENT score

- 1st validated risk stratification system to predict survival in MPE based on multicentric study involving 3 cohorts
- Calculated on the basis of pleural fluid lactate dehydrogenase, ECOG score, Serum neutrophil to lymphocyte ratio and tumour type

Clive AO, development and validation of LENT prognostic score. Thorax 2014; 69:1098

	Variable	Score
L	LDH level in pleural fluid (IU/L)	
	<1500	0
	>1500	1
E	ECOG PS	
	0	0
	1	1
	2	2
	3–4	3
N	NLR	
	<9	0
	>9	1
T	Tumour type	
	Lowest risk tumour types	0
	▶ Mesothelioma	
	▶ Haematological malignancy	
	Moderate risk tumour types	1
	▶ Breast cancer	
	▶ Gynaecological cancer	
	▶ Renal cell carcinoma	
	Highest risk tumour types	2
	▶ Lung cancer	
	▶ Other tumour types	

Risk categories	Total score
Low risk	0–1
Moderate risk	2–4
High risk	5–7

LENT score	Survival
0-1 (low risk)	319 days
2-4 (moderate risk)	130 days
5-7 (High risk)	44 days

Clive AO, development and validation of LENT prognostic score. Thorax 2014; 69:1098

Cell type	Median survival in days (95% CI)	n
Mesothelioma	339 (267 to 422)	170
Haematological malignancy	218 (160 to 484)	35
Gynaecological malignancy	203 (97 to 279)	59
Breast cancer	192 (133 to 271)	140
Renal cell carcinoma	114 (33 to 334)	22
Adenocarcinoma of unknown primary	87 (13 to 286)	11
Lung cancer	74 (60 to 92)	215
Other	71 (46 to 102)	33
Gastrointestinal cancer	61 (44 to 73)	61
Sarcoma	44 (19 to 76)	12
Melanoma	43 (23 to 72)	23
Urological cancer (bladder, prostate, testis, penile)	33 (22 to 168)	8
Overall	136 (119 to 167)	789

Clive AO, development and validation of LENT prognostic score. Thorax 2014; 69:1098

Indications for treatment

- Asymptomatic- Need not be treated
- Don’t give unnecessary discomfort to patient just to make radiograph look better
- MPE due to malignancies that respond to antitumour therapy should be treated
- Eventually almost all MPE become symptomatic
- Successful management at best is palliative and without survival benefit in most cases
- But erroneous treatment can increase discomfort and shorten survival

Approach to Treatment

- Factors to be considered:
  - Expected survival
  - Symptoms
  - Rate of reaccumulation
  - Primary tumor type and expected response to therapy
  - Degree of lung reexpansion following pleural fluid evacuation

Management options in MPE

- Simple observation
- Systemic chemotherapy for underlying malignancy
- Repeated thoracocentesis
- Chest tube drainage alone (tube thoracostomy)
- Pleurodesis
- Pleural catheters
- Surgical method
  - Pleurectomy
  - Pleuroperitoneal shunt
- Other measures
  - Intrapleural chemotherapy
  - Radiotherapy

Thoracocentesis

- Initial management in all symptomatic MPE
- Simple and effective in relieaving dyspnea
- Can be used as sole treatment strategy if slow reaccumulation(in more than a month) and life expectancy short(<3 months).
- Simultaneous assessment of lung expansion(Pleural manometry) to guide further management

Thoracocentesis

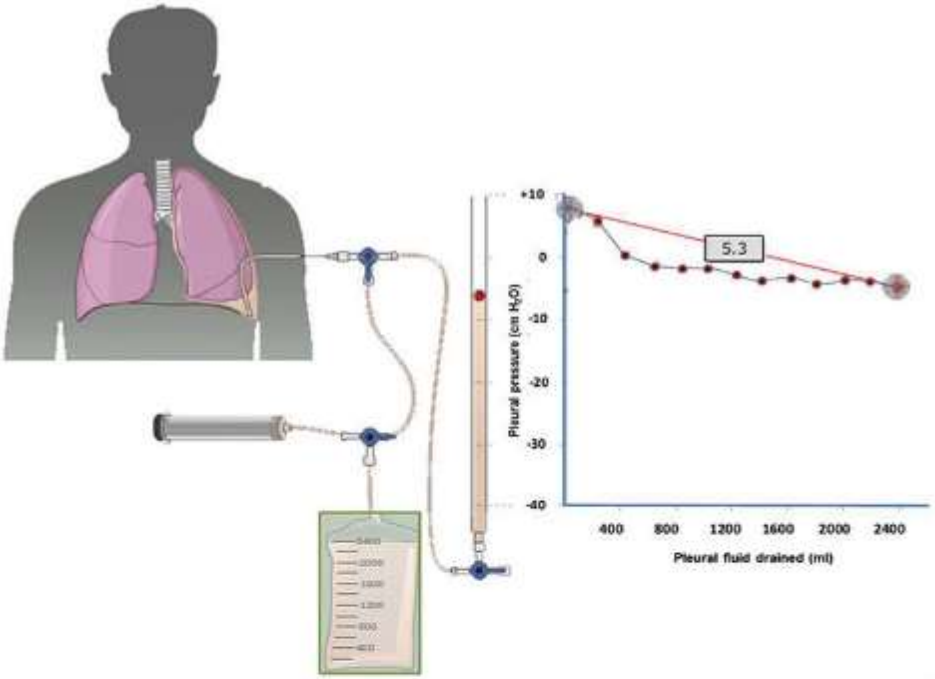
- Complications:
  - Pneumothorax
  - Infection/empyema
  - Re-expansion pulmonary edema(REPE)

