# Diagnosis and Management of Pleural Disease

장효준

한양대학교 서울 병원 흉부외과

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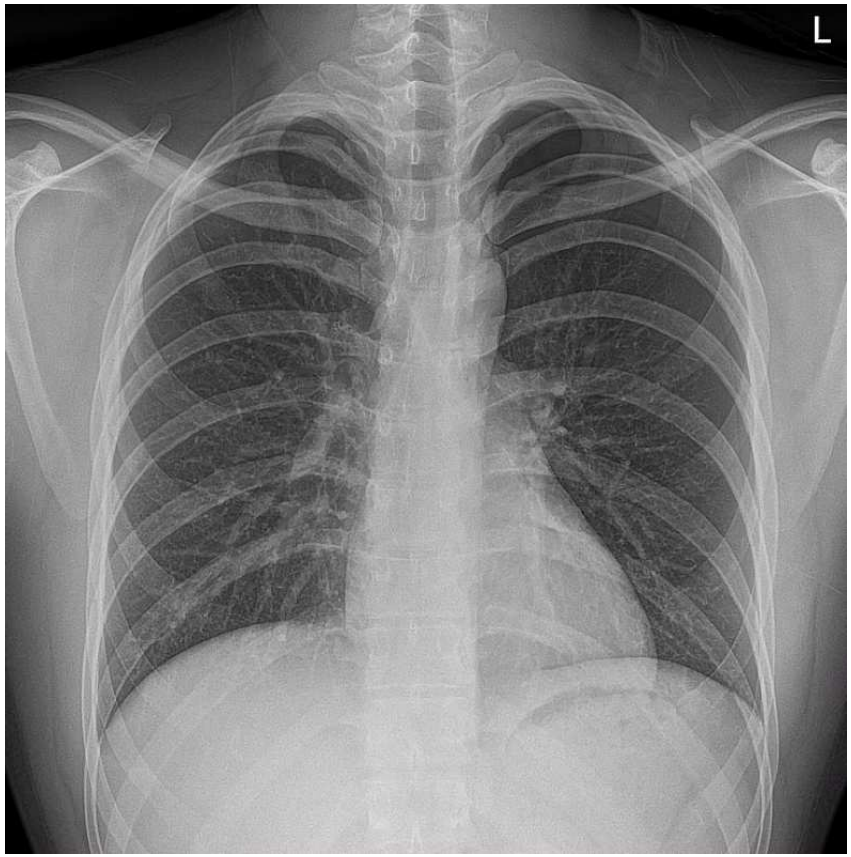
1. Spontaneous pneumothorax
2. Parapneumonic effusion and empyema
3. Malignant mesothelioma

# Spontaneous Pneumothorax

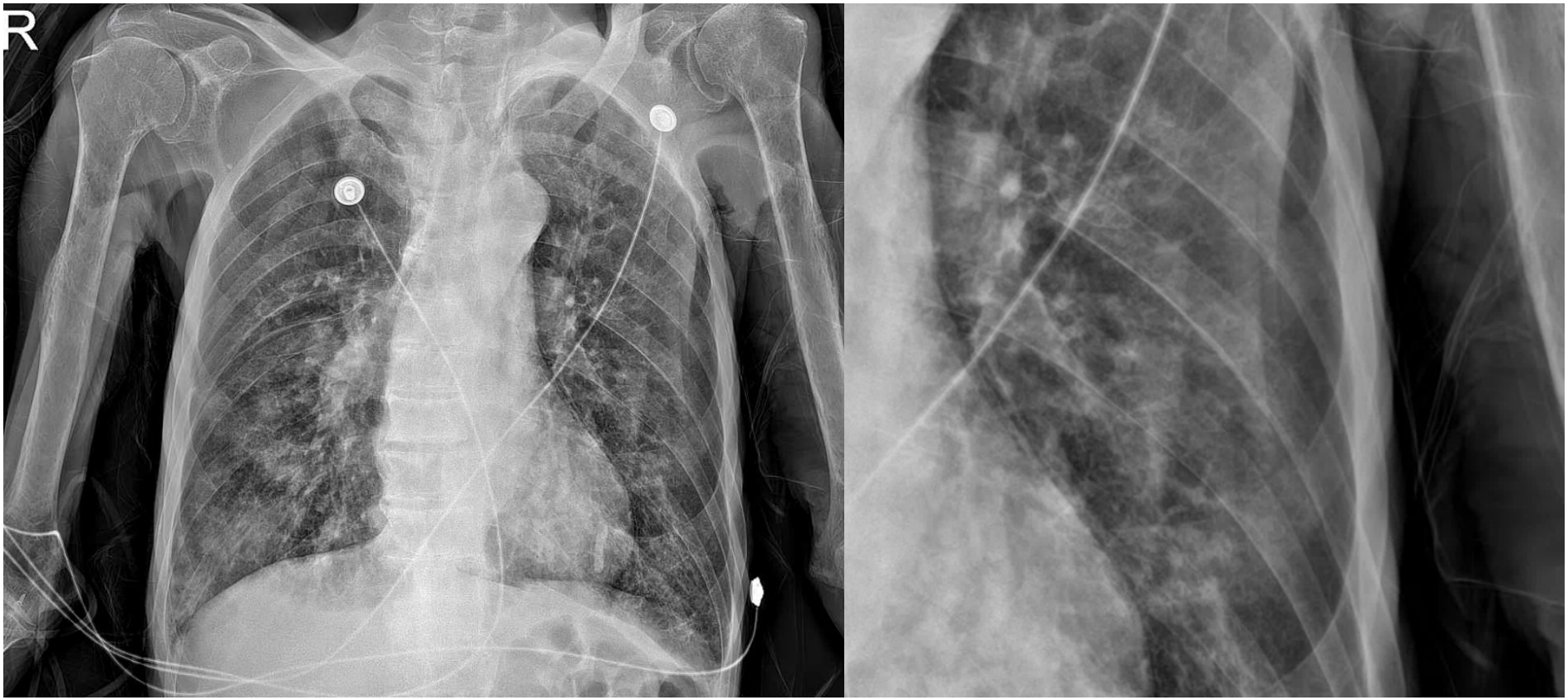
# Introduction

- Presence of air in the pleura cavity
- Common medical disease : asymptomatic ~ life threating

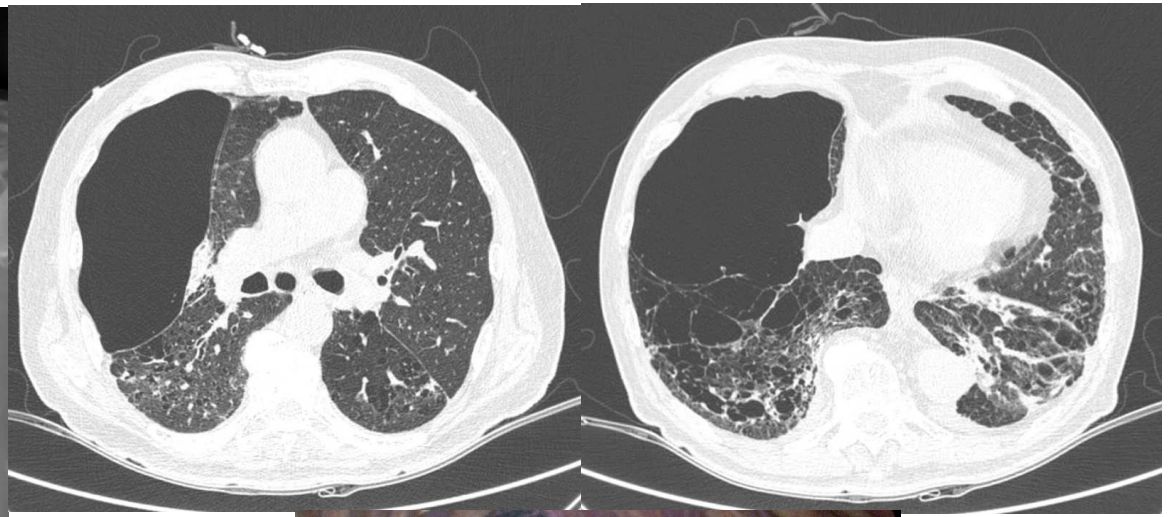
# Pneumothorax




# Skin fold



# Large bullae

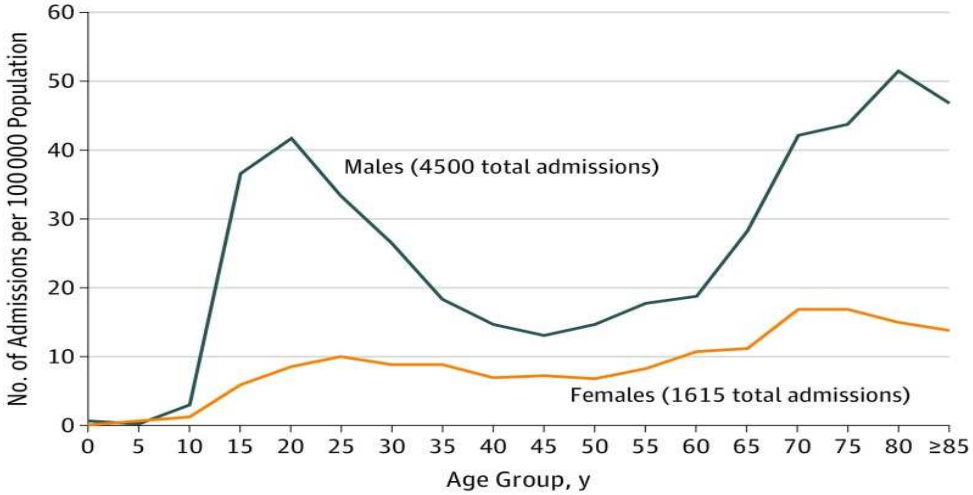
# Classification

- Spontaneous pneumothorax
  - Primary spontaneous pneumothorax(PSP)
    : without underlying lung disease
  - Secondary spontaneous pneumothorax(SSP)
    : with underlying lung disease
  - Catamenial pneumothorax
    : in conjunction with menstruation
  - Neonatal pneumothorax
    : prematurity

- Traumatic pneumothorax
  - Blunt or penetrating chest injury
  - Iatrogenic

# Epidemiology

- Incidence : 14-22/100,000 population per year
  - Male: 22.2-24/100,000 population per year
  - Female: 6.7-9.8/100,00 population per year
- Bimodal distribution



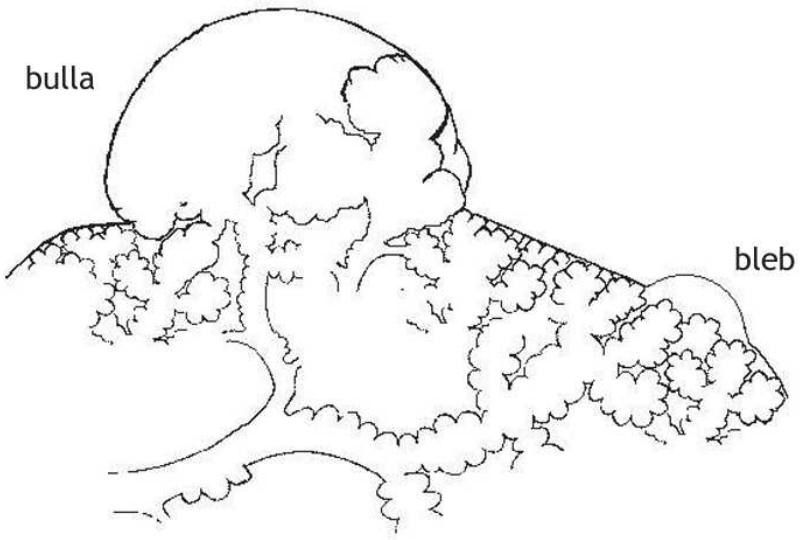

Hallifax RJ. *JAMA.* 2018;320:1471-1480.

# Primary Spontaneous Pneumothorax

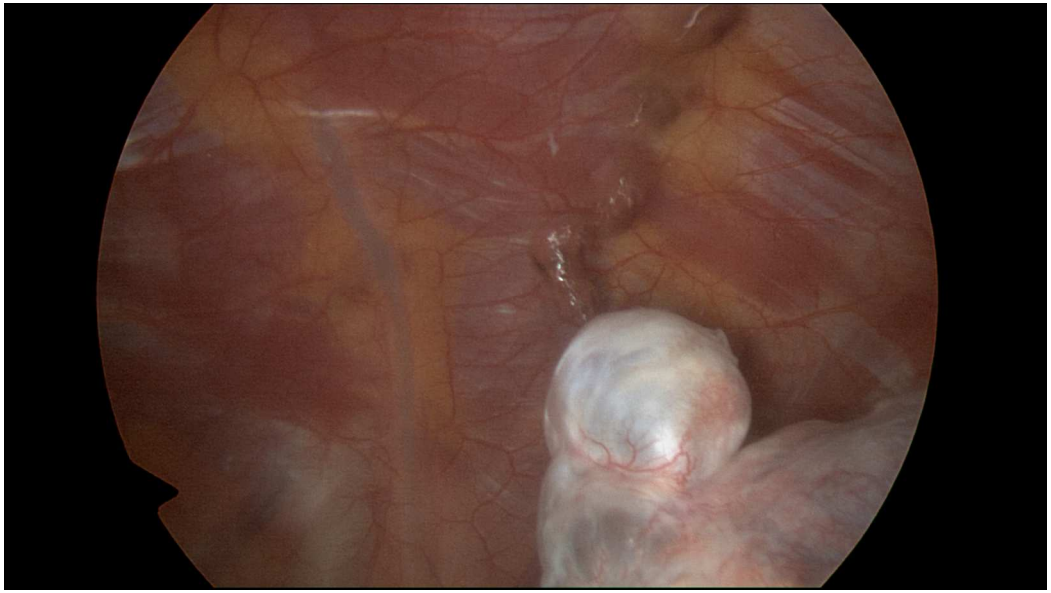
# Cause of PSP

- Subpleural blebs(<1cm) or bullae (≥1cm)
  - known as emphysema-like changes(ELC)
- Visceral pleural porosity
  - Chronic small airway inflammation

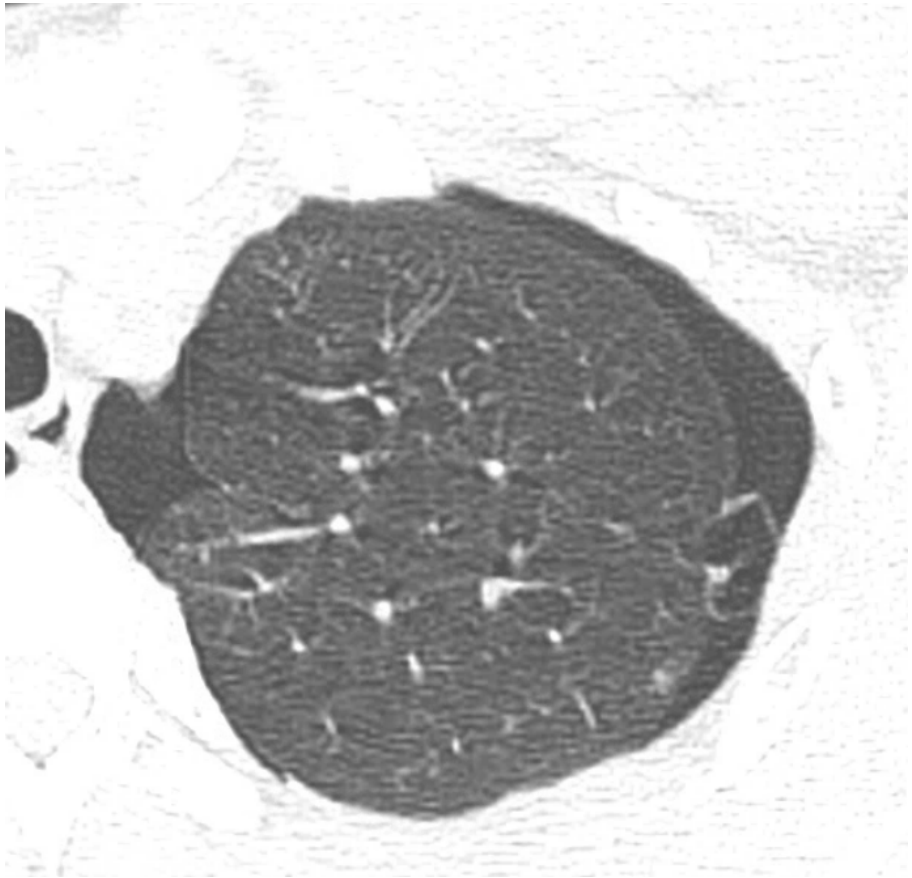
# Bleb or Bulla

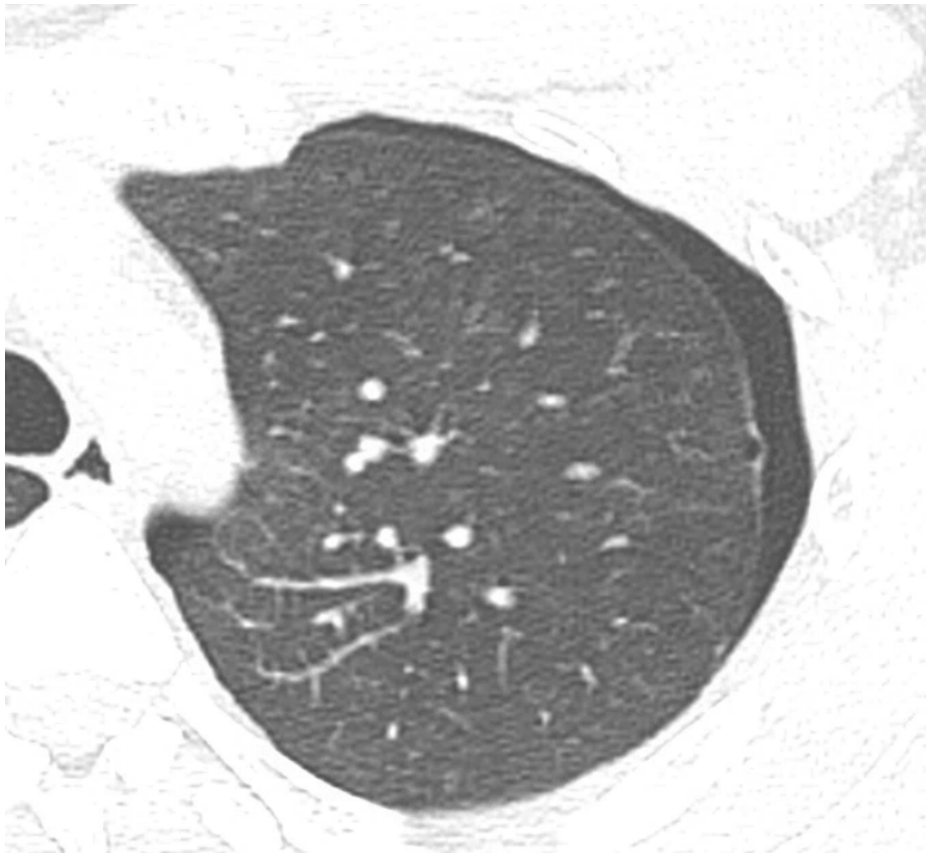


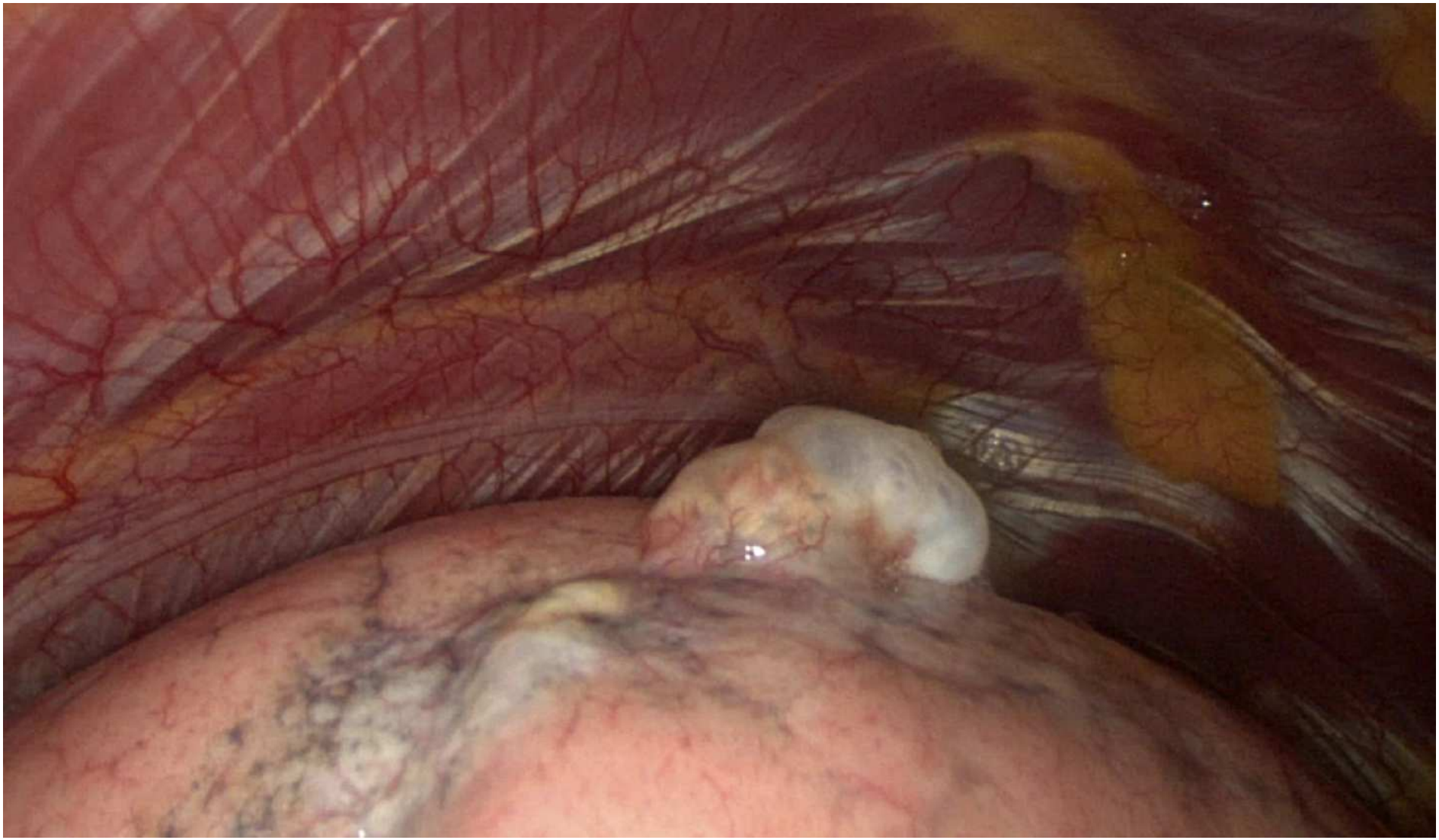

Lyra, R.D.M. Etiology of primary spontaneous pneumothorax. *J Bras Pneumol.* 2016;42:222-226.



Presence of ruptured bullae or bleb during surgery : 3.6%~73%







# Chronic small airway inflammation

- Smoking related abnormality or respiratory bronchilolitis
- Inflammatory infiltration with lymphocyte and macrophage within wall of bronchioles

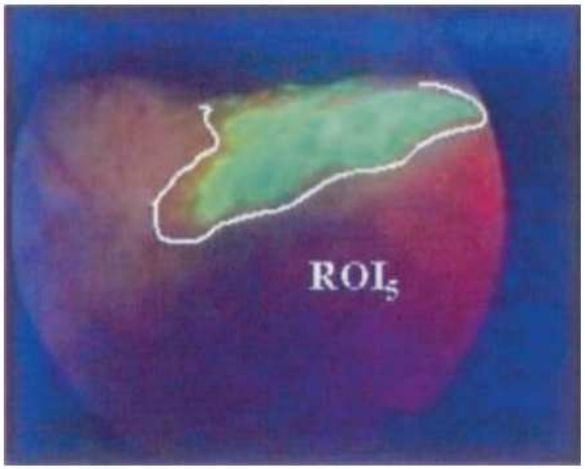
→ fibrotic change and compensatory emphysema

# Visceral pleural porosity

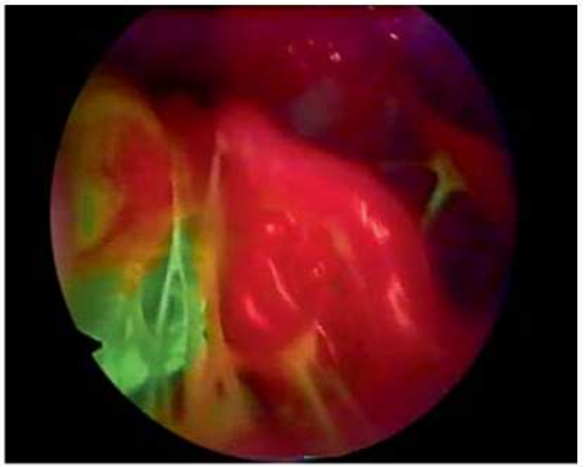
- Disruption of mesothelial cell at the visceral pleura

→ replayed by an inflammatory elastofibrotic layer

→ increased porosity → allowing an airleakage

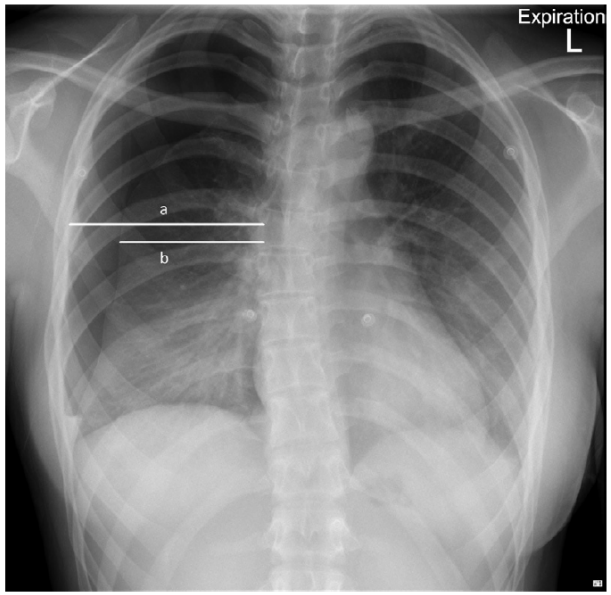



Noppen M. *Am J Respir Crit Care Med.* 2004;150:680-682.

