Diagnosis and Management of Malignant Pleural Effusions

David Hsia, M.D.
Director of Bronchoscopy and Interventional Pulmonology Services
Harbor-UCLA Medical Center

Disclosures

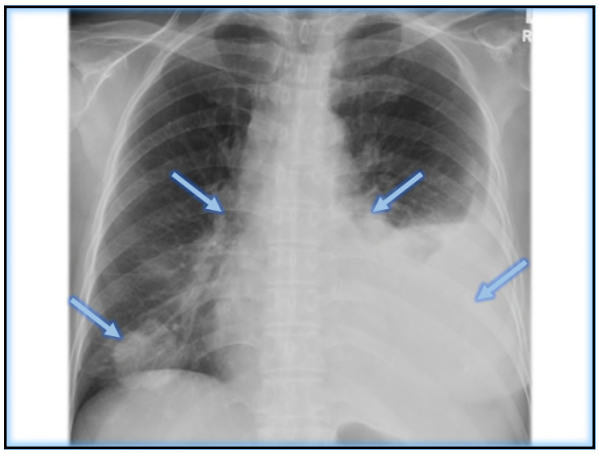
- Consultant agreements with Olympus America and VIDA Diagnostics
- Site primary investigator for PulmonX industry-sponsored trial

"… as we know, there are known knowns; there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know. But there are also unknown unknowns – the ones we don't know we don't know."

- Donald Rumsfeld

Johari Window

	Known to Self	Not Known to Self
Known to Others	Open	Blind
Not Known to Others	Hidden	Unknown



Case Presentation #1

Based on the CXR findings, what is the most appropriate initial diagnostic step?

A. Navigation bronchoscopy
B. CT guided TTNA
C. EBUS TBNA
D. U/S guided thoracentesis
E. PET-CT scan

Guidelines

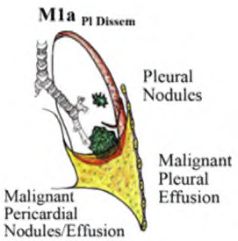
1. Adequate tissue should be obtained to accurately define the histologic type and perform molecular analysis when applicable. (ACCP, ESMO, NCCN, NICE)

2. Biopsy the pathologic site that would confer the highest stage, i.e. to biopsy a suspected metastasis. (e.g. pleural effusion M1a rather than a pulmonary lesion) (NCCN)

Concomitant staging is preferential because it avoids additional biopsies or procedures.

8th IASCLC Lung Cancer Staging Classification

T/M	Label	N0	N1	N2	N3
T1	T1a ≤1	IA1	IIB	IIIA	IIIB
	T1b >1-2	IA2	IIB	IIIA	IIIB
	T1c >2-3	IA3	IIB	IIIA	IIIB
T2	T2a Cont. Visc Pl	IB	IIB	IIIA	IIIB
	T2a >3-4	IB	IIB	IIIA	IIIB
	T2b >4-5	IIA	IIB	IIIA	IIIB
T3	T3 >5-7	IIB	IIIA	IIIB	IIIC
	T3 Invc	IIB	IIIA	IIIB	IIIC
	T3 Satell	IIB	IIIA	IIIB	IIIC
T4	T4 >7	IIIA	IIIA	IIIB	IIIC
	T4 Invc	IIIA	IIIA	IIIB	IIIC
	T4 Ipsi Nod	IIIA	IIIA	IIIB	IIIC
M1	M1a Contr Nod	IVA	IVA	IVA	IVA
	M1a Pl Dissem	IVA	IVA	IVA	IVA
	M1b Single	IVA	IVA	IVA	IVA
	M1c Multi	IVB	IVB	IVB	IVB



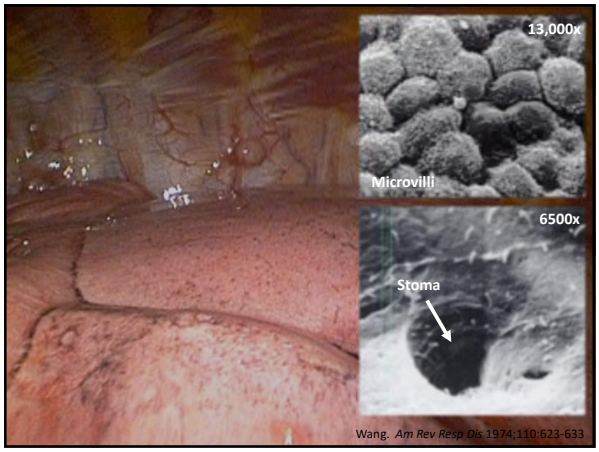
Detterbeck, et al. *Chest* 2017;151(1):193-203