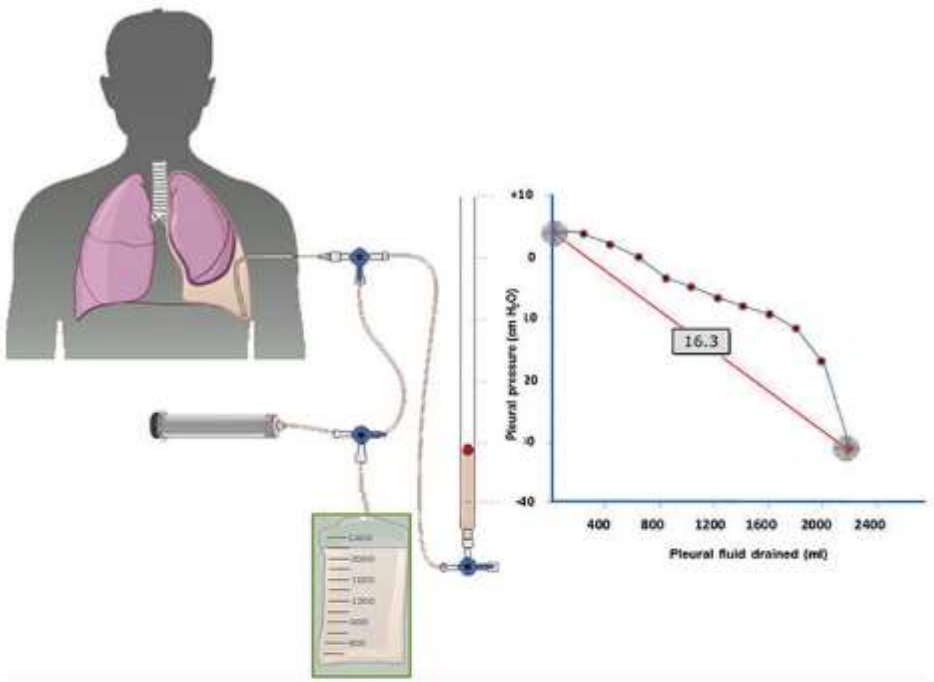
- REPE is rare complication, generally doesn't occur at less than 1.5 L. However no definite vol. or rate identified that will not cause REPE.
- Stop- when anterior chest pain or pleural pressure below -20cm H2O

Unexpandable Lung

- Inability of the lung to expand to the chest wall allowing for normal visceral and parietal pleural apposition
- Direct result of either pleural disease, endobronchial obstruction resulting in lobar collapse, or chronic atelectasis
- Trapped lung: unexpandable lung with a visceral pleural peel in the absence of malignancy or active pleural inflammation
- Lung entrapment: unexpandable lung with active pleural inflammation, infection, or malignancy

Huggins JT, The unexpandable lung. *F1000 Med Rep. 2010;2:77*


+10
0
-10
-20
-30
-40
Pleural pressure (cm H2O)
5.3
400
800
1200
1600
2000
2400
Pleural fluid drained (ml)


+10
0
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Pleural pressure (cm H2O)
16.3
400
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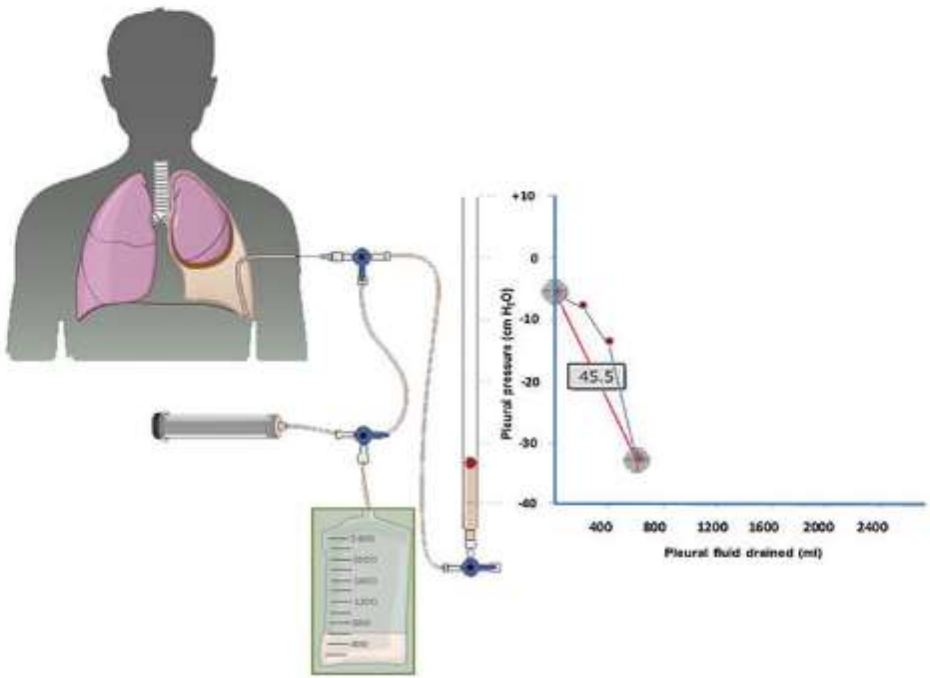
2400
Pleural fluid drained (ml)