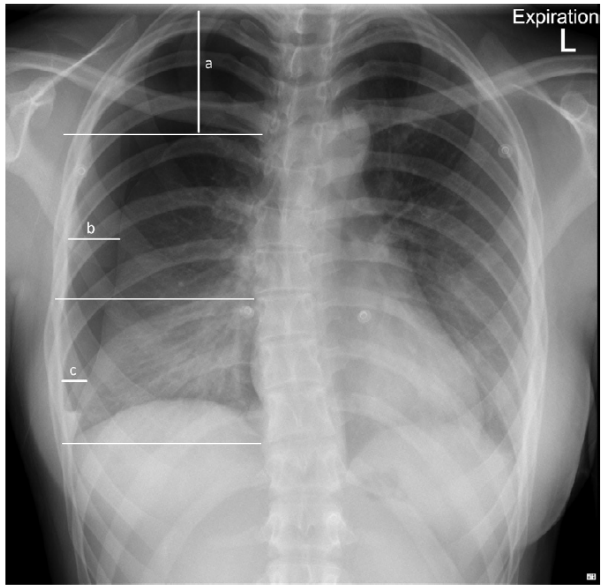


Noppen M. *Respiration.* 2008;76:121-127.

# Size of pneumothorax (1)



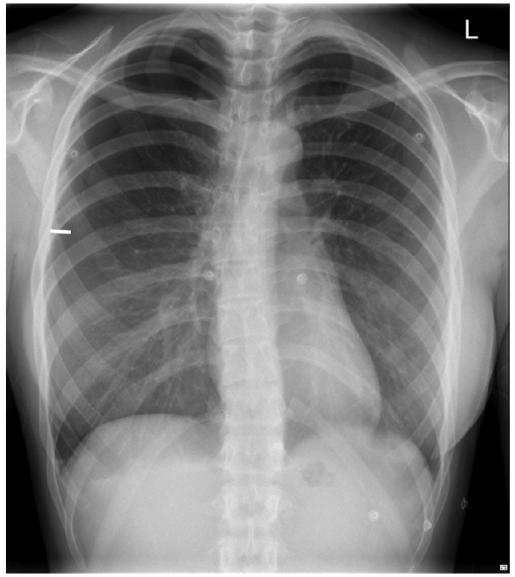

- Light method, $Y=100x[1-b^3/a^3](\%)$
- European Respiration Society (ERS) statement (2015)




- Colin formula, $Y=4.2+[4.7x(a+b+c)](\%)$
- German S3 (2018) guidelines

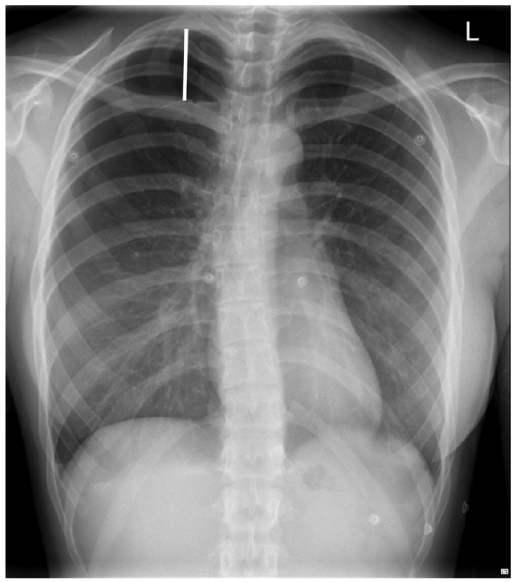
  a+b+c < 4cm: small, ≥4cm: large

# Size of pneumothorax (2)




- British Thoracic Society (BTS) guideline(2010)

  <2cm: small, ≥2cm: large




- American College of Chest Physicians (ACCP) guidelines (2001)

  <3cm: small, ≥3cm: large

# Treatment of first episode of PSP

- Conservative management
- Simple aspiration
- Closed thoracostomy
  - Ambulatory management: small chest tube with Heimlich valve

# Conservative management

- Asymptomatic patients with small pneumothorax
- ACCP (2001) guidelines
  - ER stay for 3 to 6 hours and discharge → follow up within 2 days
- German S3 (2019) guidelines
  - Check with CXR within 24 hours(outpatient) → follow up after 7 days
- Short term hospitalization for observation
  - In cases of unreliable follow up care, distant from hospital…
  - Supplemental oxygen by face mask: increasing the resorption of pneumothorax by up to 4-fold

# Simple aspiration

- Asymptomatic or minimal symptomatic patients with large pneumothorax
- Advantage
  - Lesser complication (pain, displacement, bleeding..)
  - Shorter hospitalization
  - Similar recurrence rate
- Disadvantage
  - Lesser primary success rate (failure rate: 33%)
- Conversion to closed thoracostomy
  - More than 2.5L of air aspiration, failure of aspiration in follow up CXR

# Closed thoracostomy

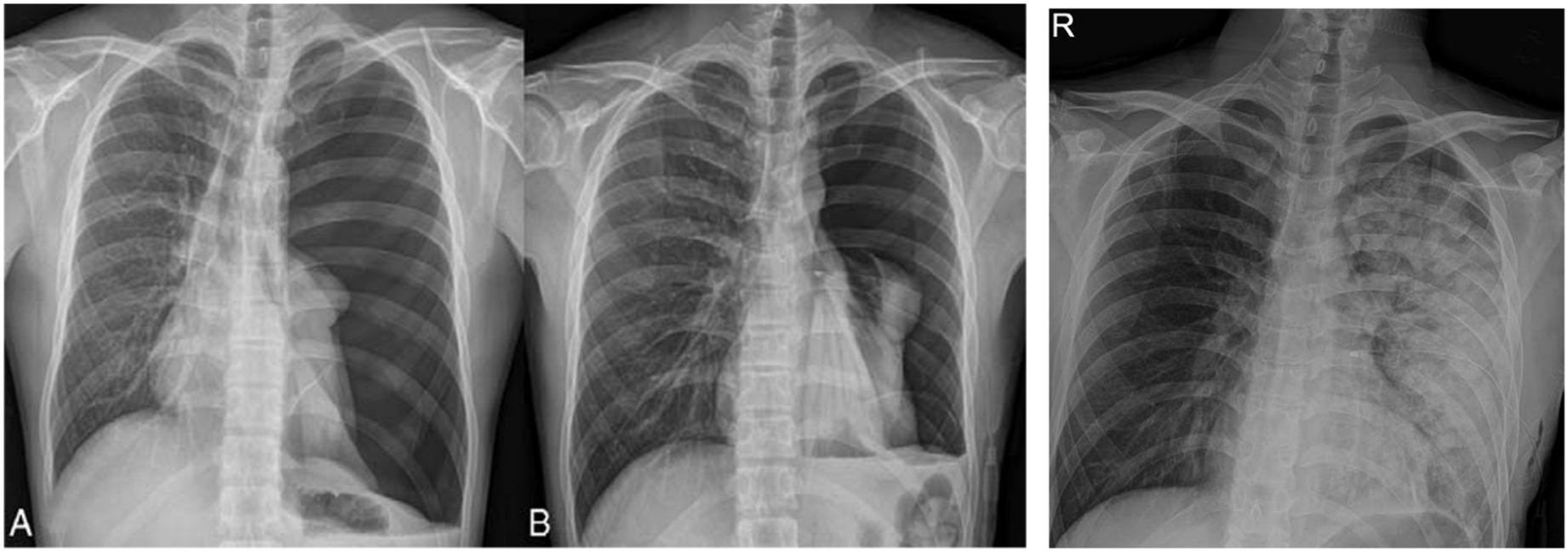
- Symptomatic patients regardless of size, clinically unstable

  → caution of tension pneumothorax

- Size of chest tube
  - Small size drain(<14Fr.) was recommended.
- Suction drain
  - Routinely suction drain: avoidance (BTS, 2010)
  - Increasing risk of re-expansion pulmonary edema (up to 14%)
  - If needed, consider delayed suction drain
- Small chest tube with Heimlich valve: ambulatory management

# Re-expansion pulmonary edema

- Sudden cough, breathless, chest tightness, foamy sputum




Song IH. *Medicine.* 2021;100:e28529.

# Definitive treatment

- To prevent recurrence
- Resection of bullous lesion
- Intraoperative pleurodesis (mechanical, cheminical)

# Indication of surgery

- BTS (2010) guidelines

➢ Recurrent pneumothorax

✓ Second ipsilateral pneumothorax

✓ First contralateral pneumothorax

➢ Synchronous bilateral spontaneous pneumothorax

➢ Persistent air leak or failure of lung re-expansion (5 -7 days)

➢ Spontaneous hemothorax

➢ Professions at risk

➢ Pregnancy

- German S3 (2019) guidelines

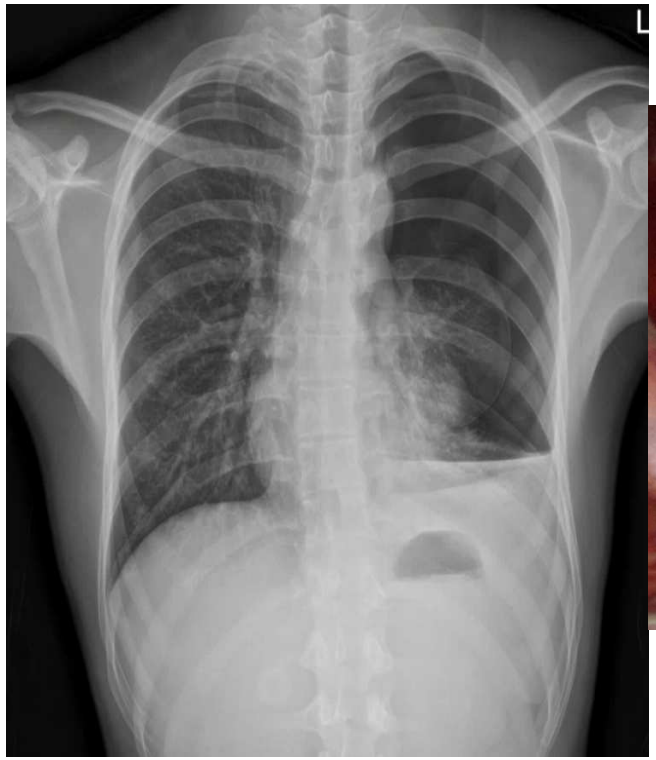
➢ At the first PSP event, consider radiological finding

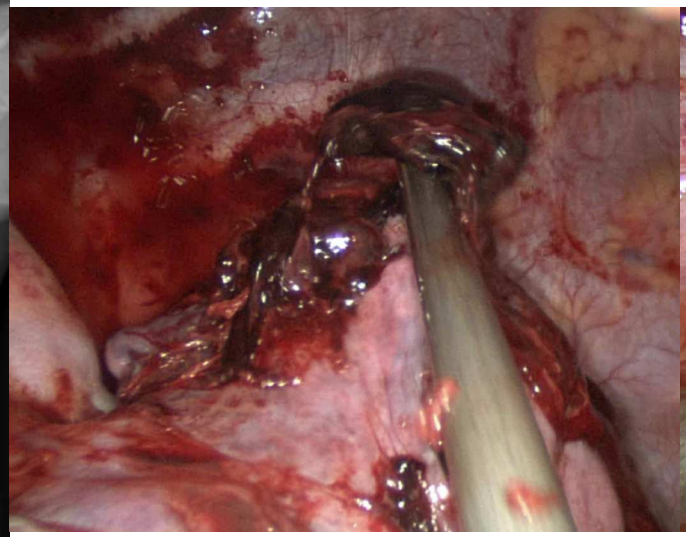
✓ Large pneumothorax

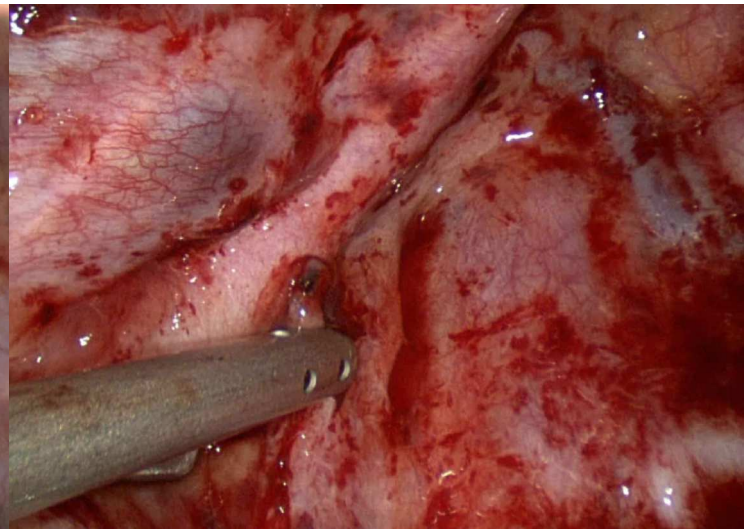
✓ Total atelectasis

✓ Pronounced bullous change

# Hydropneumothorax (hemopneumothorax)





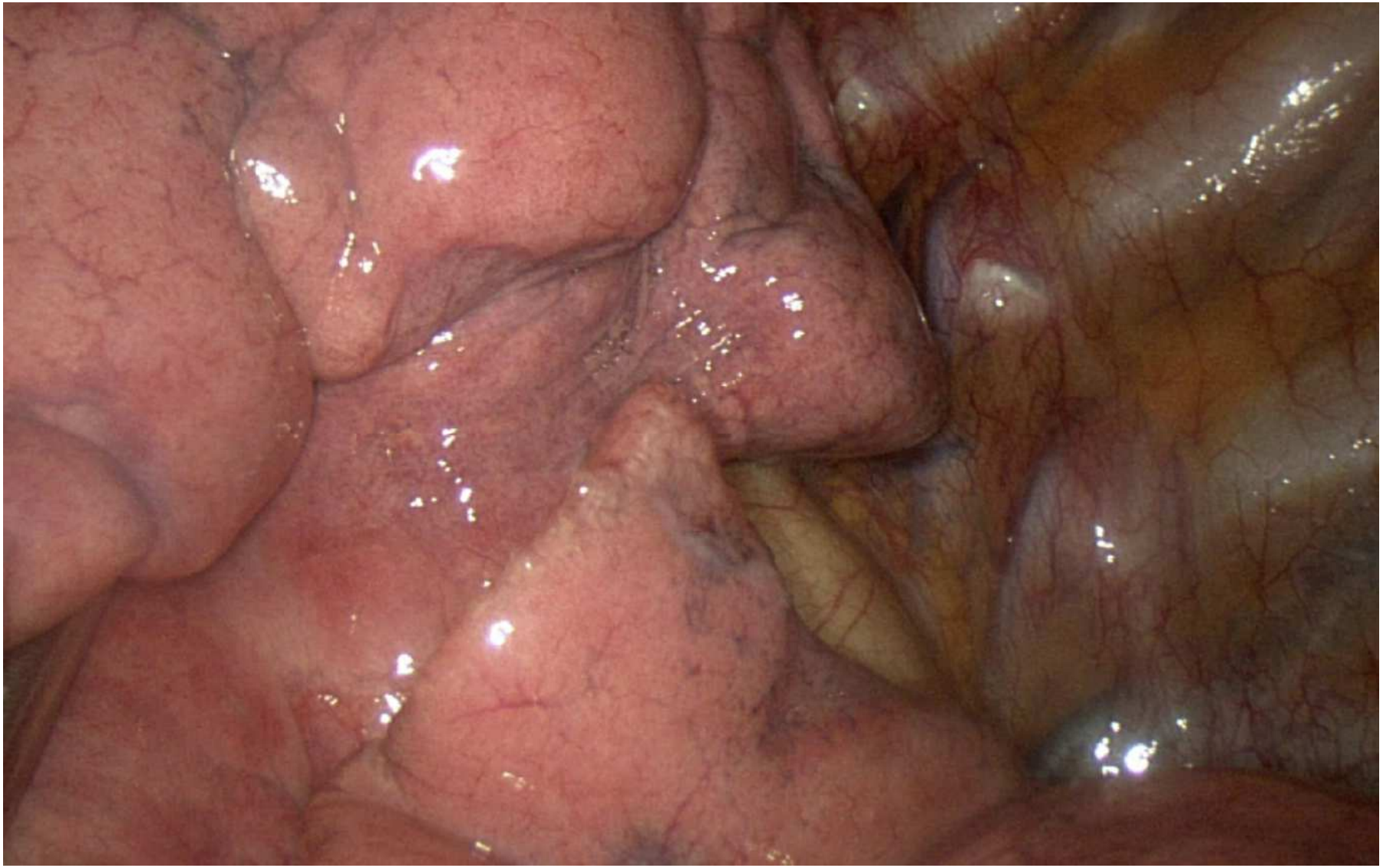
# Surgical procedure (VATS)

- Resection of lesion
  - Wedge resection or bullectomy
- Additional procedure
  - Partial pleurectomy
  - Mechanical pleurodesis
  - Chemical pleurodesis (including talc)
  - Mesh coverage on the stapler line

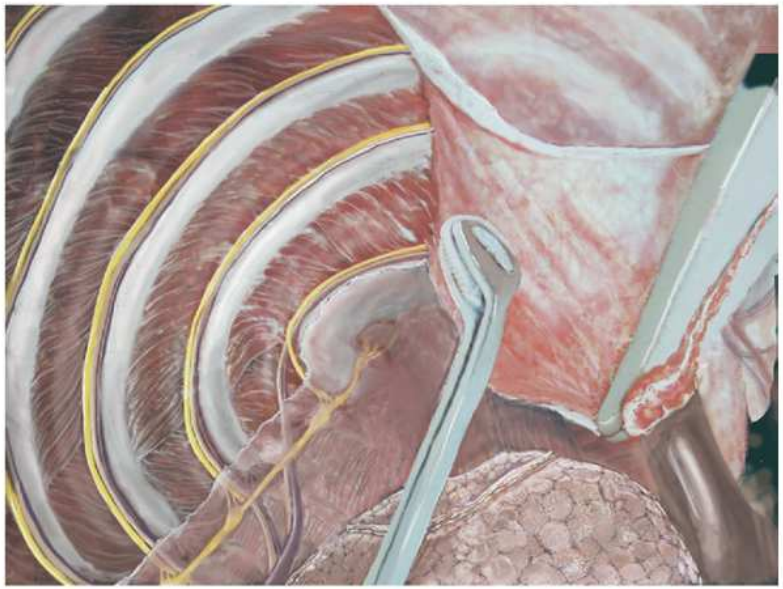
# Wedge resection

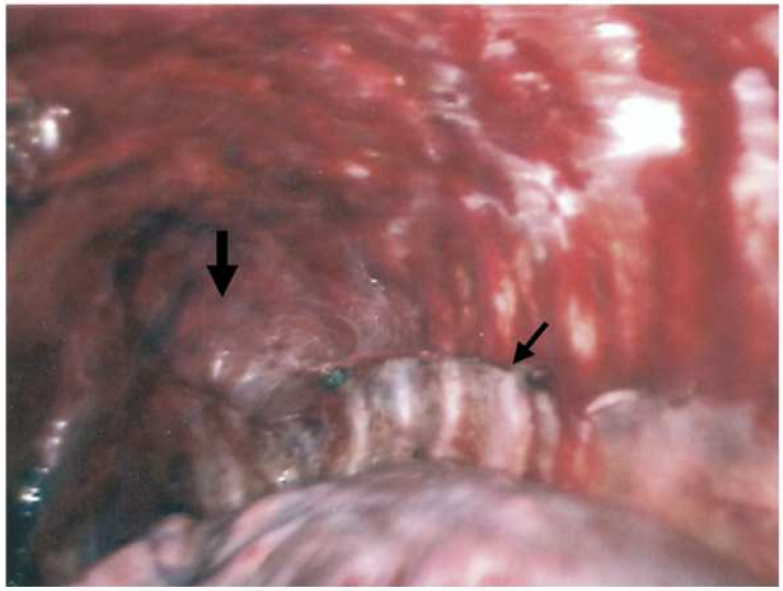
- Distance from stapler line, resected lung volume

→ associated with postoperative recurrence rate, neo bullae formation



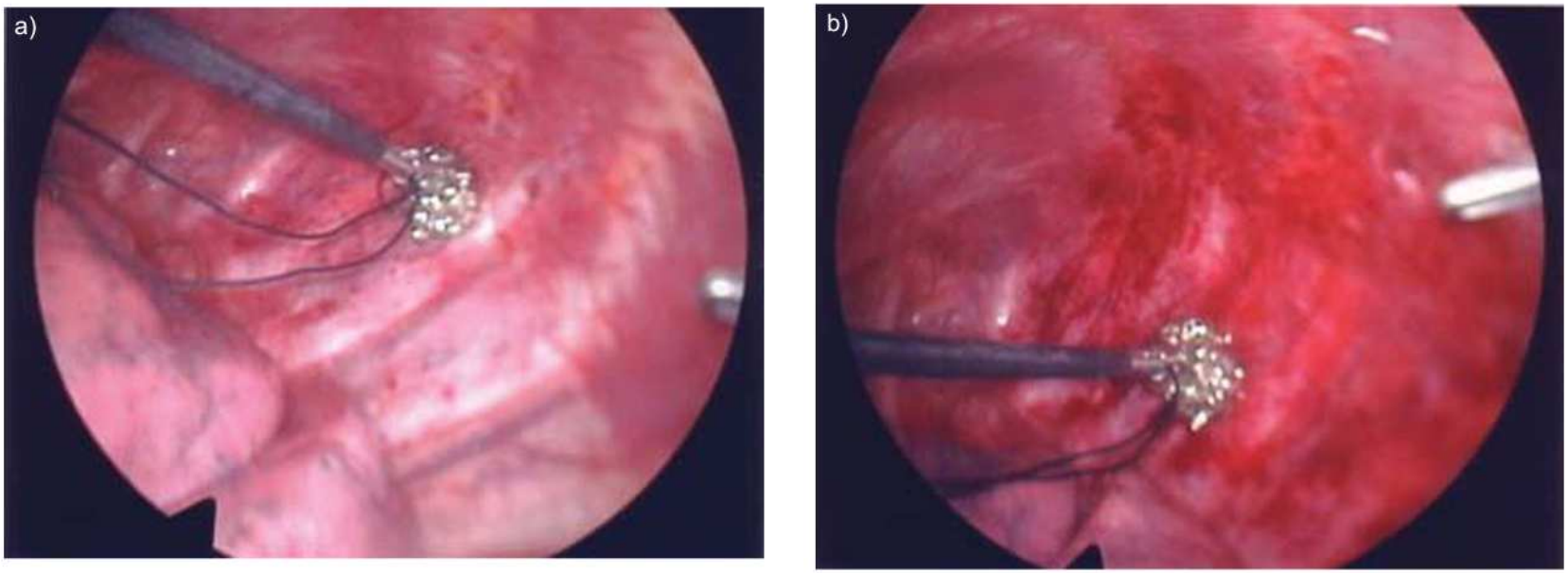
# Partial pleurectomy





Nathan DP. *Ann Thorac Surg*. 2008;85:1825-1827.

# Mechanical pleurodesis

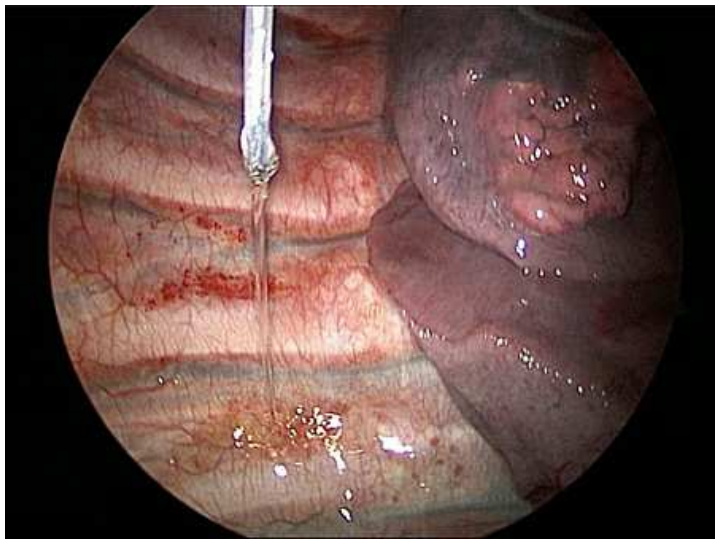


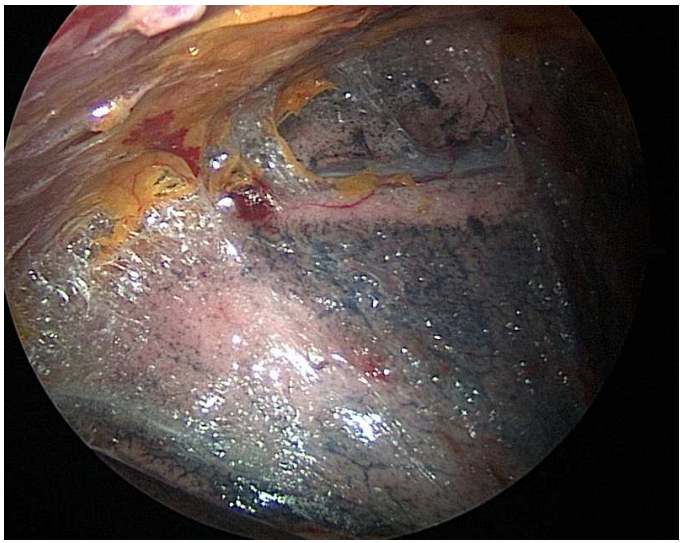

Tschopp J-M. *Eur Respir J.* 2006;28:637-650.