Epidemiology

- 126,825 admissions for MPE in the United States in 2012
  - Heathcare Cost and Untilization Project-Nationwide Inpatient Sample (HCUP-NIS)
- Mean age = 68.0 years (IQR 58.4-77.2)
- 55.8% female

Primary Malignancy	Total	Female	Male
Lung	37.8%	32.4%	44.5%
Breast	15.2%	26.8%	0.4%
GI	11.0%	8.1%	14.5%
Gynecologic	9.0%	16.1%	0%
Hematologic	11.2%	9.1%	13.8%
Other	22.2%	14.0%	32.5%
Unknown	11.2%	11.2%	11.3%

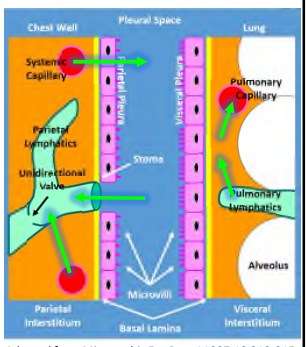
Taghizadeh, et al. *Chest* 2017;151(4):845-854



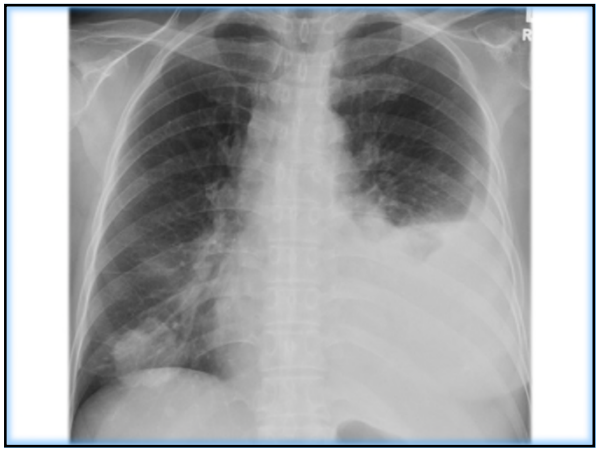
Wang. *Am Rev Resp Dis* 1974;110:623-633

Pleural Fluid

- 5-20 mL of pleural fluid
- 5-10 L of flow / day
- >75% of fluid absorbed through parietal pleura
- Normal fluid absorption can increase 20-30x



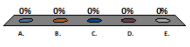
Adapted from Miserocchi. *Eur Resp J* 1997;10:219-215



Case Presentation #2

You plan to perform an U/S guided thoracentesis. On further history, the patient is on warfarin for prior PE, but is clinically asymptomatic. What is the most appropriate diagnostic step?

A. Navigation bronchoscopy
B. Percutaneous TTNA
C. EBUS TBNA
D. U/S guided thoracentesis
E. PET-CT scan



Case Presentation #2 cont'd

You plan to perform an U/S guided thoracentesis. On further history, the patient is on warfarin for prior PE, but is clinically ~~asymptomatic~~. What is the most appropriate diagnostic step?
symptomatic

A. Navigation bronchoscopy
B. Percutaneous TTNA
C. EBUS TBNA
D. U/S guided thoracentesis
E. PET-CT scan
F. Reverse anticoagulation then U/S guided thoracentesis
G. Refer to IR for thoracentesis

Complications of TTNA

Complications	SIR / ACR[1]	Core[2]	FNA[2]	TTNA[3]
Overall		38.8%	24.0%	
PTX	12-45%	25.3%	18.8%	15.0%
PTX w/ Intervention	2-15%	5.6%	4.3%	6.6%
Hemorrhage		18.0%	6.4%	1.0%
Hemoptysis	1-2%	4.1%	1.7%	

[2] Meta-analysis
- Core: 32 studies, 8,133 procedures
- FNA: 17 studies, 4,620 procedures

[3] 2006 data from 2 databases for CA, FL, MI, and NY
- 15,865 patients

[1] Gupta S, et al. *J Vasc Interv Radiol* 2010;21:969-975
[2] Heerink, et al. *Eur Radiol* 2017;27:138-148
[3] Wiener, et al. *Ann Intern Med* 2011;155(3):137-144

Complications of Guided Bronchoscopy

Complications	AQuIRE[1]	Mixed[2]	R-EBUS[3]	NAVIGATE[4]
Overall	2.2%			7.9%
PTX	1.7%	1.5%	1.0%	4.9%
PTX w/ Intervention		0.7%	0.4%	3.2%
Hemorrhage	0.2%			2.3%
Respiratory Failure	0.2%			0.6%