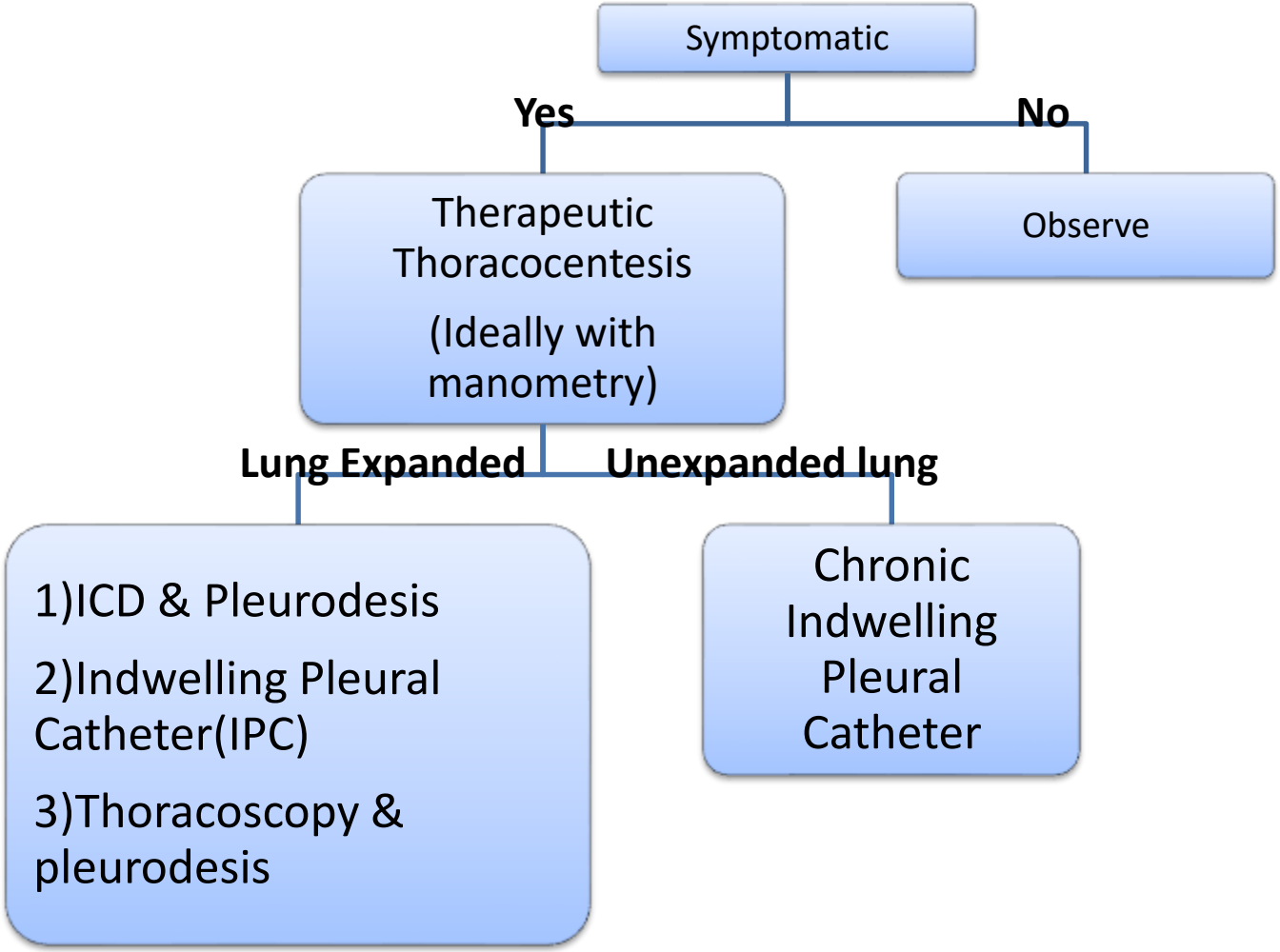

+10
0
-10
-20
-30
-40
Pleural pressure (cm H2O)
45.5
400
800
1200
1600
2000
2400
Pleural fluid drained (ml)

Unexpandable Lung

- A pleural space elastance(PEL) >19.0 cm H2O/L during the first 500 mL of pleural fluid removed(Trapped lung) is predictive of a 100% pleurodesis failure at 1 month
- PEL >14.5 in terminal stages of fluid removal (lung entrapement) also suggests high likelihood of pleurodesis failure

Lan RS,Elastance of the pleural space*Ann Intern Med.*1997;126:768–774

Management Algorithm



Pleurodesis

- Iatrogenic-induced pleural fibrosis by a sclerosing agent to obliterate the pleural space and prevent the accumulation of PF
- Talc is the most frequently used sclerosing agent
- Other agents tetracycline and its derivatives, silver nitrate, povidone-iodine, Corynebacterium parvum, bleomycin etc.