# Intraoperative chemical pleurodesis (1)

- Talc, tetracycline, bleomycin, iodine, 50% dextrose, viscum…
- Intraoperative talc pleurodesis was recommended (BTS, German S3 guidelines)
- Higher success rate
- Difficulty in reoperation
- Concern about pulmonary function

# Intraoperative chemical pleurodesis (2)





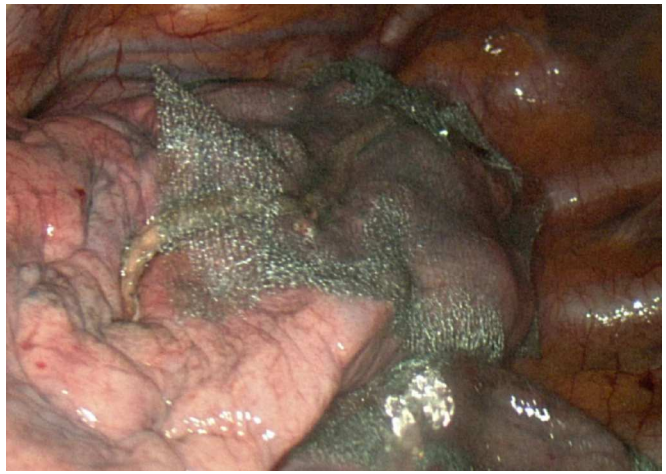
Recurrence rate : 0%

Reoperation after 6 months

Jung HS. *Sci Rep.* 2021;11:22934.

# Covering method (1)

- Absorbable polyglycolic acid(PGA) >> oxidized regenerated cellulose(ORC)



Recurrence rate : 3.4%

Recurrence rate : 17.2%

Oda R. *BMJ Open Respir Res*. 2022;9:e001231

# Covering method (2)

A B

Oda R. *BMJ Open Respir Res*. 2022;9:e001231

# Secondary Spontaneous Pneumothorax

# Cause of SSP

- Chronic obstructive pulmonary disease/emphysema
- Infection: tuberculosis, bacterial infection with lung abscess or necrotizing pneumonia, *Pneumocystis jirovecii* pneumonia(PCP), Covid-19, aspergilloma..
- Tumor: lung cancer, sarcoma..
- Interstitial lung disease: IPF, sarcoidosis..
- Connective Tissue disease: RA, marfan's syndrome, Ehlers Danlos syndrome..
- Diffuse cystic lung disease: Lymphangioleiomyomatosis(LAM), Pulmonary Langerhans cell histiocytosis (PLCH), Birt-Hogg-Dube syndrome (BHD), Lymphoid interstitial pneumonia (LIP)

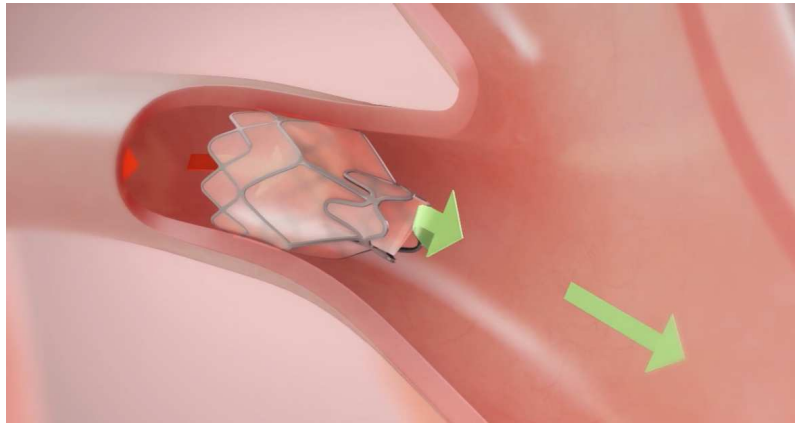
# Characteristics of SSP

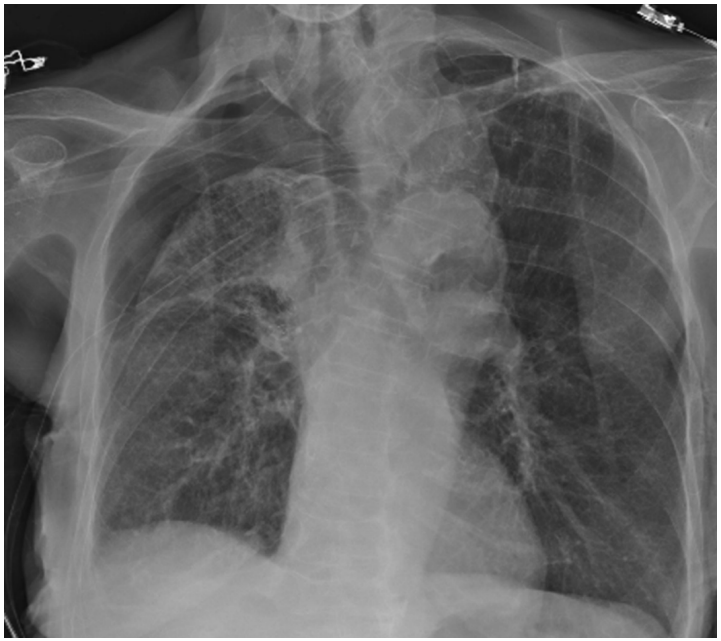
- Dyspnea severity ↑
- Rapid progression
- Diffuse lesions of lung
- Recurrence rate ↑ (more than 50%, within 6 months)
- Consider other morbidity

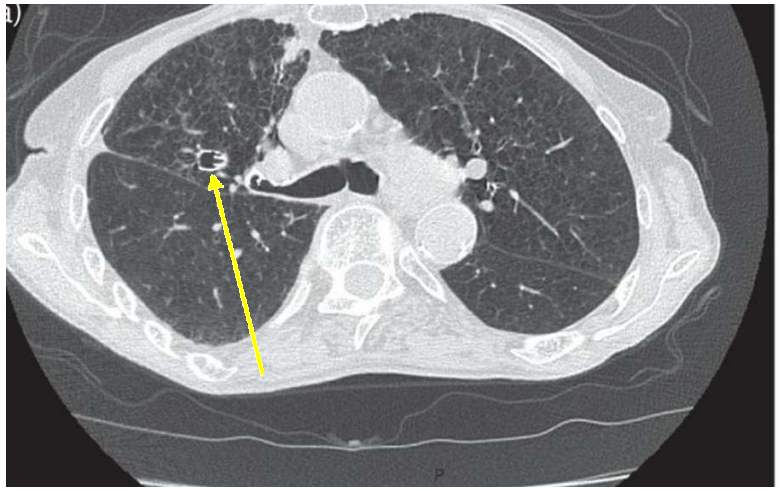
# Management of SSP

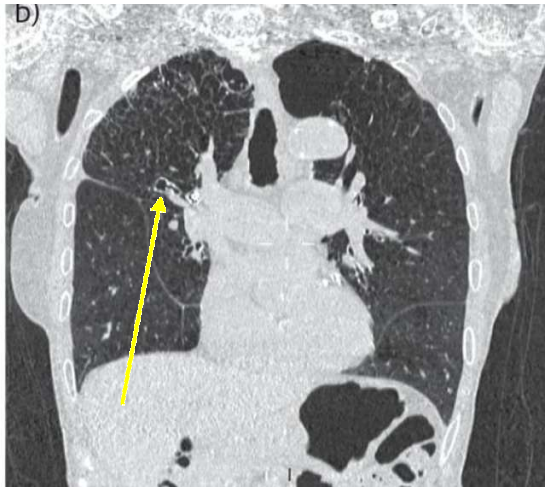
- Closed thoracostomy + hospitalization
- Consider definitive treatment
  - Surgery + intraoperative chemical pleurodesis/parietal pleurectomy
  - Bedside chemical pleurodesis
- Persistent airleakage in inoperable patients
  - Ambulatory chest tube (Heimlich valve)
  - Endobronchial valve
  - Fibrin glue under pleurography

# Endobronchial valve



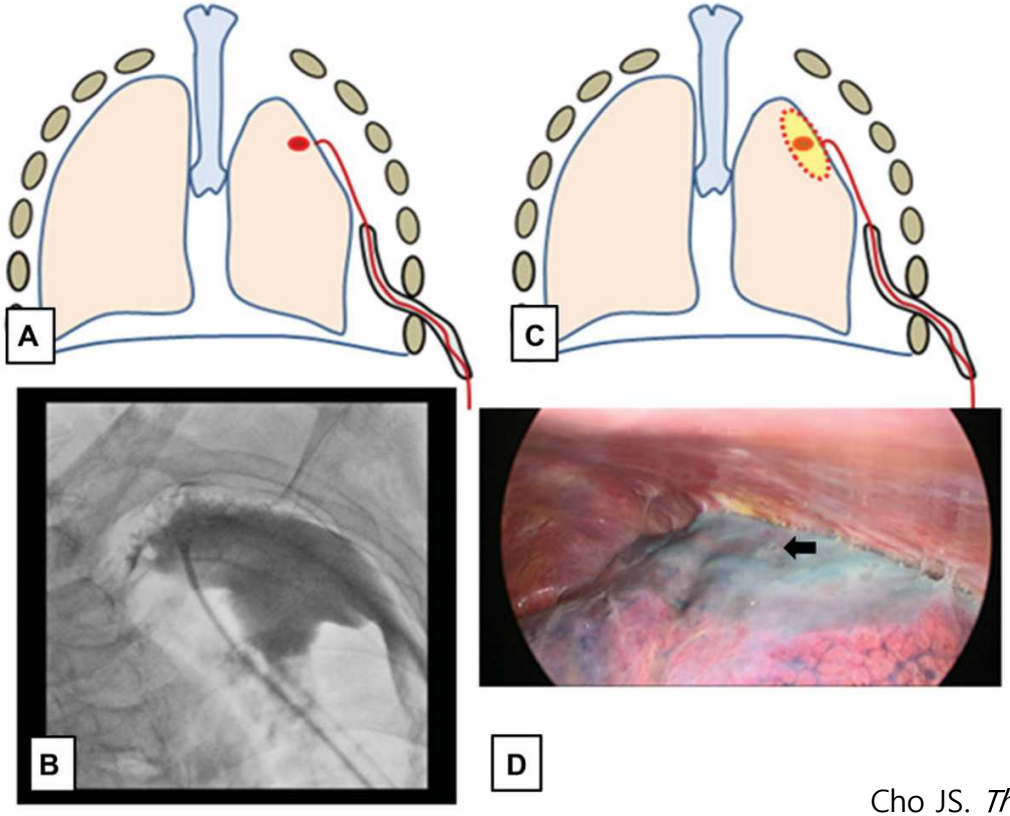






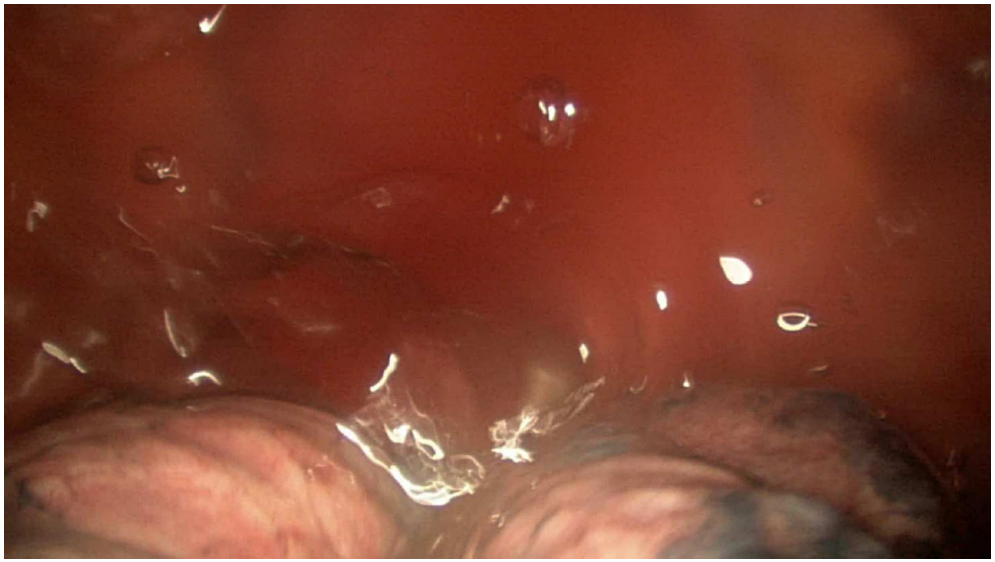

Morrison M. *Breathe.* 2016;12:61-64.

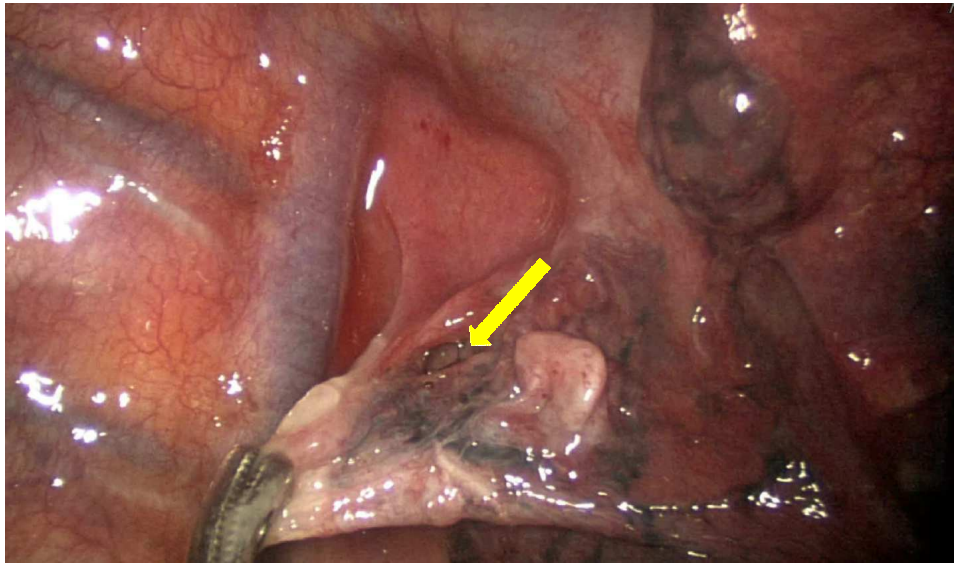
# Pleurography

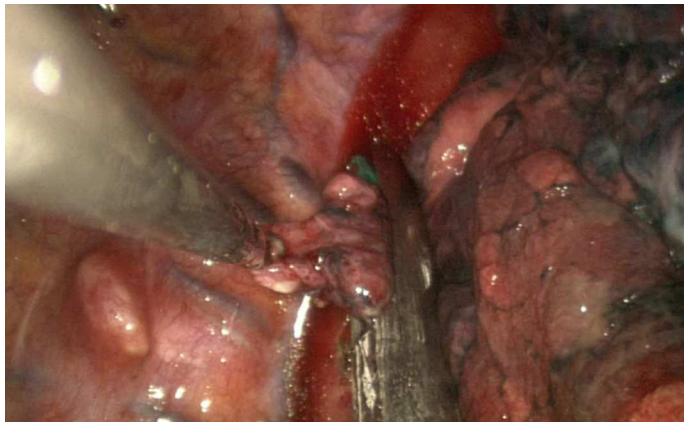



Cho JS. *Thorac Cardiovasc Surg.* 2021;69:466-469.

# Case of SSP







# Parapneumonic effusion & empyema

# Introduction

- Empyema : pus in the chest
- Cause : Pneumonia(m/c), lung abscess, postop complication, trauma, subphrenic abscess, sepsis, Tbc…
- Pneumonia -> 20~40% ; parapneumonic effusion -> 5~10% ; empyema -> 10% ; death
- Empyema incidence in pneumonia
  - pre-antibiotic era : 5% , post-antibiotic era : 2%
  - Recently increasing : old age, co-morbidity

Davies HE. *Thorax.* 2010;65 suppl :ii41-53.

# Incidence

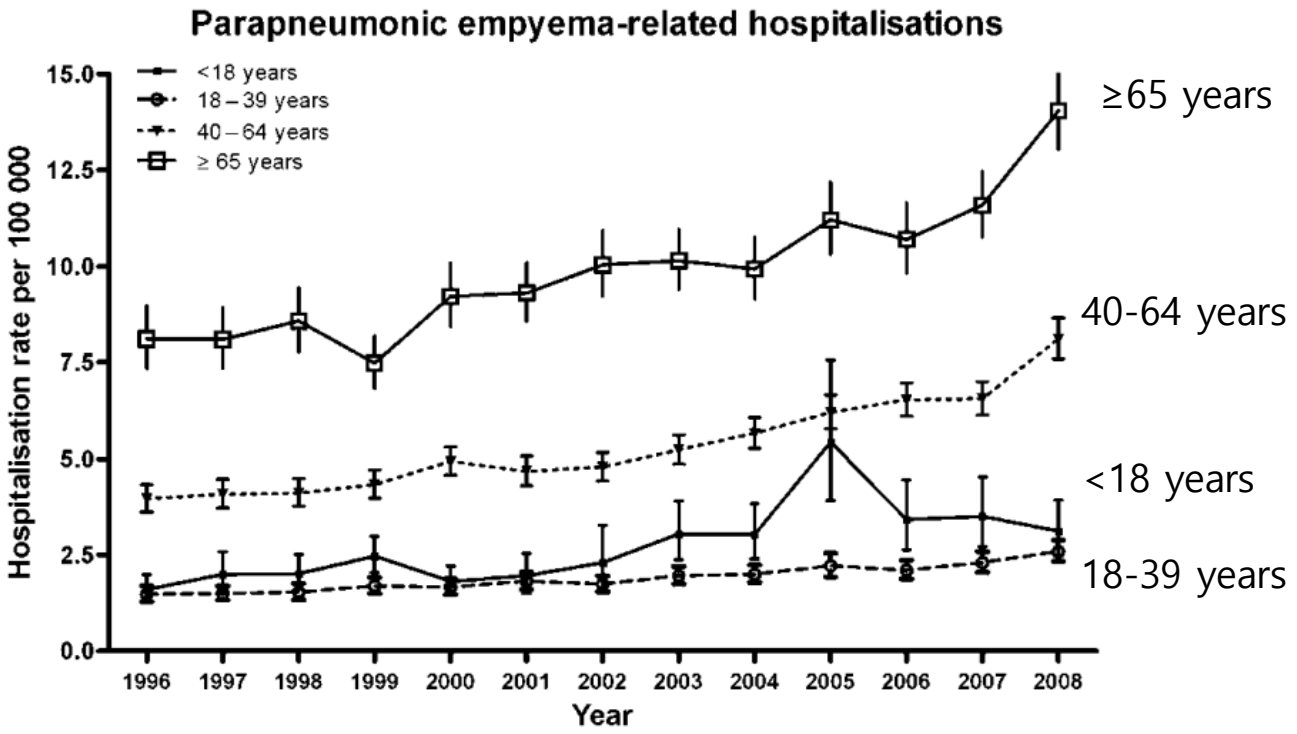
In USA

1996~2008

National hopitalisation data

In 1996, 3.04/100,000

In 2008, 5.98/100,000




Grijalva CG. *Thorax* 2011;66:663-8.

# Stage of Empyema

Stage 1

Simple parapneumonic effusion(uncomplicated), acute exudative stage, pre-empyema stage

Stage 2

Transitional fibrinopurulent stage, complicated parapneumonic effusion, empyema

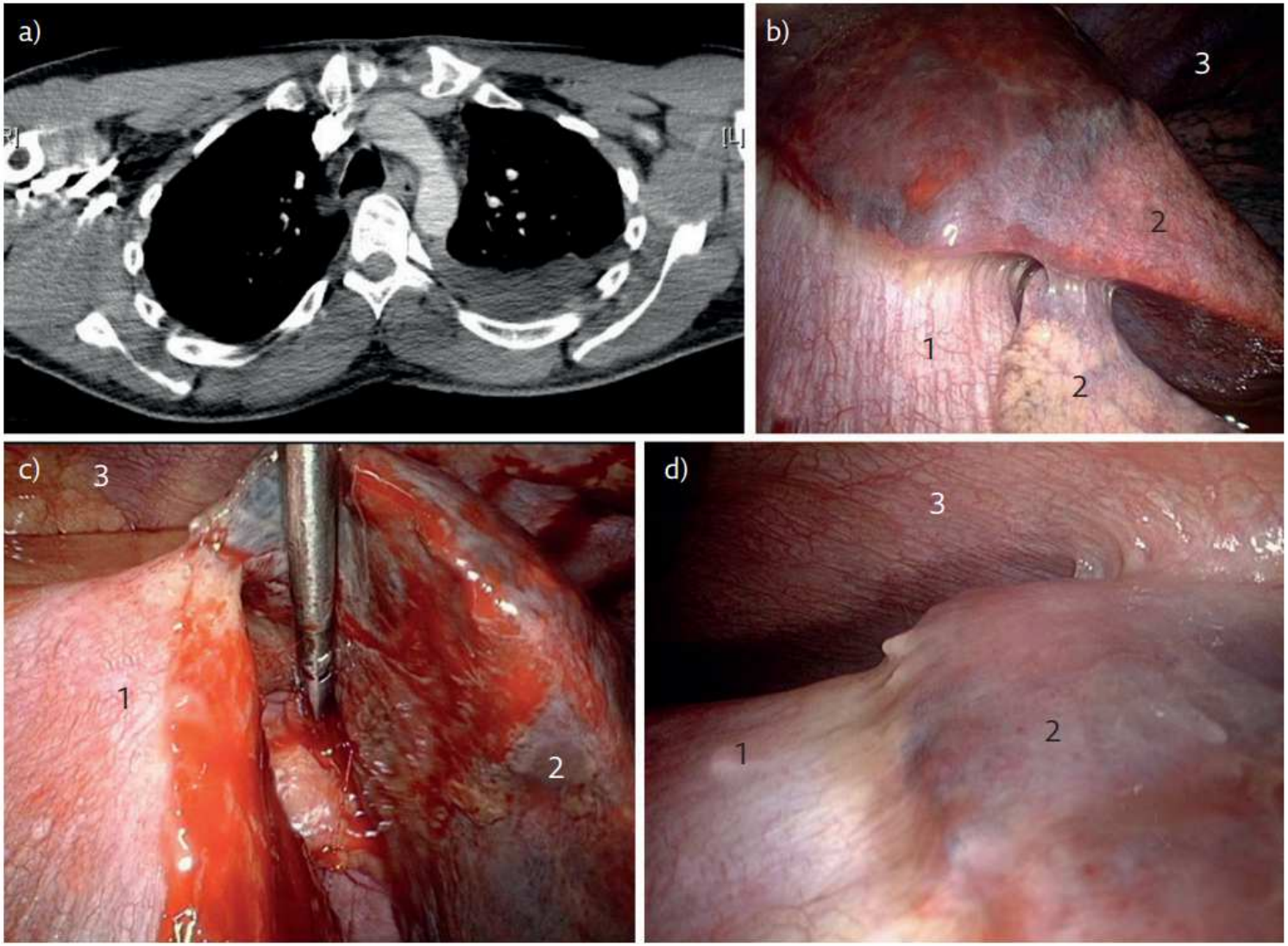
Stage 3

Chronic organizing stage, fibrothorax

# Simple Parapneumonic Effusion

- Fluid movement into pleural cavity d/t increased capillary vascular permeability
- Free flowing exudate effusion
- Pleural fluid analysis
  - Low white cell count, LDH < ½ level of serum, Normal pH, Normal glucose level
- No bacterial organism

Davies HE. *Thorax.* 2010;65 suppl :ii41-53.