Pleurodesis

- When Anticipated survival >3months
- Effective therapy that can be carried out in single procedure
- The success of pleurodesis is usually determined by the non-reaccumulation of fluid within 30 days (60-90%)
- Avoids inconvenience of intermittent drainage and long term indwelling catheter
- Painful procedure

Roberts ME, British Thoracic Society pleural disease guideline 2010. Thorax 2010;65 Suppl 2:ii32-40

Pleurodesis

- **??Controversies:**
- Tube thoracostomy Vs Thoracoscopic
- Sclerosing agent
- Analgesia
- Size of tube
- Time of removal of drain after intorducing agent
- Patient rotation after pleurodesis

Tube thoracostomy Vs Thoracoscopy

- Hospitalization is required in both
- Chest tube pleurodesis can be done in the patient's room with analgesia, thoracoscopic pleurodesis requires general anesthesia or conscious sedation
- Thoracoscopically talc poudrage is used while talc slurry is delivered through Tube thoracostomy
- Randomized clinical trials have not demonstrated superiority of one technique over another
- British Thoracic Society indicates that the two approaches have similar efficacy

Roberts ME, British Thoracic Society pleural disease guideline 2010. Thorax 2010;65 Suppl 2:ii32-40
Yim AP, Ann Thorac Surg 1996;62:1655-8

Tube thoracostomy Vs Thoracoscopy

- In a randomized trial that compared talc slurry(n=250) versus powdered talc(n=251), success rates of pleurodesis were 71% and 78%, respectively(not statistically significant, p=0.169).
- On including patients who had died before 30 days or had not achieved lung re-expansion, these rates fell to 53% and 60%, respectively(p=0.119)

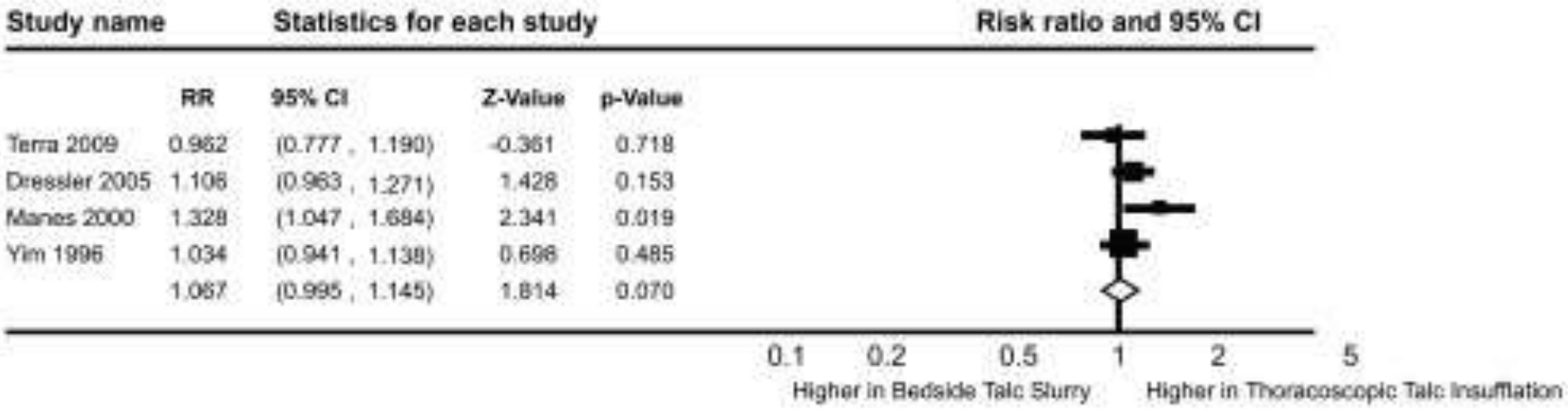
Dresler CM, Phase III intergroup study of talc poudrage
vs. talc slurry sclerosis for malignant pleural effusion Chest 2005;127:909-15

Sclerosing agent

Study	MPE and role of thoracoscopic talc insufflation/poudrage(TTI) and talc slurry(TS): A systematic review and meta-analysis
Objective	To compare rates of successful pleurodesis and rates of complication(resp. and non-resp.) between TTI and TS
Methods	Review of 137 articles of which 4 studies were included (n=454)
Results	No statistically significant difference in success of pleurodesis b/w bedside Ts (167/218pts.) Vs TTI(197/236 pts)(Pooled RR 1.06; CI 0.99-1.14, p= 0.07). The risk of respiratory complications was significantly higher in TTI group(RR-1.91,CI 1.24-2.93,p= 0.003) Risk of non resp. complications was not statistically significant between 2 groups

Srinivas et al F1000Res. 2014; 3:254

TTI Vs TS



Srinivas et al F1000Res. 2014; 3:254

TTI Vs TS

- Respiratory complications were chest pain, Pneumonia, Subcutaneous emphyseema, pulmonary edema and ARDS
- Common non respiratory complication are fever, wound infection
- The risk of acute respiratory distress syndrome using talc is directly related to the dose, particle size or other factors related to its instillation.
- Larger talc particle size (more than 15 microns) has reduced the risk of this complication
- However it increases cost

Srinivas et al, F1000Res. 2014; 3:254
Janssen JP, Lancet 2007;369:1535-9

Sclerosing agent

Objective	**To ascertain optimal treatment strategy for adults with MPE in terms of pleurodesis success**
Selection	Cochrane review of RCTs of intrapleural interventions for adults with symptomatic MPE. Finally total 62 RCTs were included with total 3428 patients
Results	Talc poudrage was highly efffective method and resulted in fewer pleurodesis failures as compared to other methods(95%Cr-I 1 to 5). Estimated ranks of commonly used agents: Talc slurry(4^{th}; 95%Cr-I 2 to 8), Iodine(5^{th}; 95%Cr-I 1 to 12), Bleomycin(8^{th}; 95%Cr-I 5 to 11), Doxycycline(10^{th}; 95%Cr-I 4 to 15)
Comments	Estimates were imprecise as evidenced by wide creditable intervals and high statistical and clinical heterogenity. High risk of bias in many studies included