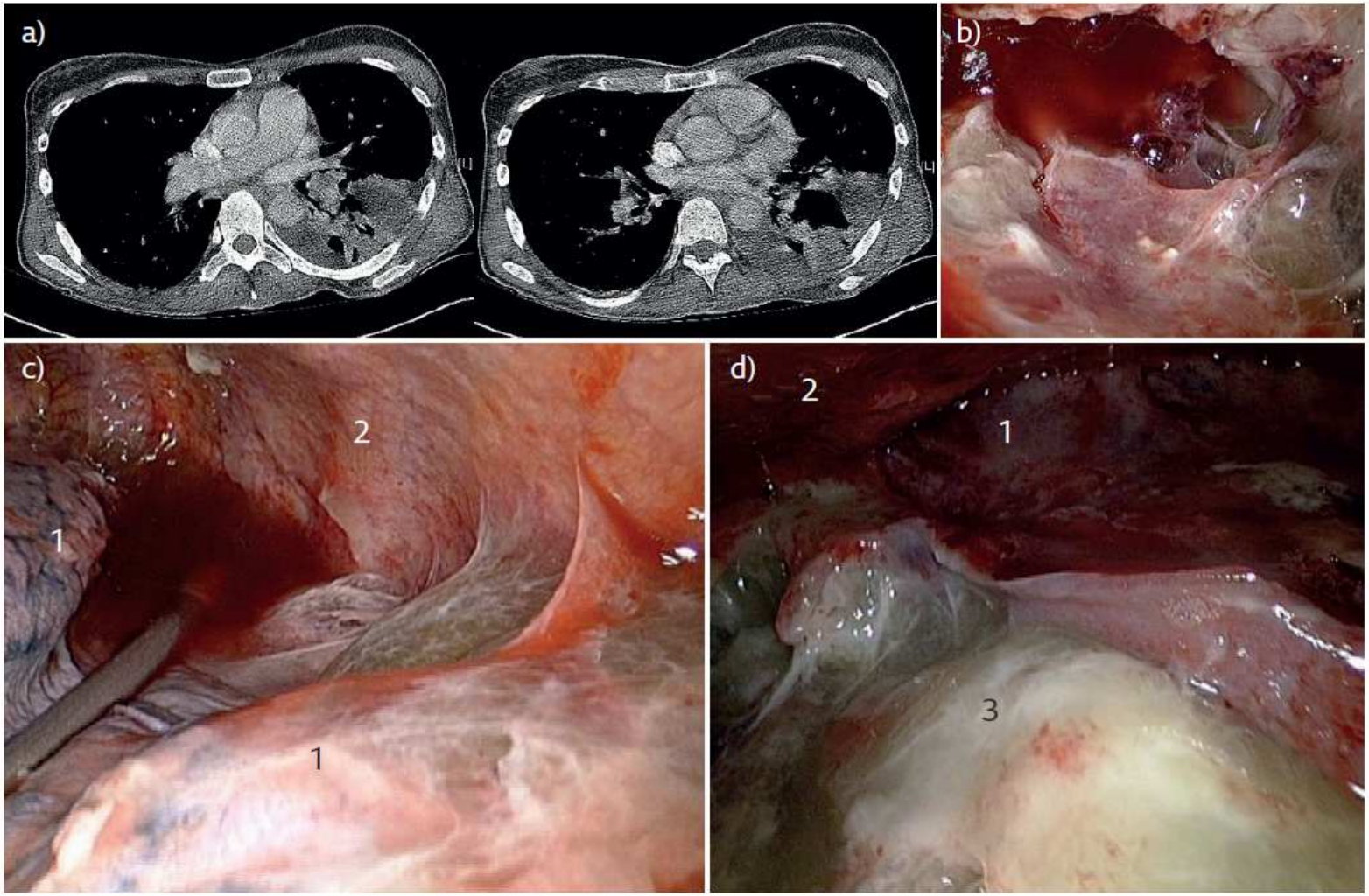



Subotic D. *Breathe.* 2018;14:302-310.

# Fibrinopurulent Stage

- Complicated parapneumonic effusion(without pus), Empyema(with pus)
- Bacterial invasion -> immune response -> migration of neutrophil, activation of the coagulation cascade ->fibrin deposit -> loculation
- Pleural fluid analysis
  - pH<7.2, glucose <40mg/dL, LDH > 1000IU/L

Davies HE. *Thorax.* 2010;65 suppl :ii41-53.

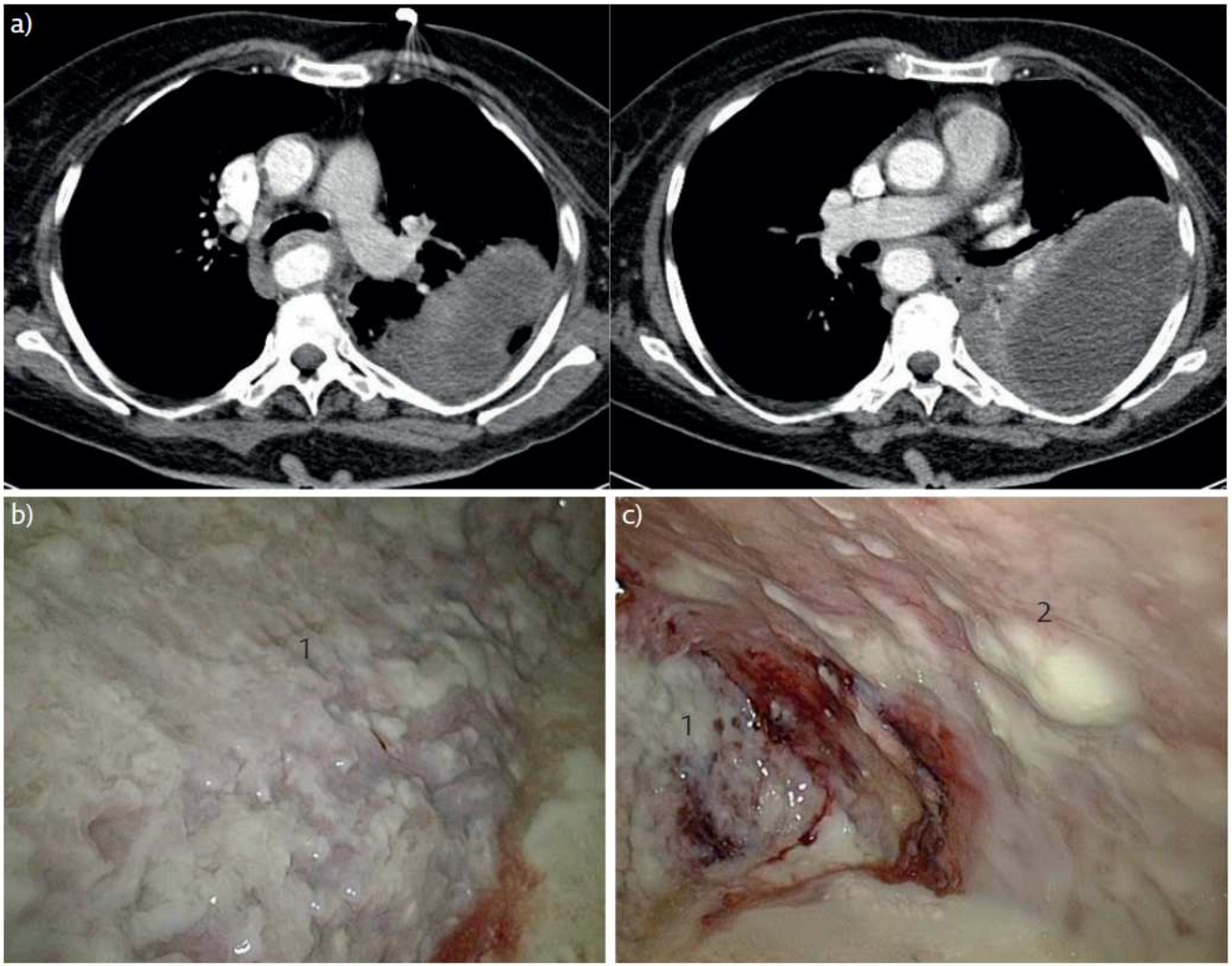



Subotic D et al. *Breathe.* 2018;14:302-310.

# Chronic Organizing Stage

- Peel : solid fibrous pleura cortex
  - Preventing re-expansion
  - Impairing lung function
  - Potential for infection

Davies HE. *Thorax.* 2010;65 suppl :ii41-53.




Subotic D. *Breathe.* 2018;14:302-310.

# Guidelines

- American College of Chest Physicians (ACCP) guidelines (2000)
- British Thoracic Society (BTS) Guidelines (2010)
- European Association for Cardio-Thoracic Surgery (EACTS) Guideline (2015)
- American Association for Thoracic Surgery (AATS) Guidelines (2017)

# Management of Empyema

- Antibiotics
- Thoracentesis
- Drainage
- Fibrinolytic therapy
- Surgical treatment

# Question in Each Stage


Thoracentesis?

Drainage?

Additional Drainage?

Fibrolytic therapy?

Timing of Surgery?

# Empirical Antibiotics

- Community-acquired
  - 2nd or 3rd cephalosporin + metronidazole
  - Aminopenicillin with β-lactamase inhibitor
- Hospital-acquired
  - MRSA, *P. aeruginosa*, anaerobes
  - Vancomycin, cefepime and metronidazole
  - Vancomycin and piperacillin/tazobactam
- Avoidance of aminoglycoside

AATS guideline 2017

# Thoracentesis

- Class III no benefit: Thoracentesis without pleural drain placement is not recommended for the treatment of parapenumonic effusion or empyema (LOE C).

AATS guideline 2017

# Pleural drainage

Class I: Image-guided pleural drain placement is useful in the treatment of early-stage, minimally septated empyema (LOE B).

Class IIa: In septated effusions, placement of small bore catheters are recommended in patients that are not surgical candidates (LOE C).

Class I: Routine drain flushing is recommended to prevent occlusion (LOE B).

Class I: Tube thoracostomy should be combined with close CT follow-up to confirm adequacy of drainage. Persistence of any undrained fluid should prompt additional drains or more aggressive management (LOE C).

AATS guideline 2017

# Fibrinolytic Therapy

- Class IIa: Intrapleural fibrinolytics should not be used routinely for complicated pleural effusions and early empyemas (LOE A).

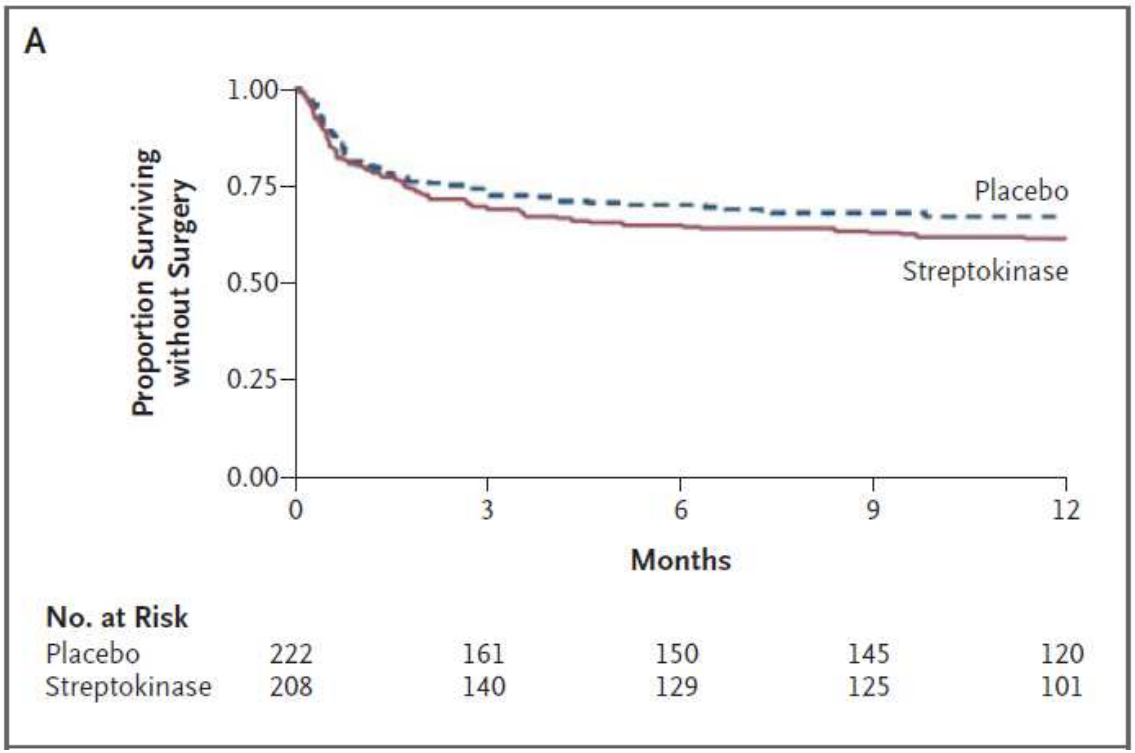
AATS guideline 2017

# Multicenter Intrapleural Sepsis Trial(MIST) I

- RCT, 52 centers in UK
- Inclusion : pleural fluid with purulent, positive on culture, positive in Gram stain or pH < 7.2
- 427 patients : streptokinase(208) vs placebo(222)
- Streptokinase : 250000IU Bid for 3 days
- Indication of surgical drainage : residual effusion + evidence of persistent infection
- Primary end point : death or surgery (3 month)
- Secondary end point : death or surgery (12 month), hospital stay, residual abnormality on CXR, dynamic lung volume, bleeding after surgery….

Maskell NA. *N Engl J Med.* 2005;352:865-74.

# Result (1)




Primary outcome : death or surgery

Streptokinase vs Placebo

At 3 month

: 31% vs 27%, p=0.43

At 12 month

: 40% vs 34%, p=0.24

Maskell NA et al. *N Engl J Med.* 2005;352:865-74.

# Result (2)

- Death (Streptokinase vs Placebo)
  - At 3 month : 16% vs 14%, $p$=0.66
  - At 12 month : 23% vs 20%, $p$=0.64
- Surgical drainage
  - At 3 month : 16% vs 14%, $p$=0.87
  - At 12 month : 18% vs 16%, $p$=0.60

Maskell NA et al. *N Engl J Med.* 2005;352:865-74.

# Discussion from MIST I

- Negative result d/t
  - Dosage of streptokinase
  - Antistreptokinase-antibody
  - Low level of plasminogen → tPA? → MIST II
  - Viscosity of pus → DNase? → MIST II

- Conclusion
  - Streptokinase should be avoided in pleural infection

Maskell NA et al. *N Engl J Med.* 2005;352:865-74.

# Surgical Outcome from MIST I

- Surgery : streptokinase + placebo
  - At 3 month : 64 (32+32)
  - At 12 month : 70 (36+34)
- Type of surgery (57)
  - 9 (5+4) : VATS drainage
  - 39 (17+22) : thoracotomy and decortication
  - 9 (5+4) : another form including rib resection
- Mortality (10%~)
  - 7 (2+5)

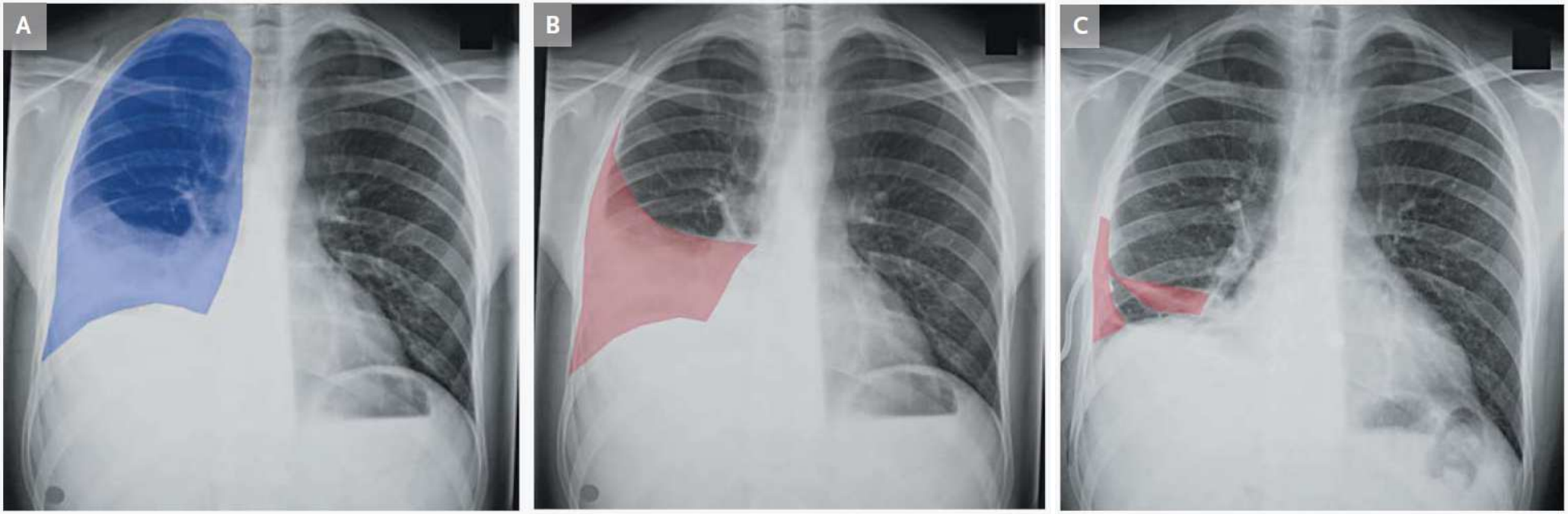
Maskell NA et al. *N Engl J Med.* 2005;352:865-74.

# Multicenter Intrapleural Sepsis Trial II

- RCT, 11 centers in UK
- Inclusion : pleural fluid with purulent, positive on culture, positive in Gram stain or pH < 7.2
- 210 patients : t-PA (48), DNase(46), t-PA+DNase(48), Placebo(51)
- t-PA : 10mg bid for 3 days, DNase : 5mg bid for 3 days
- Indication of surgical drainage : residual effusion + evidence of persistent infection
- Primary end point : area of pleura opacity in CXR from day 1 to day 7
- Secondary end point : % reduction of pleural opacity, surgical referral (3, 12 months), hospital stay, volume of drain to day 7, inflammatory maker to day 7, death (3, 12 months), adverse event

Rahman NM et al. *N Engl J Med.* 2011;365:518-26.

# Multicenter Intrapleural Sepsis Trial II




Rahman NM et al. *N Engl J Med.* 2011;365:518-26.

# Result (1)

| Outcome | t-PA | DNase | t-PA–DNase | Placebo |
|---|---|---|---|---|
| Change from baseline in hemithorax area occupied by effusion (primary outcome) — % | −17.2±24.3 | −14.7±16.3 | −29.5±23.3 | −17.2±19.6 |
| Percent difference vs. placebo (95% CI) | 2.0 (−4.6 to 8.6) | 4.5 (−1.5 to 10.5) | −7.9 (−13.4 to −2.4) | NA |
| P value | 0.55 | 0.14 | 0.005 | NA |
| Surgical referral — no. referred/total no. (%) | 3/48 (6) | 18/46 (39) | 2/48 (4) | 8/51 (16) |
| Odds ratio vs. placebo (95% CI) | 0.29 (0.07 to 1.25) | 3.56 (1.30 to 9.75) | 0.17 (0.03 to 0.87) | NA |
| P value | 0.10 | 0.01 | 0.03 | NA |
| Hospital stay — no. of days | 16.5±22.8 | 28.2±61.4 | 11.8±9.4 | 24.8±56.1 |
| Percent difference vs. placebo (95% CI) | −8.6 (−40.8 to 3.3) | 3.6 (−19.0 to 30.8) | −14.8 (−53.7 to −4.6) | NA |
| P value | 0.21 | 0.73 | <0.001 | NA |

Rahman NM et al. *N Engl J Med.* 2011;365:518-26.

# Result (3)

| Mortality | t-PA (48) | DNase (46) | t-PA-DNase (48) | Placebo (50) | *p* value |
|---|---|---|---|---|---|
| At 3 months | 4 (8%) | 6 (13%) | 4 (8%) | 2 (4%) | 0.46 |
| At 12 months | 5 (11%) | 9 (20%) | 5 (11%) | 4 (8%) | 0.37 |

Rahman NM et al. *N Engl J Med.* 2011;365:518-26.

# Conclusion from MIST II

- Benefit of t-PA–DNase therapy
  - ✓the frequency of surgical referral
  - ✓the duration of the hospital stay

- Mortality : no benefit

- This combined treatment may therefore be useful in patients in whom standard medical management has failed and thoracic surgery is not a treatment option.

Rahman NM et al. *N Engl J Med.* 2011;365:518-26.

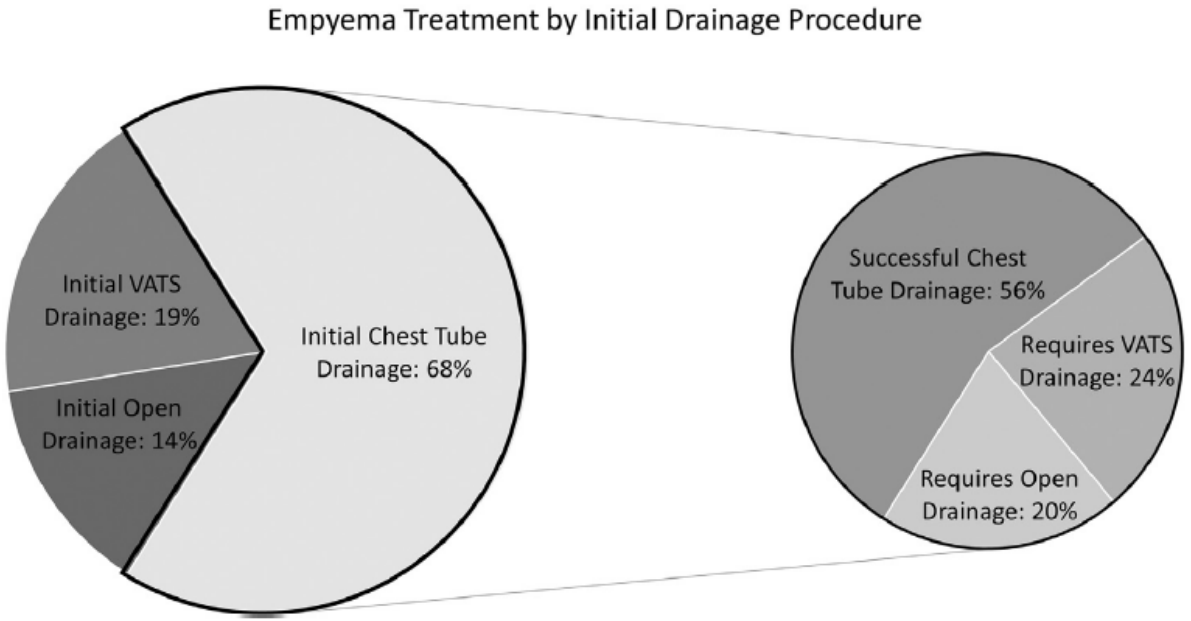
# Surgical Treatment

- Class IIa: Video-assisted thoracoscopic surgery (VATS) should be the first-line approach in all patients with stage II acute empyema (LOE B) (AATS guideline 2017).
- There is nothing to be lost in attempting VATS in all cases, provided that conversion to open thoracotomy is performed if resolution of the empyema and lung expansion is not adequately achieved (EACTS guideline, 2015).

# Type of Surgery

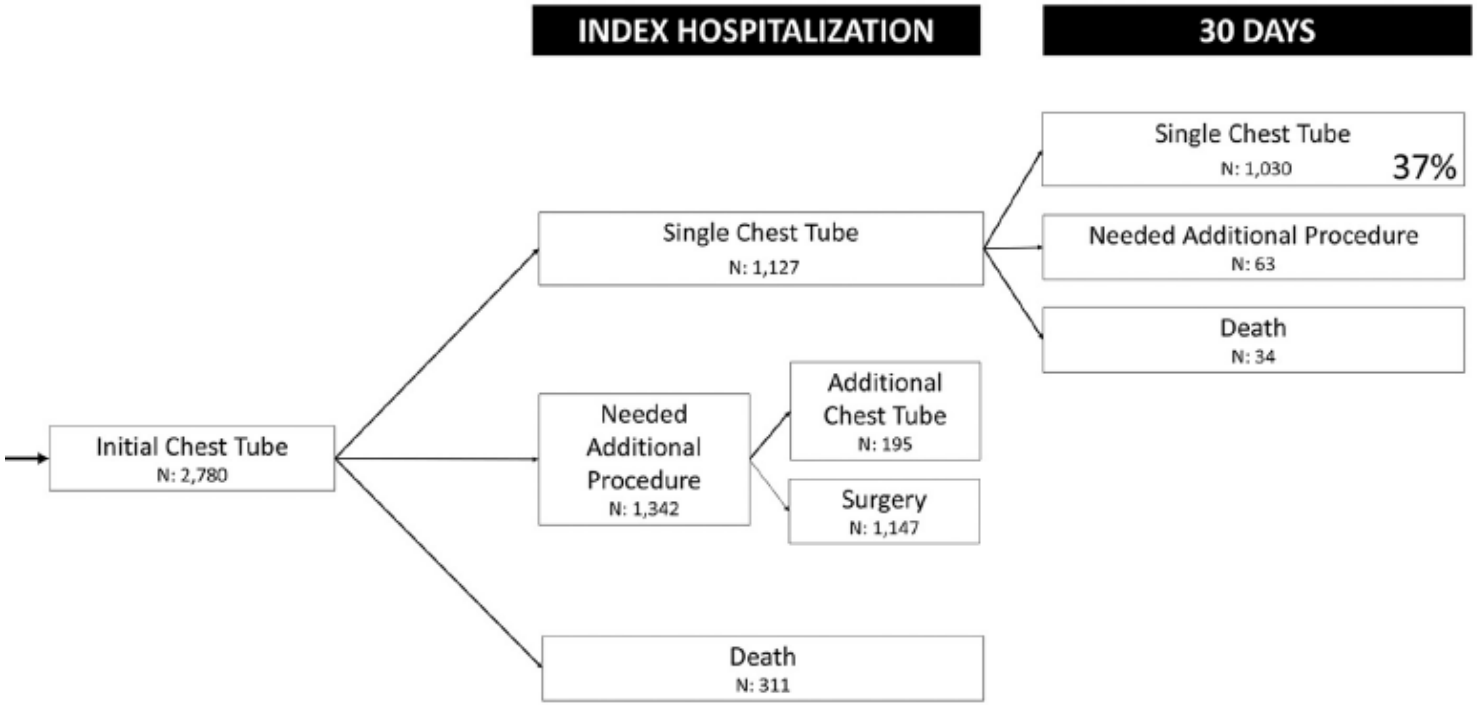
- VATS vs Open
- Debridement vs Decortication
- Goal of surgery
  - ✓Complete evacuation of potentially infected fluid
  - ✓Complete re-expansion of the lung

# Surgical Conversion from Chest Tube



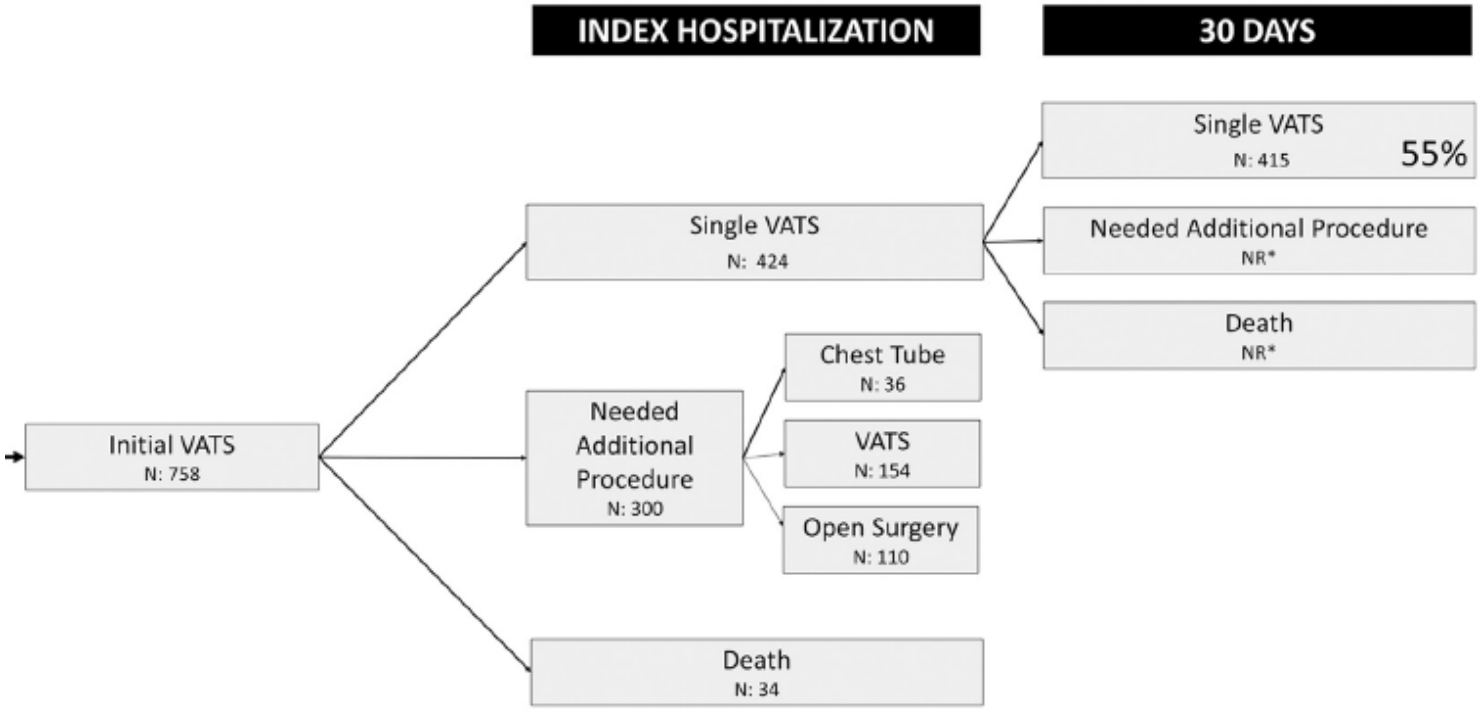

Semenkovich TR et al. *Ann Thorac Surg.* 2018;105:1589-96.