Clive AO, *Cochrane Database Syst Rev. 2016:CD010529*

Sclerosing agent

Pleurodesis efficacy	Talc poudrage ranked highest among all pleurodesis agents (rank 2 of 16 methods).# Placebo ranked lowest among all pleurodesis agents (rank 15 of 16 methods).
*OR >1 indicates higher probability of pleurodesis failure relative to comparator	Talc poudrage vs following agents: • bleomycin, OR 9.7 (2.1–44.78)* • tetracycline, OR 12.1 (1.32–111.3)* • talc slurry, OR 1.31 (0.92–1.85)* Bleomycin versus tetracycline: • tetracycline, OR 2 (1.07–3.75)* IPC versus talc slurry: • IPC OR 3.35 (1.64–6.83)*

Clive AO, *Cochrane Database Syst Rev. 2016:CD010529*

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

OBJECTIVE	**To assess the effect of chest tube size and analgesia (NSAIDs vs opiates) on pain and clinical efficacy related to pleurodesis in patients with malignant pleural effusion**
INTERVENTION	Total pts.- 320 Patients undergoing thoracoscopy (n = 206) received a 24F chest tube and were randomized to receive opiates (n = 103) vs NSAIDs (n = 103), and those not undergoing thoracoscopy (n = 114) were randomized to 1 of 4 groups (24F chest tube and opioids [n = 28]; 24F chest tube and NSAIDs [n = 29]; 12F chest tube and opioids [n = 29]; or 12F chest tube and NSAIDs [n = 28])

JAMA. 2015;314(24):2641-2653

Analgesia and Tube size

RESULTS	Pain scores in the opiate group (n = 150) vs the NSAID group (n = 144) were not significantly different (mean VAS score, 23.8mm vs 22.1 mm; *P = .40),* *but the NSAID group required more rescue analgesia* (26.3%vs 38.1%; 95%CI, 1.3-3.4; *P = .003).* *Pleurodesis failure occurred in 30* patients (20%) in the opiate group and 33 (23%) in the NSAID group, meeting criteria for noninferiority (difference, −3%; 1-sided 95%CI, −10% to ; *P = .004 for noninferiority).* *Pain* scores were lower among patients in the 12F chest tube group (n = 54) vs the 24F group(n = 56) (mean VAS score, 22.0mmvs 26.8 mm; *P = .04)* *But 12F chest tubes vs 24F chest tubes were associated with higher* pleurodesis failure (30% vs 24%), failing to meet noninferiority criteria (difference, −6%;1-sided 95%CI, −20% to ∞ ; *P = .14 for noninferiority)*

JAMA. 2015;314(24):2641-2653

Duration Of Chest Drain After Pleurodesis

- There is controversy about the length of time the chest drain must be maintained after introducing the sclerosing agent.
- Studies suggest that the withdrawal of the tube 24 h after introducing talc (instead of 72 h) does not compromise the results
- Treatment can be indivisualised

Villanueva AG, Thorax 1994;49:23-5.
Goodman A,Efficacy of short-term versus long-term chest tube drainage following talc slurry pleurodesis in patients with malignant pleural effusions: A randomised trial. Lung Cancer 2006;54:51-5

Patient Rotaion

- It is assumed that good dispersion of talc suspension contibute to final success of its treatment for which patient rotation was used
- No difference in the success rate of pleurodesis has been observed between rotated or nonrotated patients in clinical trials