# Fate of Initial Chest Tube



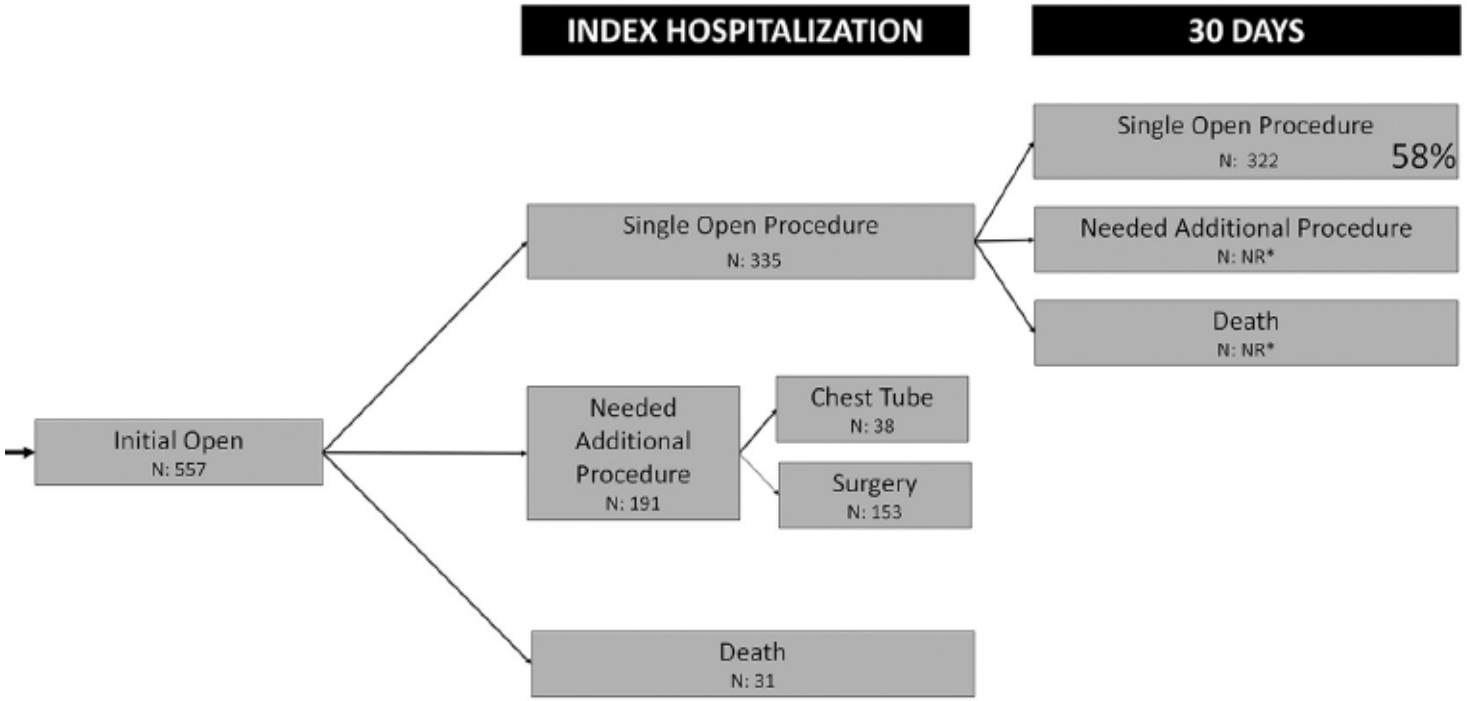

Semenkovich TR et al. *Ann Thorac Surg.* 2018;105:1589-96.

# Fate of Initial VATS




Semenkovich TR et al. *Ann Thorac Surg.* 2018;105:1589-96.

# Fate of Initial Open




Semenkovich TR et al. *Ann Thorac Surg.* 2018;105:1589-96.

# Outcomes according to Initial Treatment

| | | Drainage or Decortication | | |
|---|---|---|---|---|
| | Chest Tube | VATS | Open | |
| Outcome Measure | No. (%) or median (IQR) (N = 4,095) | | | *p* |
| Patients | 1,563 (38.2) | 1,313 (32.1) | 1,219 (29.8) | |
| Length of stay, days | 14 (9–22) | 12 (9–19) | 15 (10–21) | <0.001 |
| Mortality rate | | | | |
| Index hospitalization | 241 (15.4) | 62 (4.7) | 73 (6.0) | <0.001 |
| 30 days | 286 (18.3) | 71 (5.4) | 83 (6.8) | <0.001 |
| 90 days | 322 (20.6) | 83 (6.3) | 91 (7.5) | <0.001 |
| 30-day readmission rate | | | | |
| For any reason | 276 (20.9) | 144 (11.5) | 154 (13.4) | <0.001 |
| For empyema | 96 (7.3) | 48 (3.8) | 47 (4.1) | <0.001 |
| 90-day readmission rate | | | | |
| For any reason | 391 (29.6) | 236 (18.9) | 236 (20.6) | <0.001 |
| For empyema | 113 (8.9) | 55 (4.4) | 63 (5.6) | <0.001 |
| 30-day reintervention rate | 80 (6.1) | 24 (1.9) | 24 (2.1) | <0.001 |
| 90-day reintervention rate | 113 (8.8) | 37 (3.0) | 45 (4.0) | <0.001 |

Semenkovich TR et al. *Ann Thorac Surg.* 2018;105:1589-96.

| Outcome | Overall N = 7316 | Thoracotomy decortication N = 2881 | VATS decortication N = 4435 | *P* value |
|---|---|---|---|---|
| Duration of procedure (min) | 95.0 (68.0-134.0) | 114.0 (82.0-158.0) | 85.0 (60.0-118.0) | <.0001 |
| Length of stay (d) | 12.0 (8.0-18.0) | 13.0 (9.0-20.0) | 11.5 (8.0-17.0) | <.0001 |
| Time (d) from admit to surgery | 4.0 (2.0-7.0) | 4.0 (2.0-8.0) | 4.0 (2.0-7.0) | .0001 |
| **Postoperative length of stay (d)** | **7.0 (5.0-11.0)** | **8.0 (6.0-13.0)** | **7.0 (5.0-11.0)** | **<.0001** |
| **Prolonged postoperative LOS (>19 d)** | **707 (9.7%)** | **343 (11.9%)** | **364 (8.2%)** | **<.0001** |
| Any postoperative event | 2875 (39.3%) | 1306 (45.3%) | 1569 (35.4%) | <.0001 |
| Unexpected reoperation | 281 (3.8%) | 129 (4.5%) | 152 (3.4%) | .0224 |
| Air leak >5 d duration | 257 (3.5%) | 117 (4.1%) | 140 (3.2%) | .0401 |
| Atelectasis requiring bronchoscopy | 235 (3.2%) | 117 (4.1%) | 118 (2.7%) | .0009 |
| Pulmonary embolus | 26 (0.4%) | 10 (0.3%) | 16 (0.4%) | .9236 |
| Ventilator support >48 h | 497 (6.8%) | 242 (8.4%) | 255 (5.7%) | <.0001 |
| Reintubation | 198 (3.7%) | 102 (4.7%) | 96 (3.0%) | .0019 |
| Tracheostomy | 199 (2.7%) | 104 (3.6%) | 95 (2.1%) | .0002 |
| Other pulmonary events | 207 (2.8%) | 81 (2.8%) | 126 (2.8%) | .9407 |
| Respiratory failure | 154 (4.8%) | 80 (6.5%) | 74 (3.7%) | .0003 |
| Wound infection | 5 (0.2%) | 4 (0.4%) | 1 (0.1%) | .1152 |
| Unexpected admission to ICU | 260 (3.6%) | 102 (3.5%) | 158 (3.6%) | .9602 |
| New renal failure per RIFLE criteria | 164 (3.1%) | 69 (3.6%) | 95 (2.9%) | .1828 |
| Red cell transfusion (intraoperative, postoperative) | 1926 (26.3%) | 1012 (35.1%) | 914 (20.6%) | <.0001 |
| Respiratory failure or ARDS | 314 (4.3%) | 154 (5.3%) | 160 (3.6%) | .0003 |

Towe CW et al. *J Thorac Cardiovasc Surg.* 2019;157:1288-97.

| Outcome | Overall N = 7316 | Thoracotomy decortication N = 2881 | VATS decortication N = 4435 | *P* value |
|---|---|---|---|---|
| Discharge location | | | | |
| **Home** | **5394 (73.7%)** | **2044 (70.9%)** | **3350 (75.5%)** | |
| Extended care, TCU, rehabilitation | 1140 (15.6%) | 486 (16.9%) | 654 (14.7%) | |
| Other hospital | 138 (1.9%) | 70 (2.4%) | 68 (1.5%) | |
| Nursing home | 311 (4.3%) | 137 (4.8%) | 174 (3.9%) | |
| Hospice | 54 (0.7%) | 17 (0.6%) | 37 (0.8%) | |
| Other | 77 (1.1%) | 37 (1.3%) | 40 (0.9%) | .0002 |
| Readmission −30 d of procedure (January 1, 2009, to December 31, 2011) | 144 (6.9%) | 60 (6.4%) | 84 (7.3%) | .4094 |
| Readmission −30 d of discharge (January 1, 2012, to June 31, 2016) | 452 (8.7%) | 156 (8.0%) | 296 (9.0%) | .2889 |
| Discharged with chest tube | 675 (9.2%) | 288 (10.0%) | 387 (8.7%) | .0664 |
| **Operative mortality** | **228 (3.1%)** | **106 (3.7%)** | **122 (2.8%)** | **.0257** |
| **Any major postoperative event** | **1138 (15.6%)** | **520 (18.0%)** | **618 (13.9%)** | **<.0001** |
| Any cardiovascular complications | 494 (6.8%) | 223 (7.7%) | 271 (6.1%) | .0066 |
| Any gastrointestinal complications | 246 (3.4%) | 111 (3.9%) | 135 (3.0%) | .0608 |
| Any urologic complications | 250 (3.4%) | 99 (3.4%) | 151 (3.4%) | .9421 |
| Any neurologic/psychiatric complications | 258 (3.5%) | 100 (3.5%) | 158 (3.6%) | .8357 |

Towe CW et al. *J Thorac Cardiovasc Surg.* 2019;157:1288-97.

| Risk factor | Major morbidity | | Discharge location other than home | | Postoperative LOS >19 d | | Mortality | |
|---|---|---|---|---|---|---|---|---|
| | Adjusted OR (95% CI) | *P* value | Adjusted OR (95% CI) | *P* value | Adjusted OR (95% CI) | *P* value | Adjusted OR (95% CI) | *P* value |
| Dialysis | | | 1.60 (1.11-2.29) | .0113 | | | 2.23 (1.33-3.77) | .0026 |
| eGFR < 60 | 1.81 (1.54-2.12) | <.0001 | 1.48 (1.23-1.79) | <.0001 | 2.25 (1.82-2.77) | <.0001 | 1.94 (1.38-2.74) | .0002 |
| COPD | 1.26 (1.09-1.46) | .0019 | 1.30 (1.10-1.53) | .0018 | 1.42 (1.15-1.76) | .0013 | 1.49 (1.08-2.04) | .0139 |
| ASA risk class: III/IV/V/VI vs I/II | 2.07 (1.66-2.60) | <.0001 | 2.28 (1.70-3.07) | <.0001 | 4.51 (2.60-7.82) | <.0001 | 10.15 (1.41-73.12) | .0215 |
| Zubrod: in bed/bedridden/moribund vs normal activity/fully ambulatory | 1.84 (1.62-2.09) | <.0001 | 2.34 (2.01-2.73) | <.0001 | 2.33 (1.88-2.88) | <.0001 | 2.46 (1.69-3.57) | <.0001 |
| VATS | 0.69 (0.60-0.78) | <.0001 | 0.74 (0.64-0.85) | <.0001 | 0.79 (0.65-0.96) | .0162 | 0.74 (0.56-0.99) | .0444 |
| Days from admission to surgery per 1-d increase when ≤5 d | 1.02 (0.98-1.06) | .4244 | 1.01 (0.96-1.06) | .7732 | 1.09 (1.02-1.16) | .0127 | 1.20 (1.07-1.33) | .0015 |
| Days from admission to surgery per 1-d increase when >5 d | 1.02 (1.01-1.04) | .0011 | 1.07 (1.06-1.09) | <.0001 | 1.07 (1.05-1.09) | <.0001 | 1.02 (1.00-1.05) | .0782 |
| Procedure time per 10-min increase | 1.05 (1.04-1.06) | <.0001 | | | 1.03 (1.02-1.05) | <.0001 | | |

Towe CW et al. *J Thorac Cardiovasc Surg.* 2019;157:1288-97.

*Table 2. Identification of Predictors for Conversion Thoracotomy in 178 Patients With Presumed Stage II Empyema Accessed by Video-Assisted Thoracoscopic Surgery by Use of a Univariate and a Multivariate Analysis With a Multiple Stepwise Logistic Regression*

| | Univariate Analysis | | Multivariate Analysis | |
|---|---|---|---|---|
| Risk Factors | *p* Value | Odds Ratio[a] | *p* Value | Odds Ratio[a] |
| Age | 0.07 | 0.98 | 0.62 | 0.99 |
| Sex (male) | 0.01 | 0.44 | 0.54 | 0.69 |
| Etiology | | | | |
| Postpneumonic | 0.004 | 2.47 | 0.56 | 0.72 |
| Postoperative | 0.04 | 0.43 | | |
| Posttraumatic | 0.18 | 0.54 | | |
| Postembolic | 0.77 | 0.83 | | |
| Tuberculosis | 0.18 | 0.40 | | |
| Bacteria | 0.78 | 0.92 | | |
| Gram positive | 0.03 | 0.51 | 0.08 | 0.29 |
| Gram negative | <0.0001 | 6.60 | <0.01 | 5.77 |
| Time interval | | | | |
| T | <0.0001 | 2.17 | <0.0001 | 2.35 |

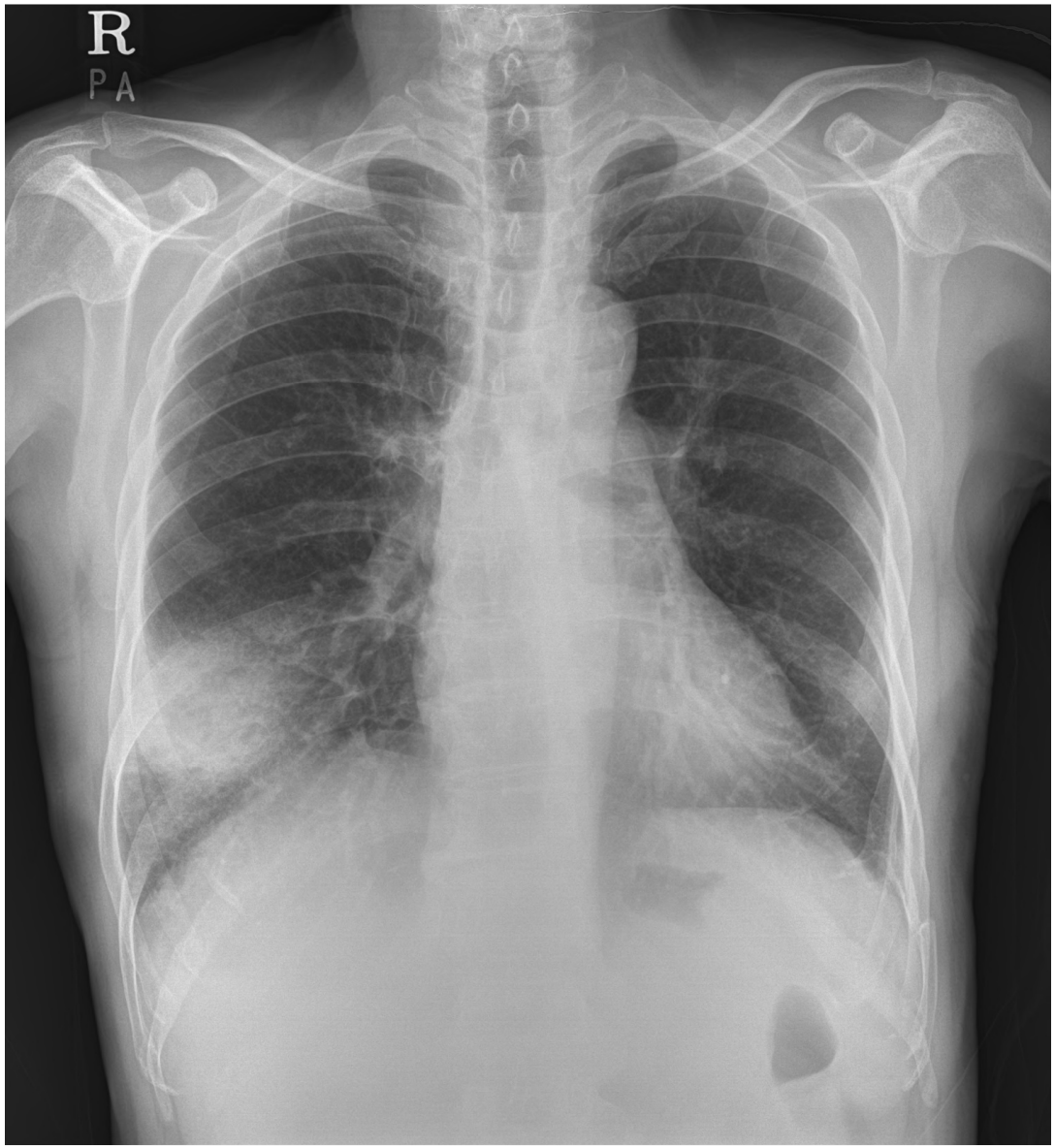
Lardinois D et al. *Ann Thorac Surg.* 2005;79:1851-6.

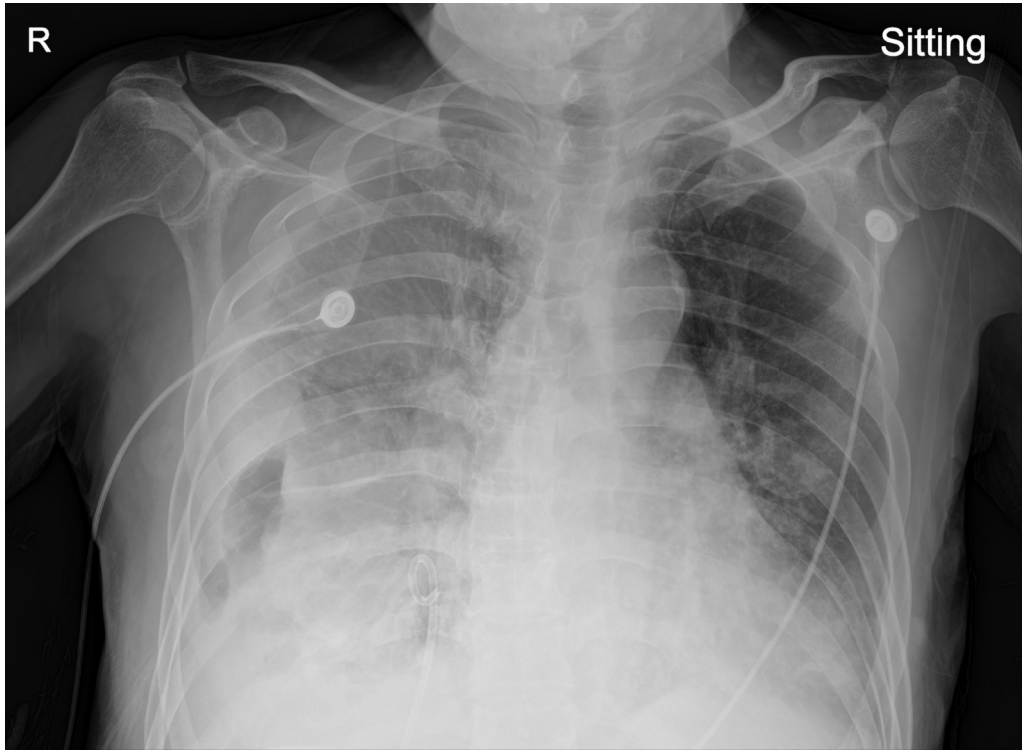
Case 1

M/71

HTN, DM, carotid a stenosis, heavy alcoholics

Necrotizing pneumonia, RLL

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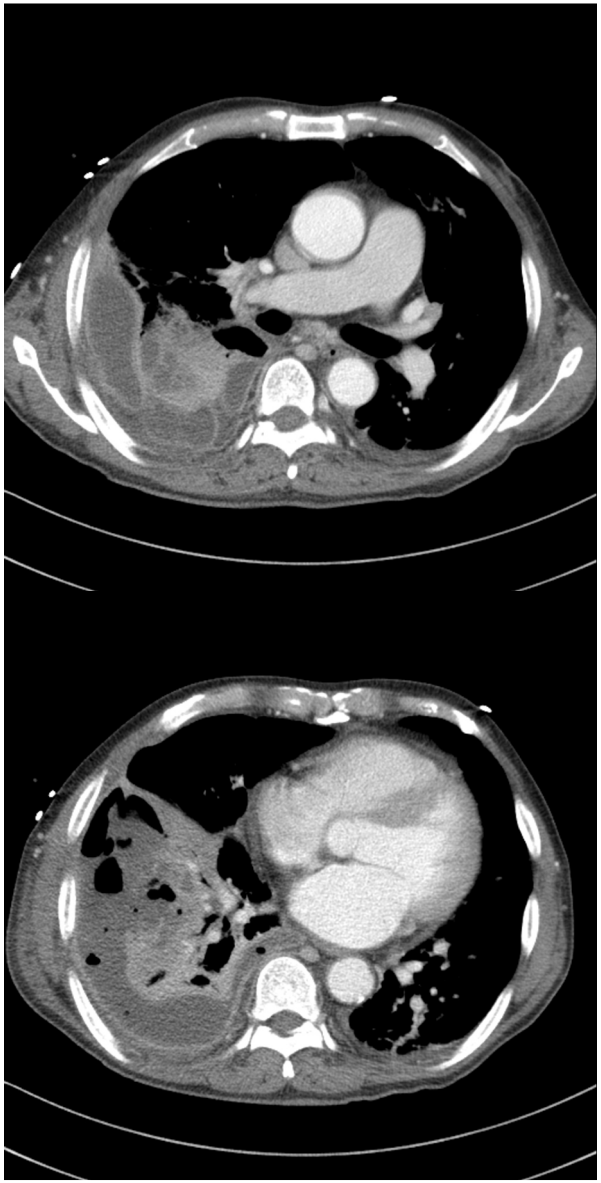
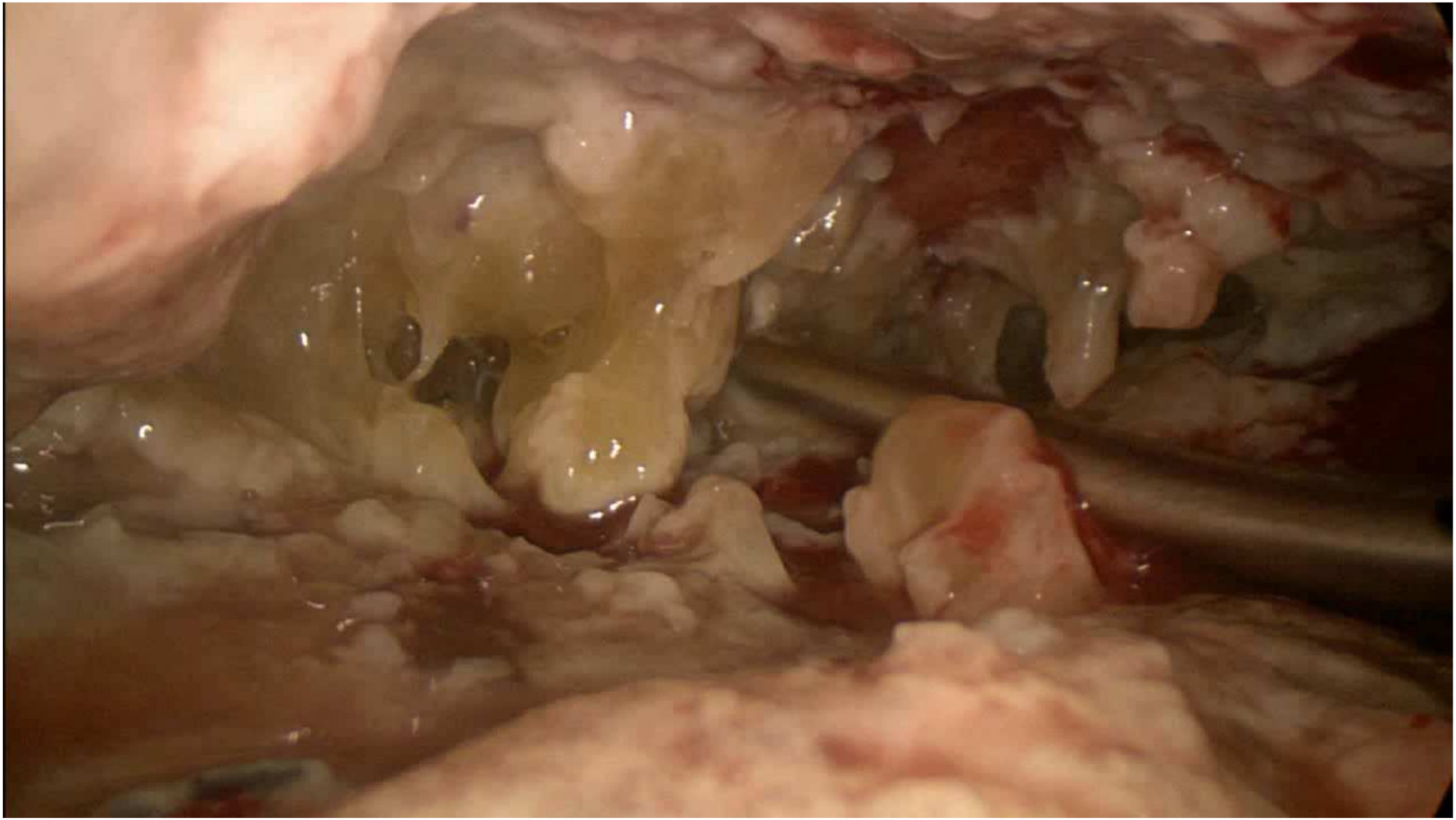
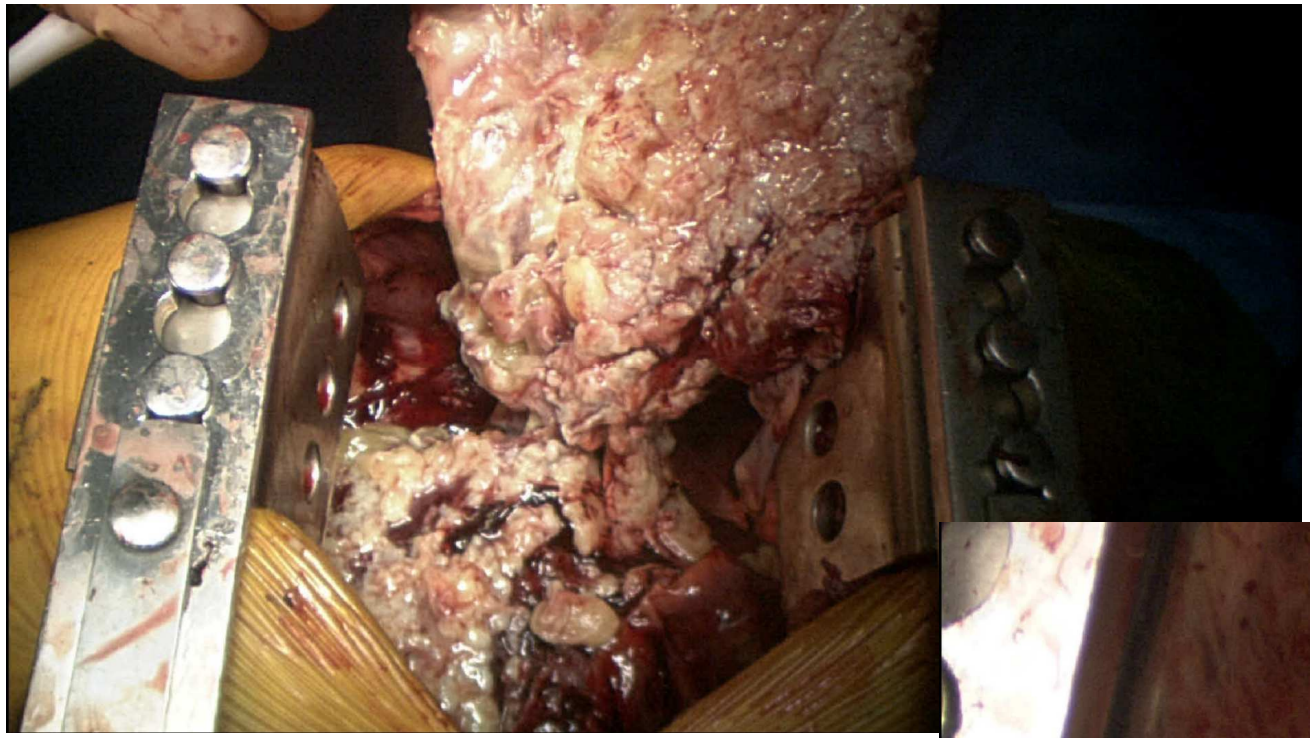
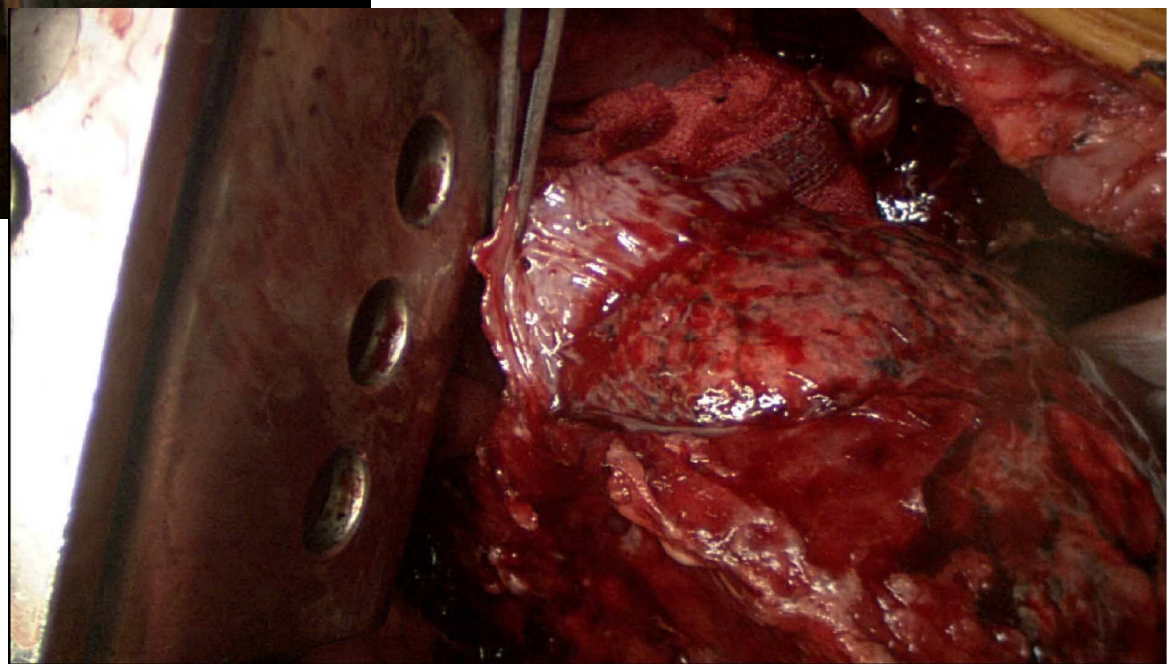
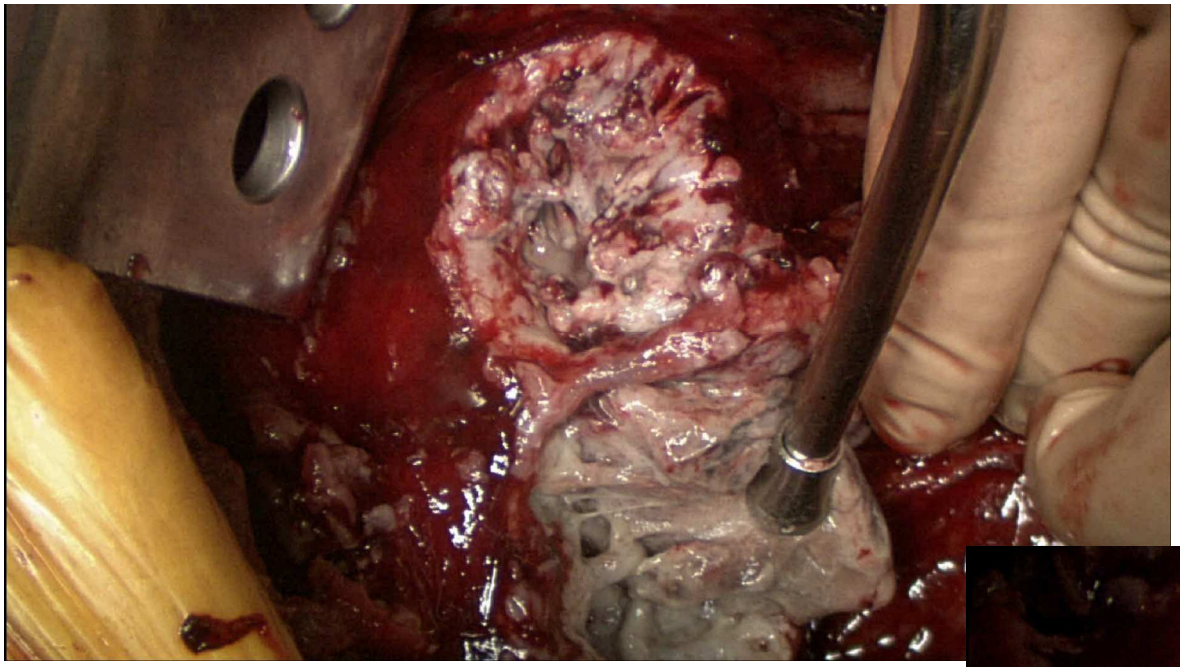
Sitting

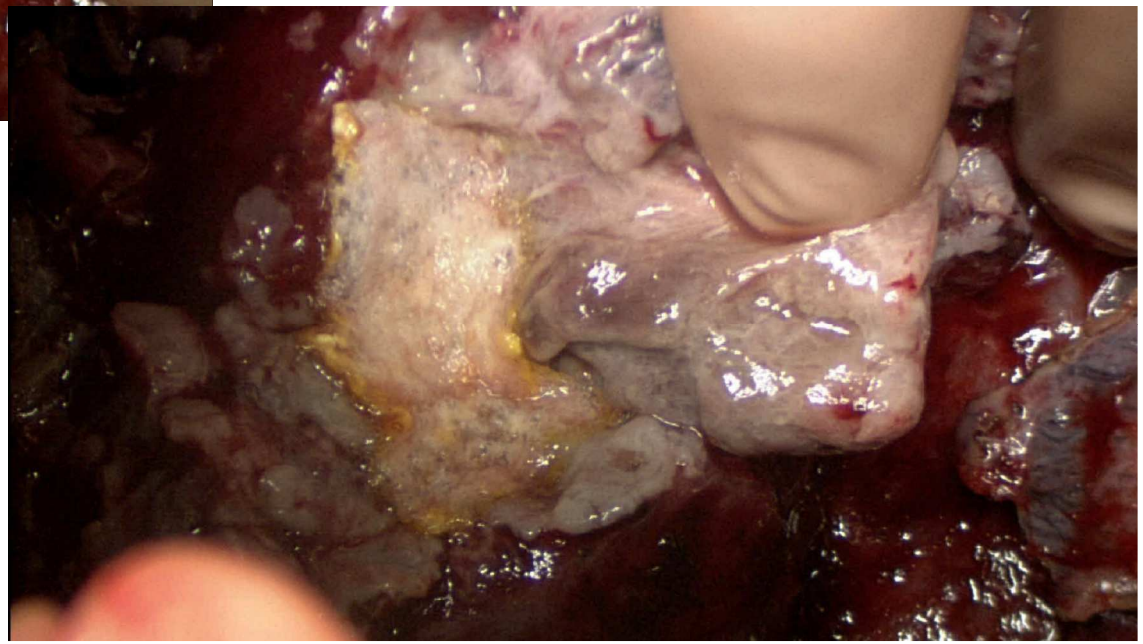


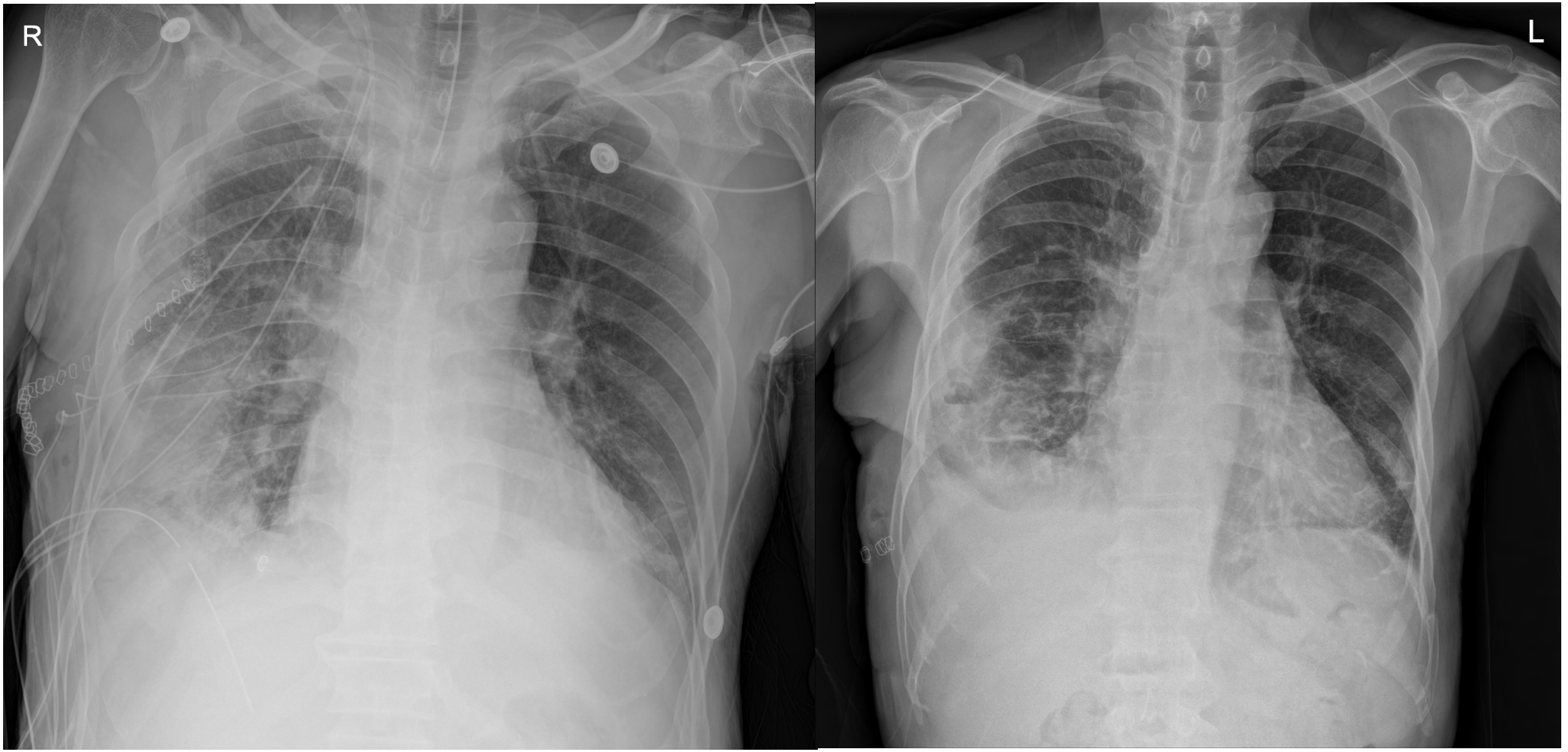








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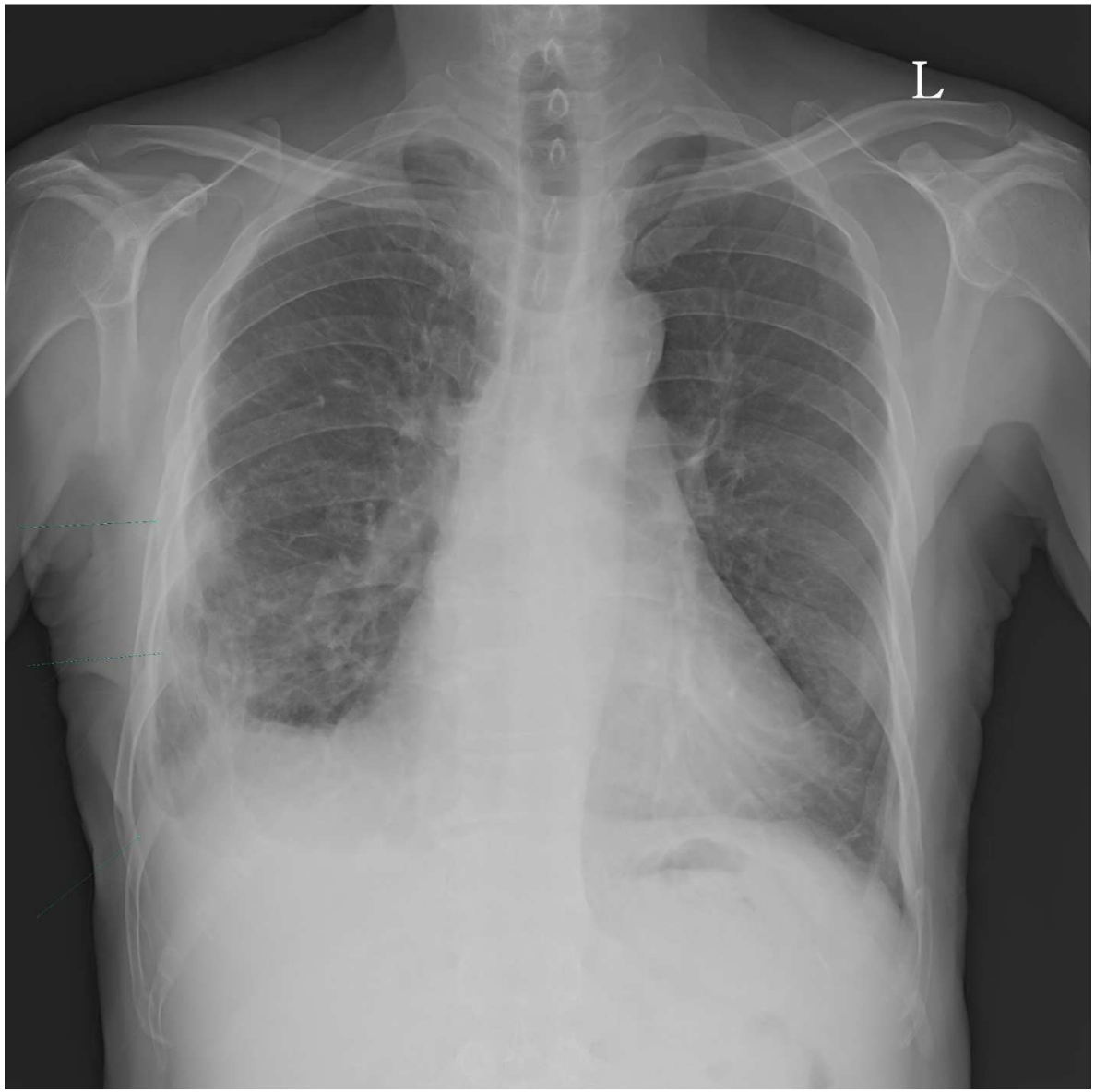
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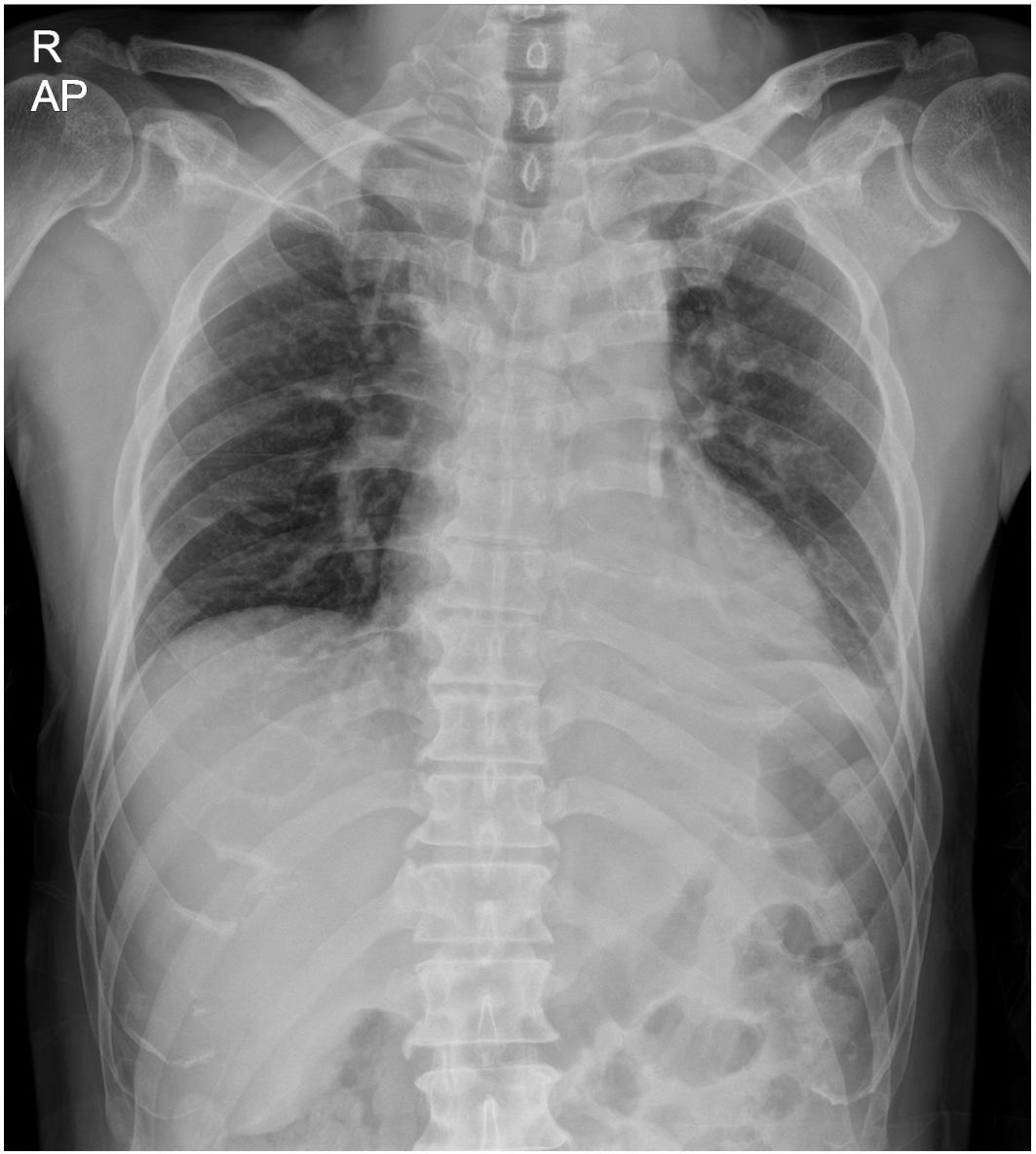
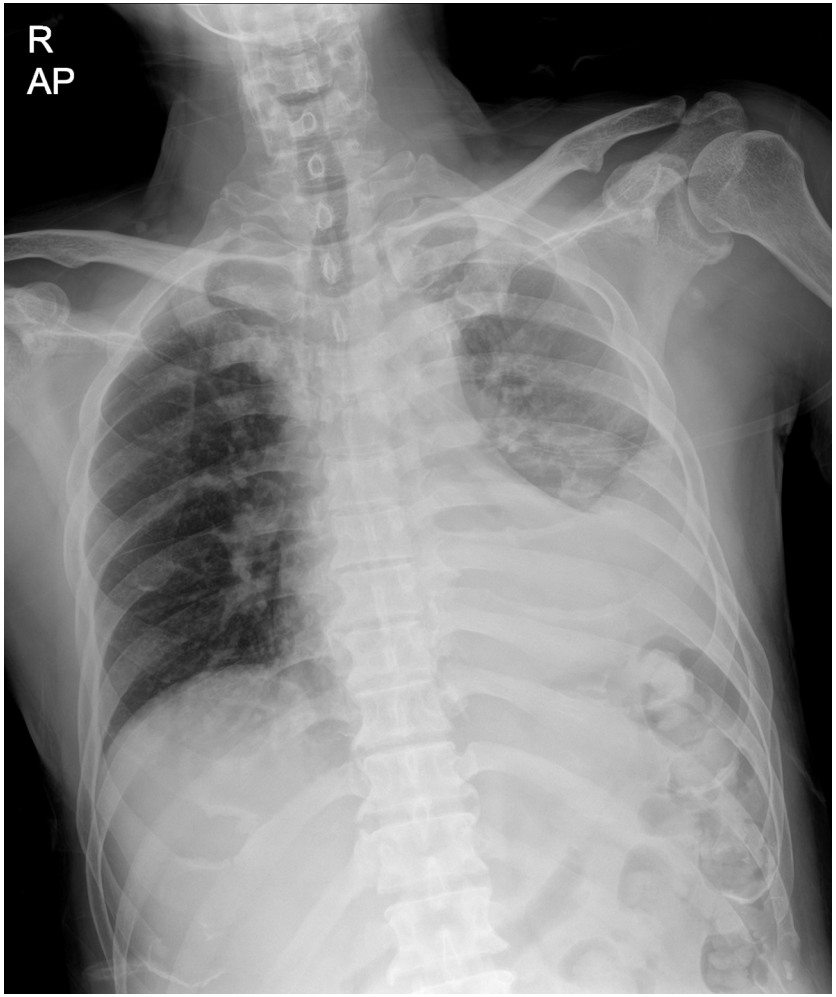
Case 2

M/56

No underlying Dz.