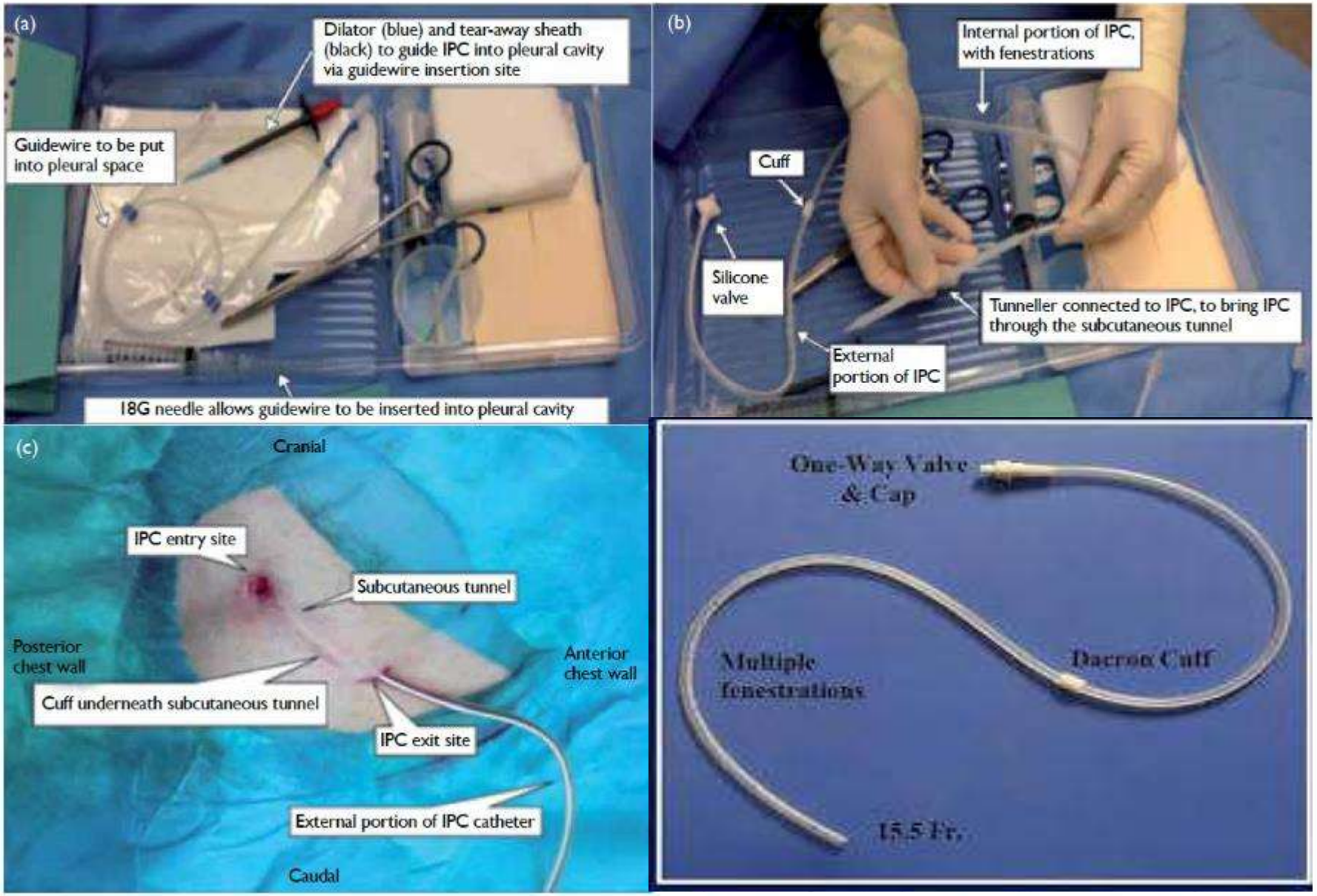
Mager HJ, Distribution of talc suspension during treatment of MPE with talc pleurodesis. Lung Cancer 2002;36:77-81

Indwelling Pleural Catheter(IPC)

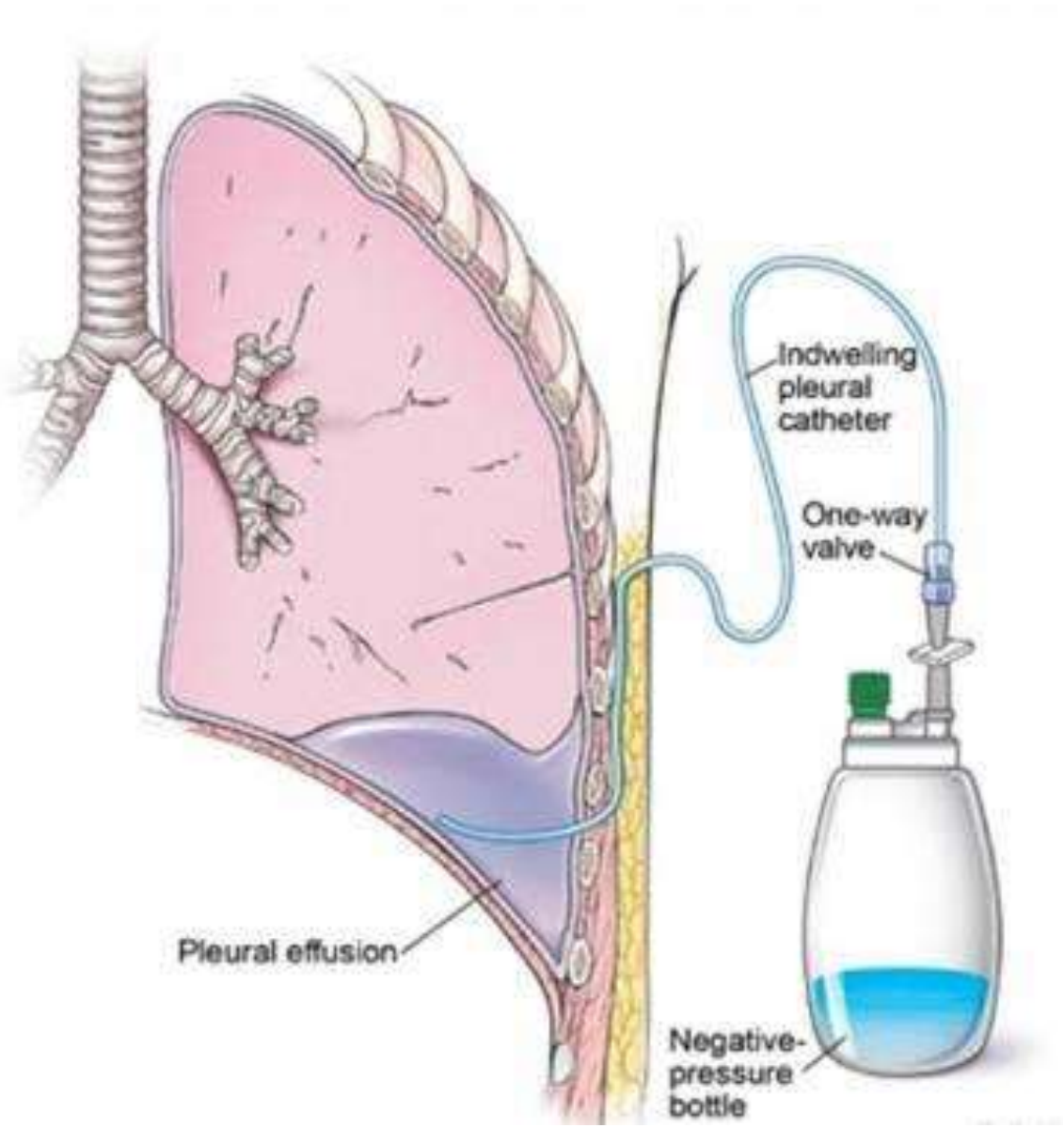
- Tunneled pleural catheter system (Pleur X-Care fusion)
- A 15.5 Fr catheter that may be placed in outpatient setting under local anesthesia
- Subcutaneously secured indwelling silicone tubes ending in a one-way valve
- Drainage is performed daily or alternate day by the patient, family members or visiting healthcare professionals

Davies HE,The TIME2 randomized controlled trial. JAMA 2012;307:2383-9.
Fysh ET, Chest 2012;142:394-400

Indwelling Pleural Catheter(IPC)



Indwelling Pleural Catheter(IPC)



Indwelling Pleural Catheter(IPC)

- Maintain lung expansion through continuous drainage of fluid rather than obliteration of the pleural space
- As effective as pleurodesis in the first-line treatment of MPE
- Can also be used when pleurodesis fails or is contraindicated because of a trapped lung
- Spontaneous pleurodesis may be achieved in approx 50-70% after 2-12 weeks
- Also being used to administer the sclerosing agent

Ahmed L;Chest 2014;146:e190-4
Van Meter ME; J Gen Intern Med 2011;26:70-6

Indwelling Pleural Catheter(IPC)

- Complications are minor and rates are low(5-27%)
  - infection along catheter tract(1-12%)
  - Bleeding
  - Pneumothorax
  - catheter blockage
  - catheter fracture

Fysh ET *et al. Clinical outcomes of indwelling pleural* Catheter; Chest 2013;144:1597-602
Lui MM;Complications of indwelling pleural catheter use and their management. BMJ Open Respir Res 2016;3:e000123

Pleurodesis via IPC

- Case series of 24 patients
- Underwent talc pleurodesis via IPC performed as an opd procedure
- Successful in 22 patients(92%)
- Complications- wound site infection(1), recurrent effusion(1), hydropneumothorax(1)

Ahmed L et al; Chest 2014; 146(6):e190

IPC Vs Pleurodesis

- Relief of dyspnea (Modified Borg score) after treatment:
  - Both were efficacious(n= 88, $p<0.01$)
  - But difference was not statistically significant between IPC and pleurodesis($p=0.16$ for rest dyspnea, $p=0.72$ for exercise)
- after 6 weeks:
  - Pleurodesis pts. had significantly less dyspnea($p=0.002$)

Boshuizen et al; RCT comparing IPC with talc pleurodesis lung cancer 2017;108:9

IPC Vs Pleurodesis

- A study of 250 pts. after IPC showed improved dyspnea in 89% (39% resolved; 50% partial relief)
- Few total hospital days(6.5 vs 18,n=65 p=0.002) with IPC as compared to pleurodesis
- Fewer reinterventions(13.5% vs 32.3%) with IPC as compared to pleurodesis

Boshuizen et al; RCT comparing IPC with talc pleurodesis lung cancer 2017;108:9
Fysh ET Chest 2012; 142(2):394

IPC Vs Pleurodesis

- IPCs are preferred in patients with limited survival (<3 months) and those who prefer outpatient management
- Pleurodesis is more cost-effective in those with longer survival and those who want immediate treatment without chaos of regular drainage

Penz ED et al; Chest 2014;146:991-1000

Status in India

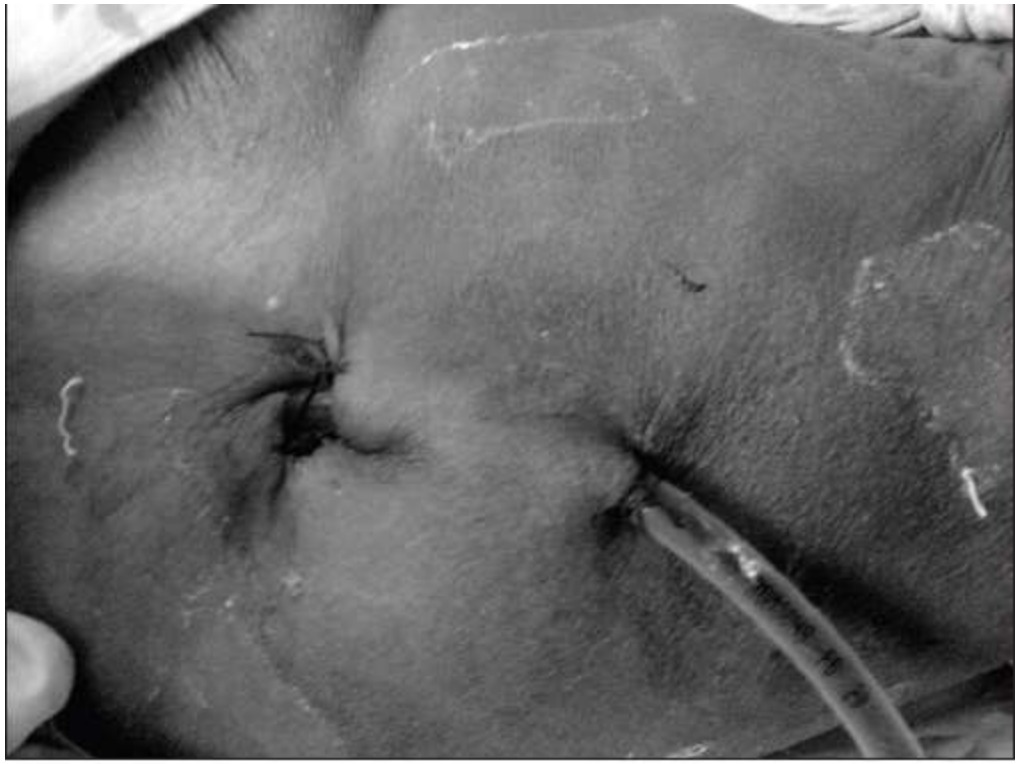
- Available at very few places
- Expensive(full kit costs 27,000-40,000/-)
- Each time a vacuum bag has to be used- 2500-3000/- per use
- Being used at few centres
- Modified version being used at one centre