Pneumonia, LLL

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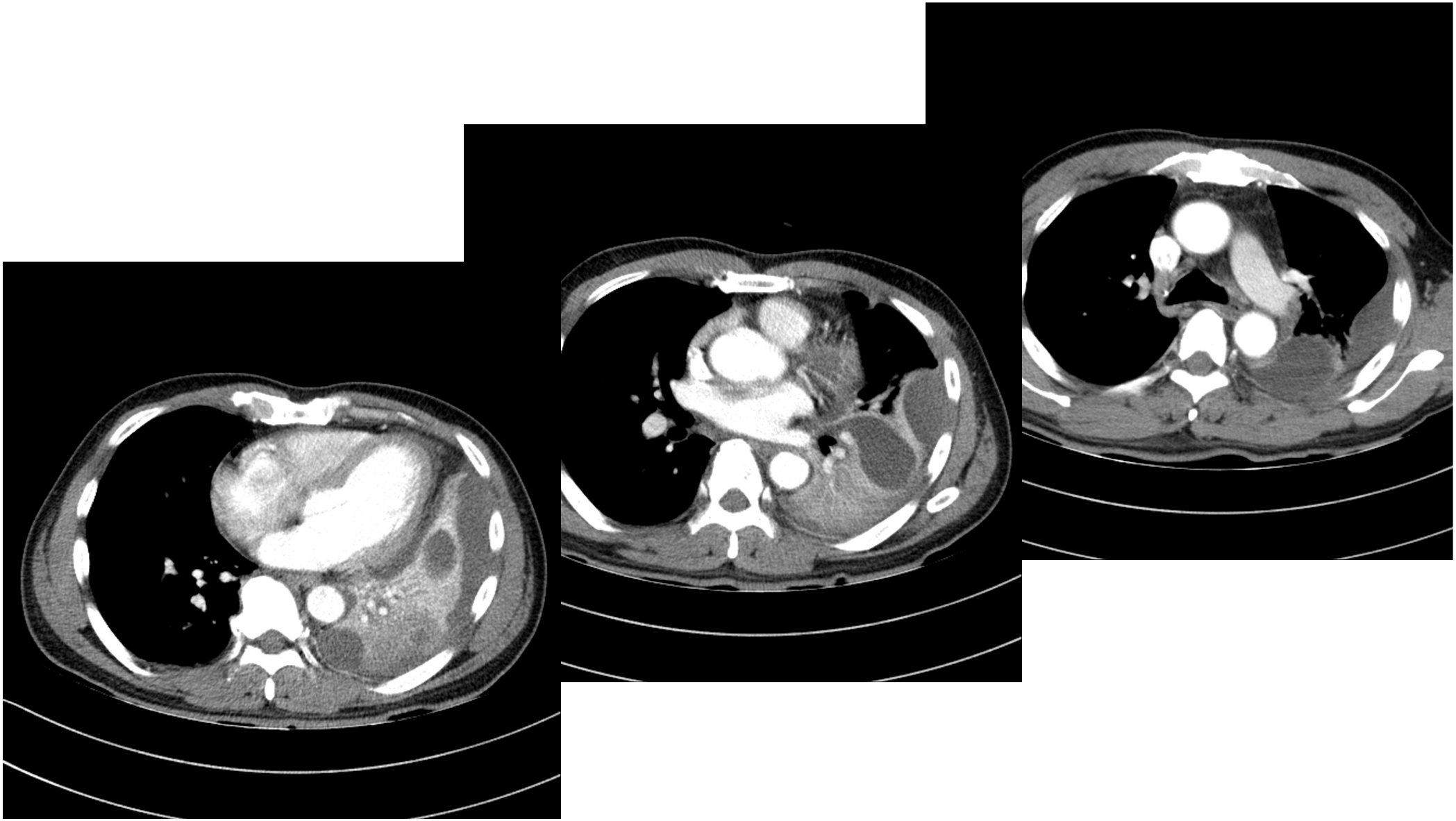
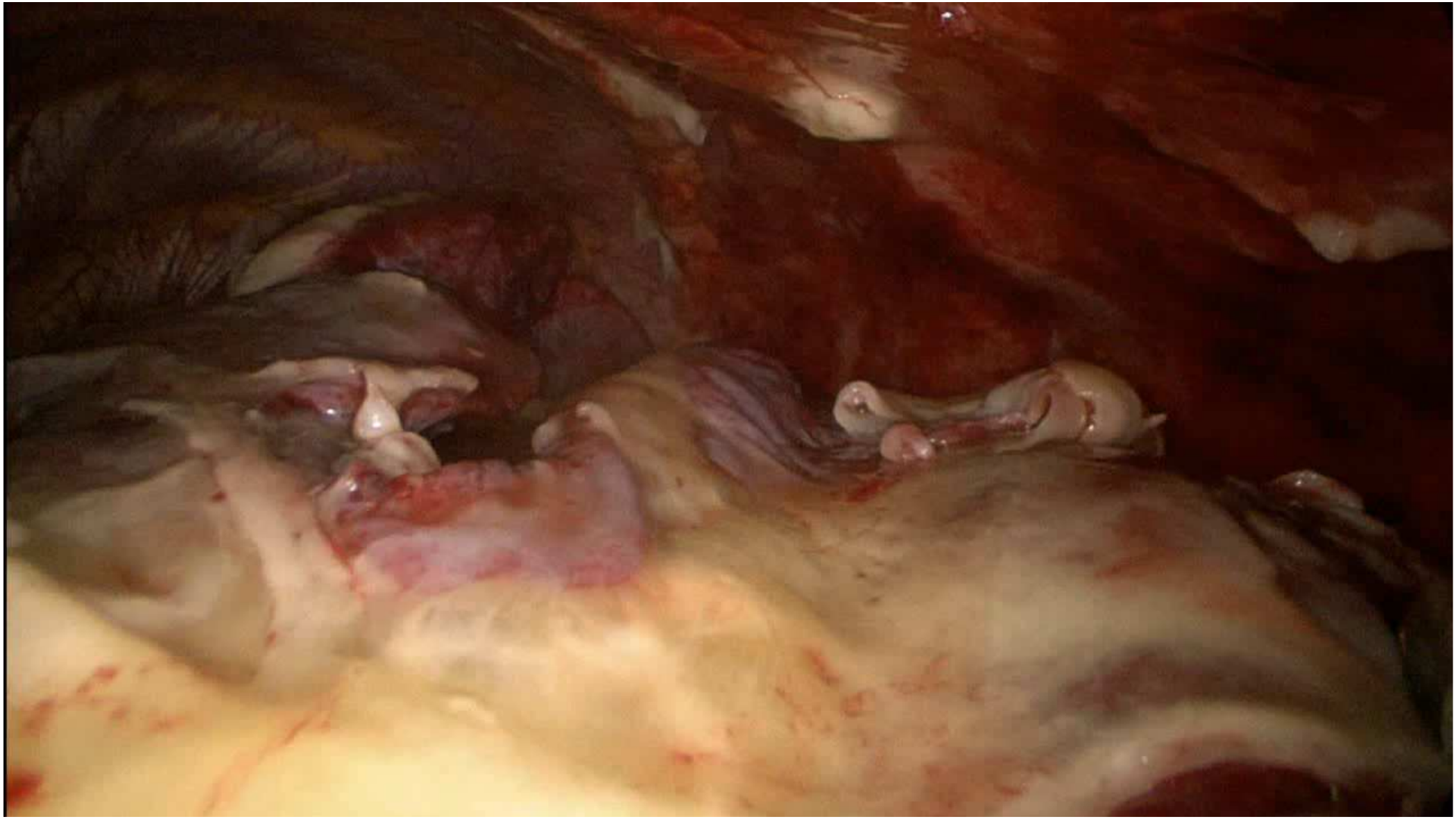
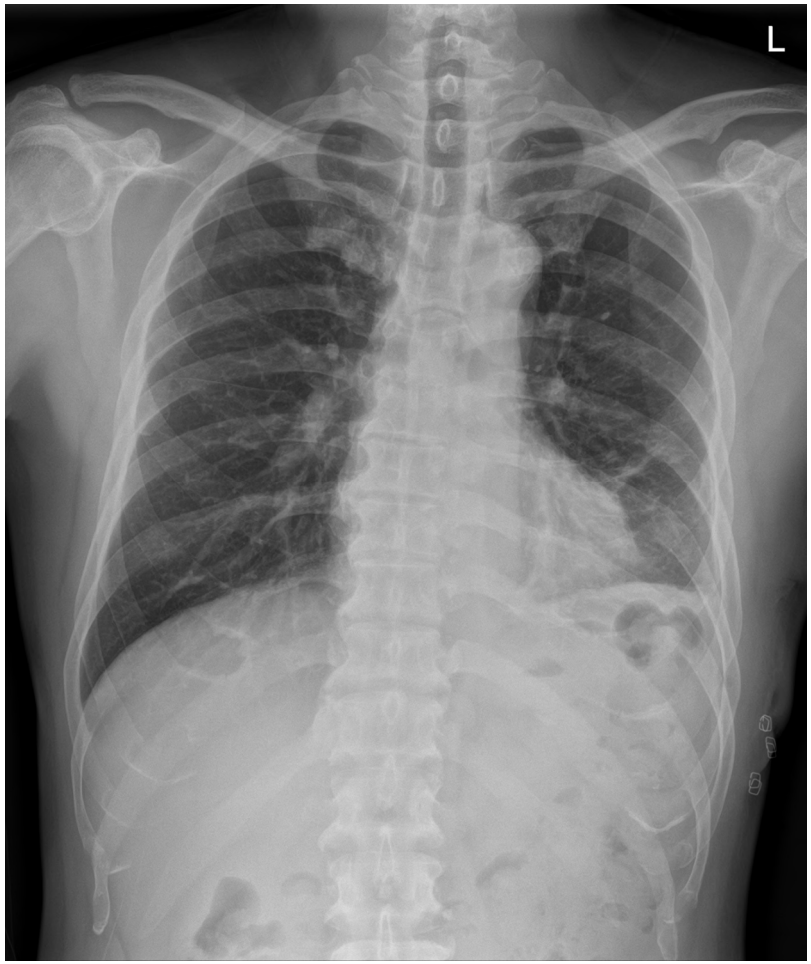




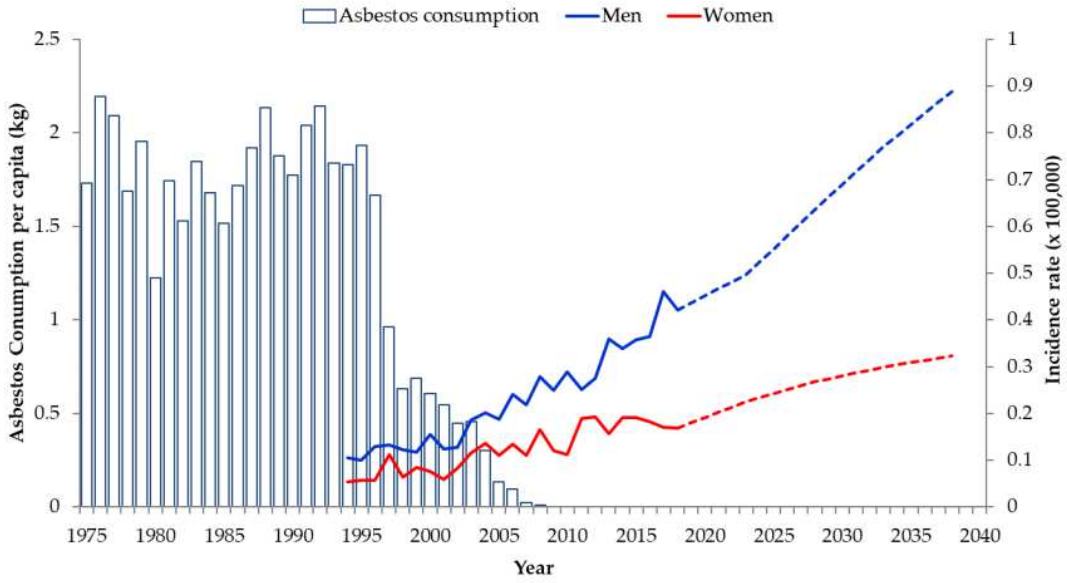

R


L

# Malignant Mesothelioma

# Introduction

- Rare pleura tumor
- 20-40 years later occurrence after asbestos exposure



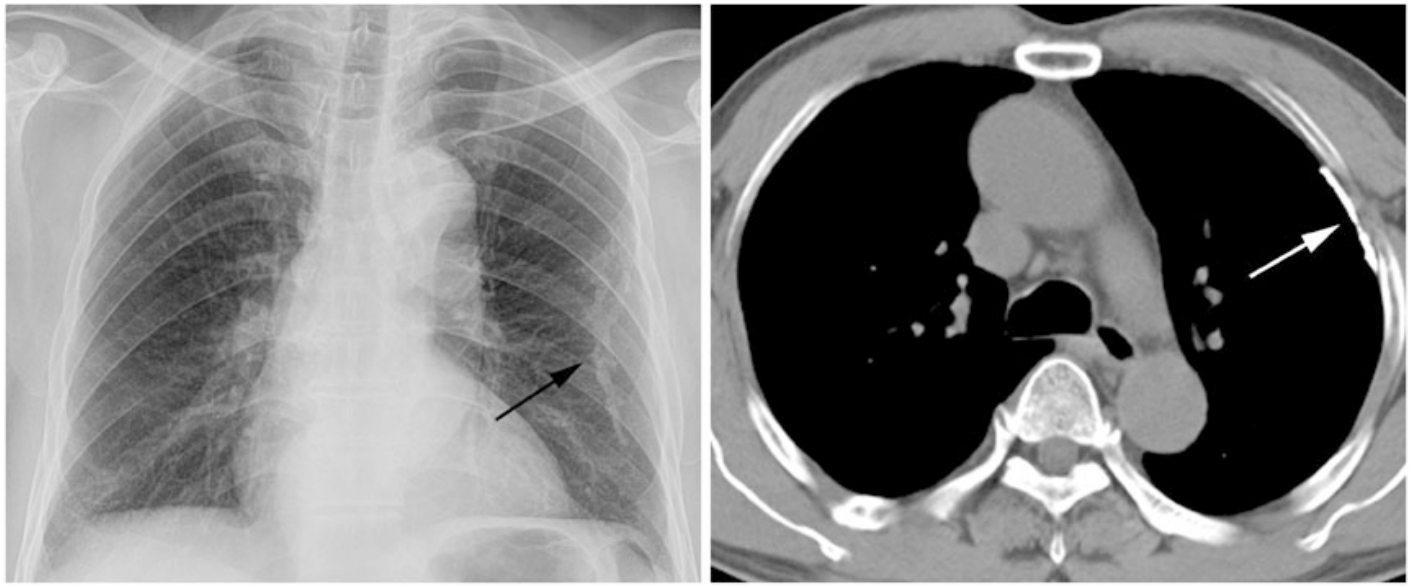

Kwak K. *Int J Environ Res Public health*. 2021;18:6614.

# Etiology

- Asbestos (m/c)
- Mantle radiation
- Erionite
- Genetic factor: mutation in BAP1 gene

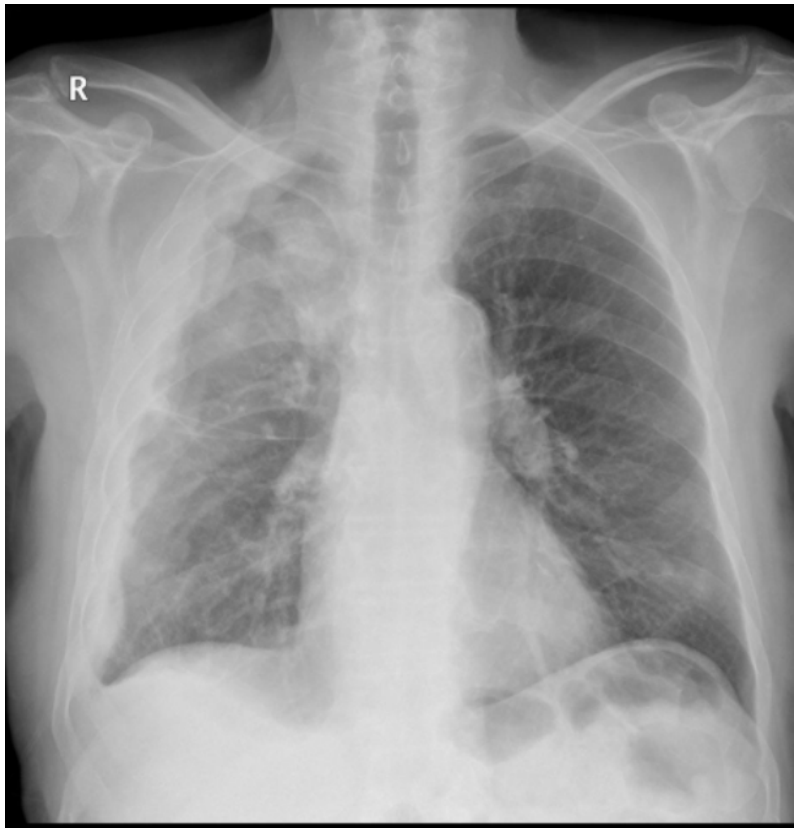
# Pleural plague

- Marker of asbestos exposure

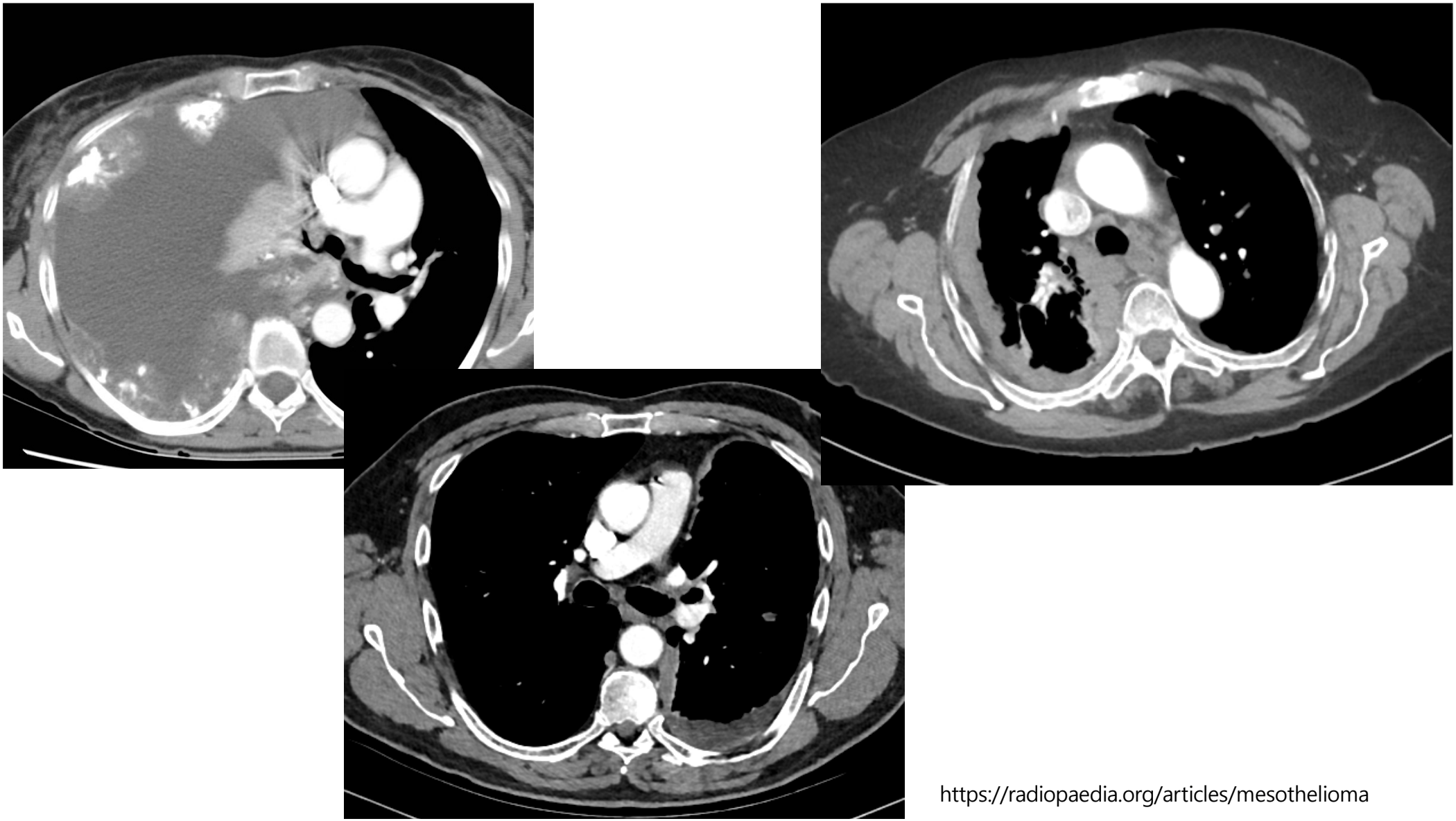


Kim Y. *Korean J Radiol.* 2015;16:1142-1152.

# Radiologic finding




https://radiopaedia.org/articles/mesothelioma



https://radiopaedia.org/articles/mesothelioma

# Effusion cytology

- Epithelioid
  - Effusion (+)
- Sarcomatoid
  - Effusion (-)

- Diagnostic sensitivity : 30%~75%
- Immunohistochemical markers
- (+): Calretinin, WT-1, D2-40, cytokeratin 5/6
- (-): TTF-1, CEA

# Pleural biopsy

- VATS biopsy: gold standard
  - sensitivity of 95%, specificity of 100%, negative predictive value of 94%
- CT-guided needle biopsy: nodular lesion (+)
- Open pleural biopsy: obliterated pleural space
- Biopsy tract recurrence ↑ ↑

# TNM Stage (1)

| Stage | Definition |
|---|---|
| Primary tumor (T) | |
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| T1 | Tumor limited to the ipsilateral parietal ± visceral ± mediastinal ± diaphragmatic pleura |
| T2 | Tumor involving each of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least one of the following features:<br>• involvement of diaphragmatic muscle<br>• extension of tumor from visceral pleura into the underlying pulmonary parenchyma |
| T3 | Describes locally advanced but *potentially resectable* tumor. Tumor involving all of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least one of the following features:<br>• involvement of the endothoracic fascia<br>• extension into the mediastinal fat<br>• solitary, completely resectable focus of tumor extending into the soft tissues of the chest wall<br>• nontransmural involvement of the pericardium |
| T4 | Describes locally advanced *technically unresectable* tumor. Tumor involving all of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least one of the following features:<br>• diffuse extension or multifocal masses of tumor in the chest wall, with or without associated rib destruction<br>• direct transdiaphragmatic extension of tumor to the peritoneum<br>• direct extension of tumor to the contralateral pleura<br>• direct extension of tumor to mediastinal organs<br>• direct extension of tumor into the spine<br>• tumor extending through to the internal surface of the pericardium with or without a pericardial effusion, or tumor involving the myocardium |

Rusch V. *J Thorac Oncol.* 2016;11:2112-2119.