Case Report

Indwelling pleural drain for mobile management of malignant pleural effusion-combining benefits of both methods

Dinesh Mehta, Anshu Gupta[1], Sameer Singhal, Sachin Bansal

Departments of Respiratory Medicine and [1]Pharmacology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Ambala, Haryana, India



Modified IPC

- Size 18 Fr ICD was used
- The patient was mobile without any need for carrying the icd bag with icd *in situ* continuously and remained comfortable with the tube for 4 months till the end of life
- Indwelling portex icd offers a low cost, easily available and successful alternative to thoracoscopy and indwelling pleural catheter for persistent malignant pleural effusions in a selected subset of patients

Surgical methods

- For patients having failed chemical pleurodesis
  - Radical total/subtotal pleurectomy and decortication
  - Pleuroperitoneal shunt

Pleurectomy

- Rarely performed for non-mesolthelioma MPE
- Lack of evidence of efficacy over less invasive procedures
- Long recovery time
- Does not improve survival
- Patient should be good surgical candidate and having long expected survival

Ohta Y et al, J surg oncol. 2005;91(4):237

Pleurectomy

- Subtotal pleurectomy can be performed thoracoscopically
- Radical total pleurectomy/decortication requires thoracotomy
- Virtually always effective in obliterating pleural space for control of MPE
- One case series of 19 patients showed efficacy of 91%

Kara M, use of single incision thoracoscopicc pleurectomy in MPE; Acta Chir Belg 2013 jul; 113(4): 270-4

Pleuroperitoneal shunt

- Rarely used
- Failed pleurodesis, lung entrapment or malignant chylothorax- nutritional advantage
- Performed thoracoscopically under GA
- Can also be done by interventional radiological techniques
- Denver shunt- unidirectional flow from pleural space; shunt pumping chamber subcutaneusly over costal margin

Genc O. Eur J Cardiothorac Surg 2000; 18:143

Pleuroperitoneal shunt

- Relatively safe
- Palliation achieved in 73-90%
- Shunt failure common
  - Catheter occlusion(7.5%)
  - Infection (4.3%)
  - Malignant seeding at site of insertion

Genc O. Eur J Cardiothorac Surg 2000; 18:143

Anti Tumour Therapy

- Breast Ca, Lymphoma, Small cell ca may respond to chemotherapy
- EGFR mutant NSCLC with MPE can experience control with TKI
- A study of 60 patients with NSCLC and MPE in which 34 received TKI (20 TKI alone, 14 TKI with talc pleurodesis)
- Time for effusion to reaccumulate was 9.9 months(TKI) vs 11.7 months(TKI+TP) p=0.59 suggesting efficacy of TKI
- Risk of resistance after 1 year of therapy with TKI

Verma A, Curr Drug Discov Technol. 2016; 13(2): 68
Janne PA, NEJM 2015;372(18):1689

Anti Tumour therapy

- VEGF- critical cytokine in formation of MPE
- Bevacizumab(Anti VEGF) was studied in non-squamous NSCLC as intrapleural agent and systemic agent in different studies along with chemotherapy
- Preliminary data suggests that some NSCLC may respond to bevacizumab

Marquez et al, Clin Transl Oncol 2016; 18:760
Masago et al, Mol Clin Oncol 2015;3:415
Du N et al, Oncol Rep 2013; 29:2332

Pleurodesis should not be attempted in patients receiving antiVEGF therapy
Pleurodesis requires angiogenetic factors

Radiotherapy

- May be helpful when Mediastinal LN disease is cause of pleural effusion(paramalignant) as in lymphoma
- Mediastinal radiation also helpful in chylothorax

Take Home Message

- Malignant pleural effusion(MPE) is a common cause of exudative pleural effusions
- Appearance of MPE is poor prognostic sign with median survival 3-12 moths
- Survival depends on multiple factors including underlying tumour type and patient performance status
- Treatment approach becomes palliative rather than curative
- Treatment should be indivizualised and goal should be patient comfort

Take Home Message

- IHC and flow cytometry are being increasingly used for diagnosis
- Indwelling pleural cathters(IPCs) have shown promising results in management of MPE. However cost of treatment makes it less popular in resource limited settings
- New generation Anti Tumour Therapy shows promising results and gives hope for future research