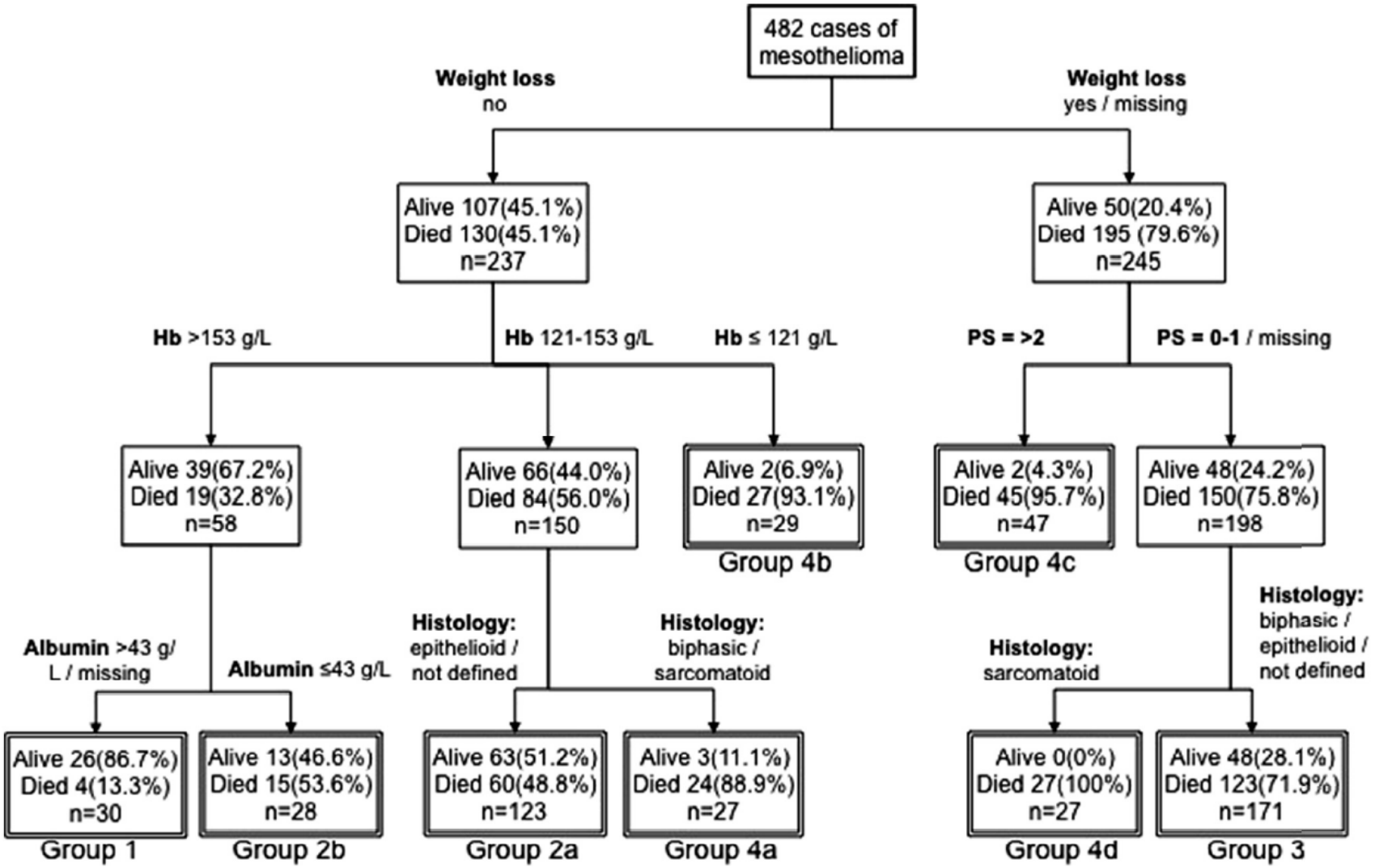
# TNM Stage (1)

| | |
|---|---|
| Regional lymph nodes (N) | |
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastases |
| N1 | Metastases in the ipsilateral bronchopulmonary, hilar, or mediastinal (including the internal mammary, peridiaphragmatic, pericardial fat pad, or intercostal lymph nodes) lymph nodes |
| N2 | Metastases in the contralateral mediastinal, ipsilateral, or contralateral supraclavicular lymph nodes |
| Distant metastasis (M) | |
| M0 | No distant metastasis |
| M1 | Distant metastasis present |

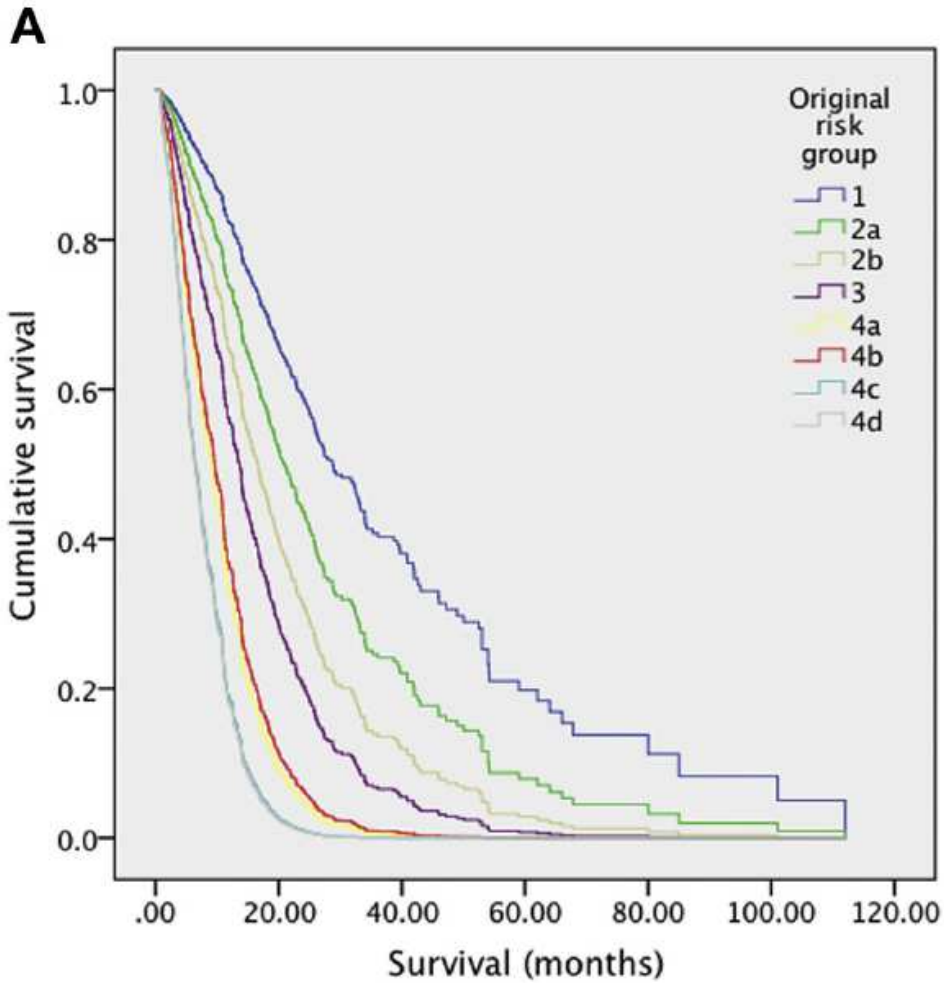
Rusch V. *J Thorac Oncol.* 2016;11:2112-2119.

# Pre-op evaluation

- Chest and abdomen CT with contrast
- PET-CT (before pleurodesis)
- Mediastinoscopy or EBUS
- Chest MRI
- VATS (for contralateral thorax)
- Laparoscopy(for transdiaphragmatic extention)




Brims F.J.H. *J Thorac Oncol.* 2016;11:573-582.




Brims F.J.H. *J Thorac Oncol.* 2016;11:573-582.

# Indication of Surgery

- NCCN guideline 2022
  - cStage I-IIIA and epitheloid histology
  - Considered for biphasic histology with early stage
- ERS/ESTS/EACTS/ESTRO guideline 2020
  - In prospective randomised control clinical trial or in national/international registries
  - EP/D >> EPP

NCCN guideline 2022

# Surgery

- Goal: cytoreduction surgery, macroscopic complete resection
- Type
  - Extrapleural pneumonectomy (EPP)
  - Extended pleurectomy/decortication(EP/D)
  - Pleurectomy/decortication (P/D)

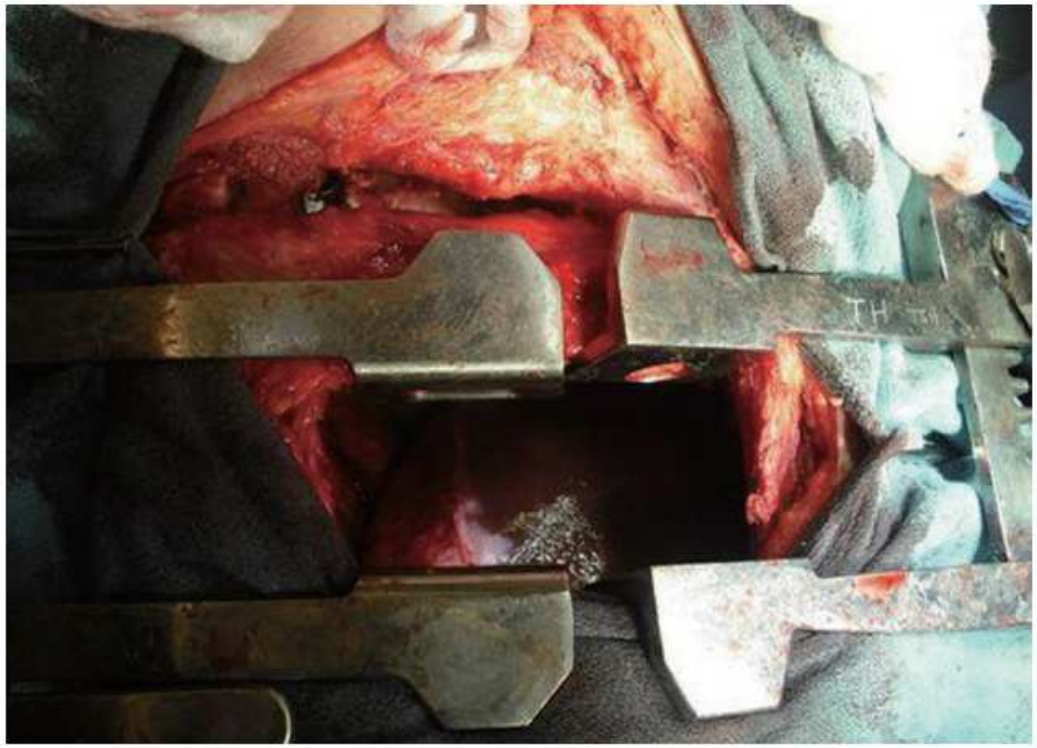
    : sparing pericardium and diaphragm

  *Partial pleurectomy

    : partial removal for diagnostic or palliative

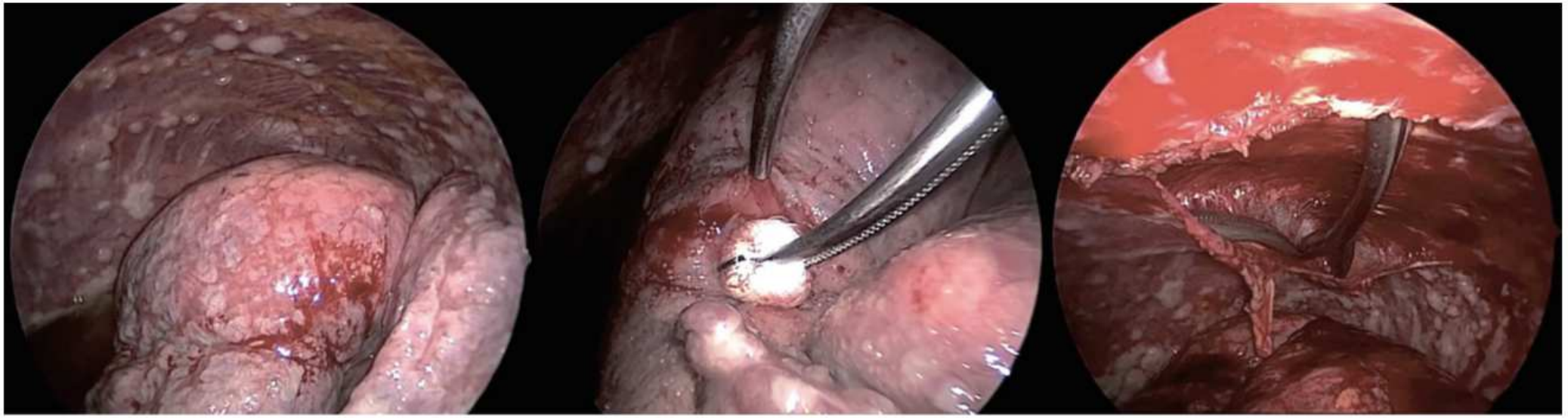
Rice D. *J Thorac Oncol.* 2011;6:1304-1312.

# EPP



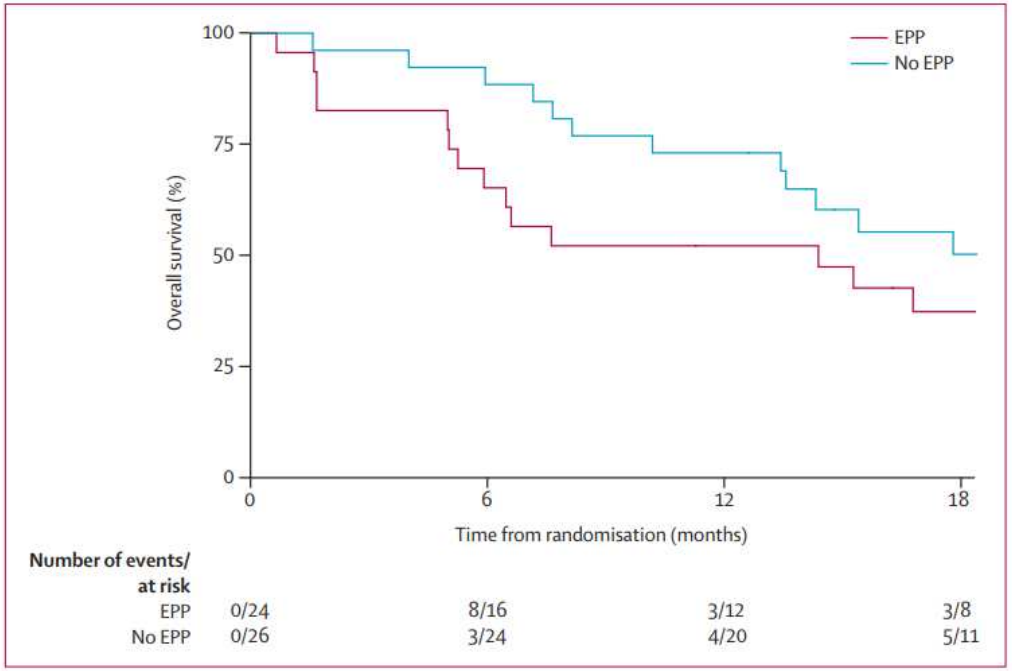
Collaud S. *Ann Cardiothorac Surg.* 2012;1:537-543.

# P/D



Ali J.M. *Shanghai Chest.* 2018;2:46.

# Mesothelioma and Radical Surgery (MARS) trial

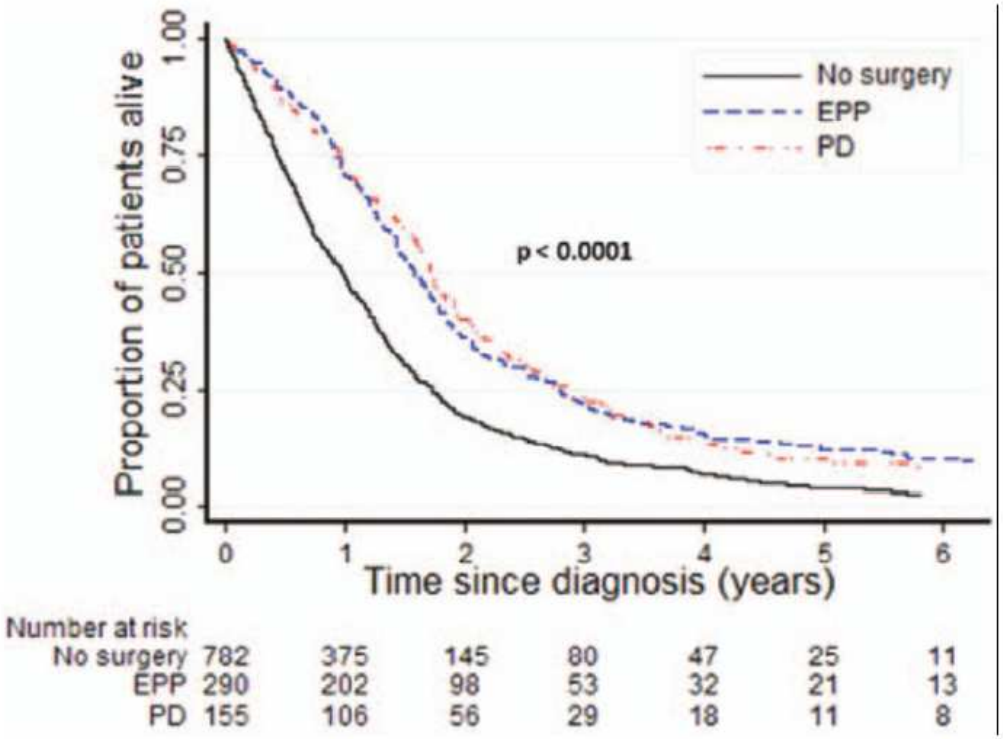



1-year recurrence free survival

EPP vs no EPP: 34.8% vs 42.3%

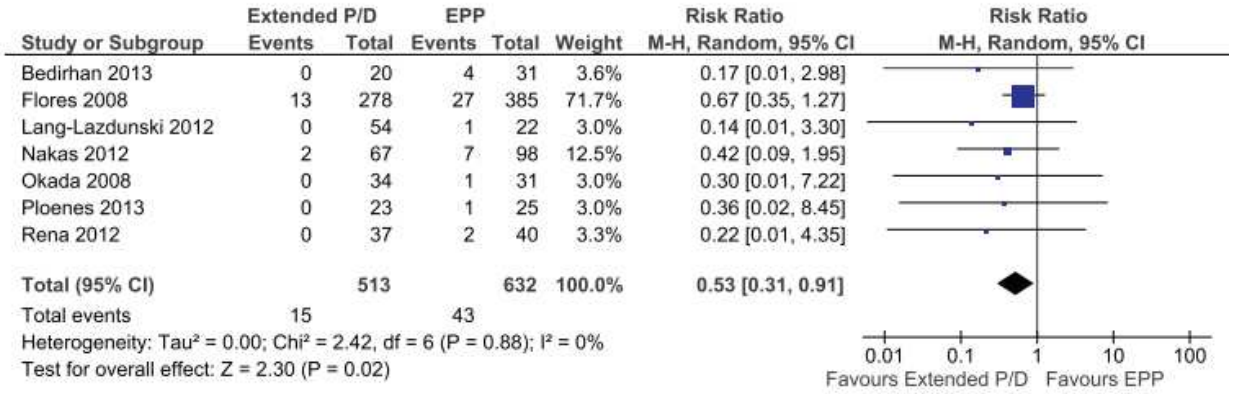
Treasure T. *Lancet Oncol.* 2011;12:763-772.

# *A Multicenter Retrospective Analysis of 1365 Consecutive Patients*




Bovolato P. *J Thorac Oncol.* 2014;9:390-396.

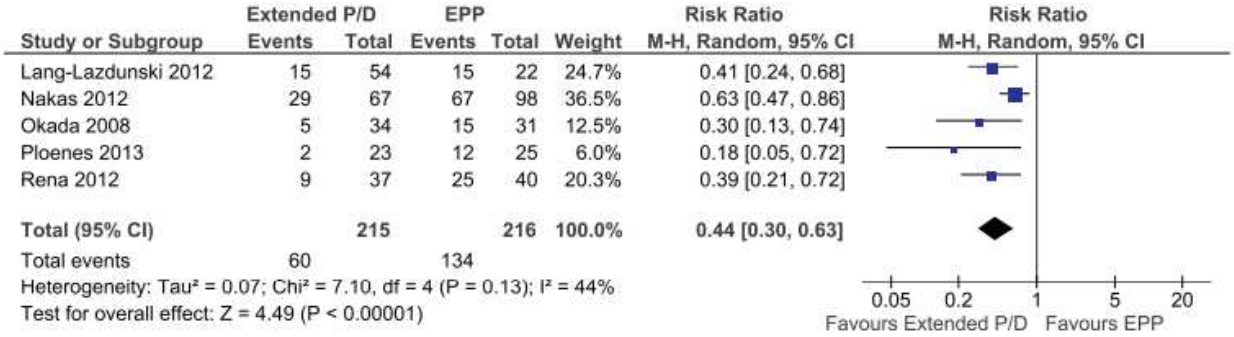
# EPP vs EP/D



| Study or Subgroup | Extended P/D Events | Total | EPP Events | Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Bedirhan 2013 | 0 | 20 | 4 | 31 | 3.6% | 0.17 [0.01, 2.98] |
| Flores 2008 | 13 | 278 | 27 | 385 | 71.7% | 0.67 [0.35, 1.27] |
| Lang-Lazdunski 2012 | 0 | 54 | 1 | 22 | 3.0% | 0.14 [0.01, 3.30] |
| Nakas 2012 | 2 | 67 | 7 | 98 | 12.5% | 0.42 [0.09, 1.95] |
| Okada 2008 | 0 | 34 | 1 | 31 | 3.0% | 0.30 [0.01, 7.22] |
| Ploenes 2013 | 0 | 23 | 1 | 25 | 3.0% | 0.36 [0.02, 8.45] |
| Rena 2012 | 0 | 37 | 2 | 40 | 3.3% | 0.22 [0.01, 4.35] |
| **Total (95% CI)** | | **513** | | **632** | **100.0%** | **0.53 [0.31, 0.91]** |
| Total events | 15 | | 43 | | | |

Heterogeneity: Tau² = 0.00; Chi² = 2.42, df = 6 (P = 0.88); I² = 0%
Test for overall effect: Z = 2.30 (P = 0.02)





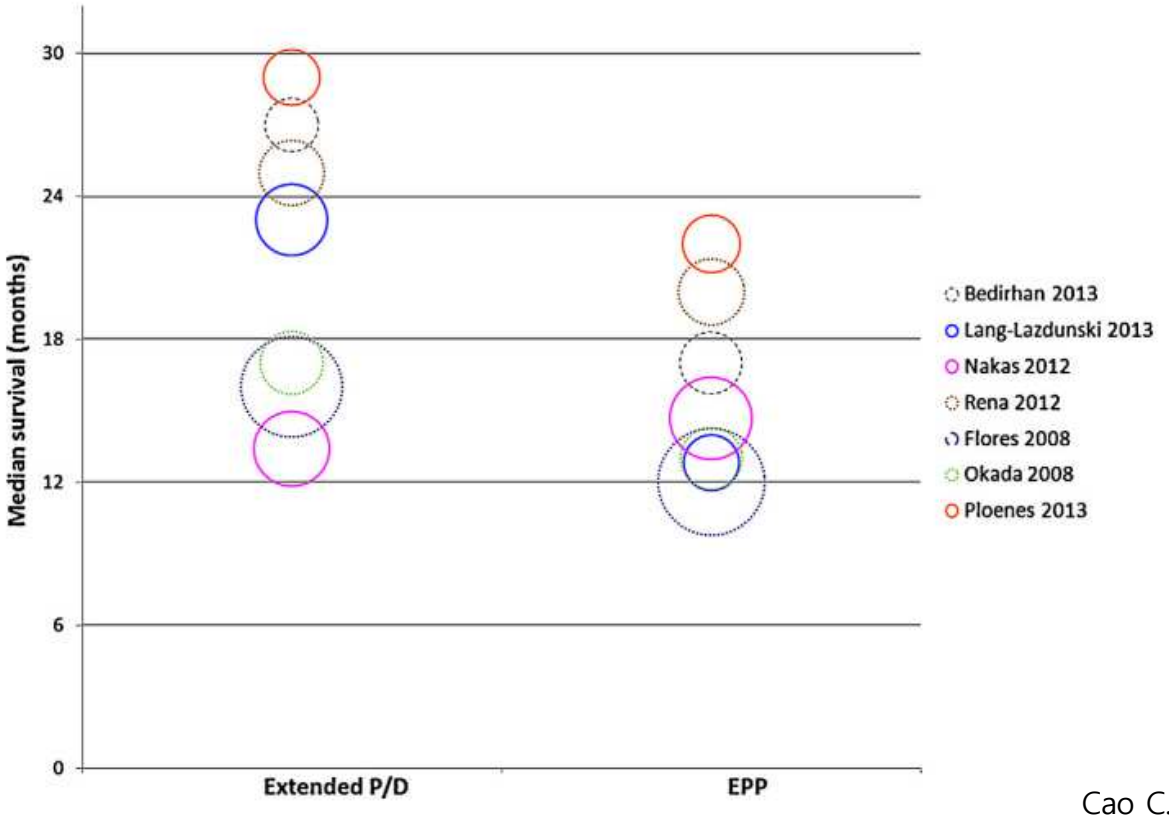
| Study or Subgroup | Extended P/D Events | Total | EPP Events | Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Lang-Lazdunski 2012 | 15 | 54 | 15 | 22 | 24.7% | 0.41 [0.24, 0.68] |
| Nakas 2012 | 29 | 67 | 67 | 98 | 36.5% | 0.63 [0.47, 0.86] |
| Okada 2008 | 5 | 34 | 15 | 31 | 12.5% | 0.30 [0.13, 0.74] |
| Ploenes 2013 | 2 | 23 | 12 | 25 | 6.0% | 0.18 [0.05, 0.72] |
| Rena 2012 | 9 | 37 | 25 | 40 | 20.3% | 0.39 [0.21, 0.72] |
| **Total (95% CI)** | | **215** | | **216** | **100.0%** | **0.44 [0.30, 0.63]** |
| Total events | 60 | | 134 | | | |

Heterogeneity: Tau² = 0.07; Chi² = 7.10, df = 4 (P = 0.13); I² = 44%
Test for overall effect: Z = 4.49 (P < 0.00001)



Cao C. *Lung Cancer.* 2014;83:240-245.

# EPP vs P/D




Cao C. *Lung Cancer.* 2014;83:240-245.

# Mesothelioma and Radical Surgery 2 (MARS 2) trial

- Ongoing
- (Extended) P/D vs no surgery
- N=264

Lim E. *BMJ open.* 2020;10:e038892.