[1] Ost, et al. *Am J Respir Crit Care Med* 2016;193(1):68-77
[2] Wang Memoli, et al. *Chest* 2012;142(2):385-393
[3] Steinfort, et al. *Eur Respir J* 2011;37:902-910
[4] Khandhar, et al. *BMC Pulm Med* 2017;17:59

Complications of TBBx with Antiplatelet Agents

- Clopidogrel is a contraindication to TBBx
  - Bleed risk higher in clopidogrel vs. control group: 89% vs. 3.4%
  - Higher bleed risk for all categories of bleeding
    - Mild: 27% vs. 1.5%
    - Moderate: 34% vs. 1.5%
    - Severe: 27% vs. 0.3%
- Aspirin alone does not significantly increase bleed risk
  - Bleed risk similar on ASA (1.8%) vs. control group (2.9%)

Ernst, et al. *Chest* 2006;129(3):734-737
Herth, et al. *Chest* 2002;122(4):1461-1464

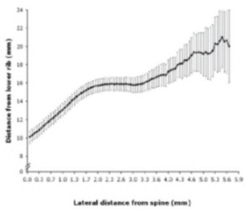
Thoracentesis – Hemorrhage

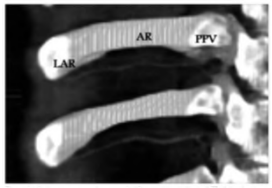
- Risk of hemorrhage with thoracentesis is < 0.4%
- No difference in hemorrhage based on INR or platelets
  - 1076 U/S-guided thoracentesis
  - No difference for INR ≥ 2.0, 2.5, or 3.0 (No hemorrhage)
  - No difference for platelets ≤ 100K, 50K, or 25K
- No difference in hemorrhage with transfusion of FFP or platelets
  - 1009 U/S-guided thoracentesis with INR ≥ 1.6 and/or platelets ≤ 50K
  - No difference for transfusion-corrected versus uncorrected patients (0.4%)
- Small case series with low hemorrhage risk
  - Clopidogrel
  - Uremia

Patel and Joshi. *AJR Am J Roentgenol* 2011;197:W164-8
Hibbert, et al. *Chest* 2013;144:456-63

Variability of Intercostal Artery Location

- Posteriorly, the intercostal artery is more exposed as it moves laterally
  - Degree of exposure correlates with age
- 86% of intercostal arteries were not "shielded" by the overlying rib
  - Measured at 3 positions along the back to axilla (133 points on 50 patients)





Helm, et al. *Chest* 2013;143(3):634-639
Dewhurst, et al. *Diagn Interv Radiol* 2012;18:221-224
Salamonsen, et al. *Respirology*. 2013;18(6):942-947

Intercostal Arteries are Not Straight

Table 1. Tortuosity grading system for the posterior intercostal artery within the intercostal space (n=248)

Tortuosity	Description	Grade	Intercostal space n (%)
	Linear	0	32 (7.4)
	Slight curve	1	152 (35.5)
	Wavy	2	169 (39.4)
	Sinusoidal	3	75 (17.5)

Dewhurst, et al. *Diagn Interv Radiol* 2012;18:221-224

Collateral Branches

- Up to 80% of intercostal arteries may have a collateral branch
- Collateral branches tend to increase in size anteriorly

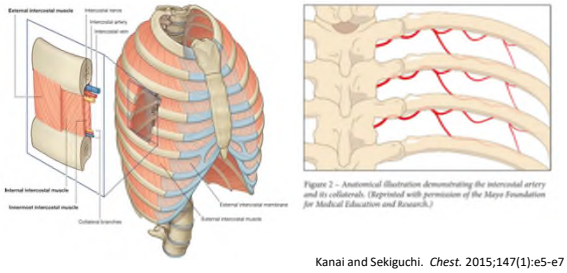


Figure 2 – Anatomical illustration demonstrating the intercostal artery and its collaterals. (Reprinted with permission of the Mayo Foundation for Medical Education and Research.)

Kanai and Sekiguchi. *Chest.* 2015;147(1):e5-e7

Avoiding Intercostal Vessels

- Rather than aiming superior to the rib, use ultrasound and aim for the middle of the intercostal space

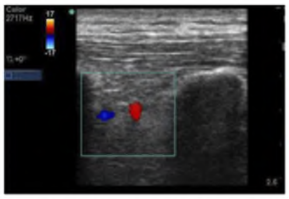


Figure 1 – Vascular ultrasonography with color Doppler demonstrating the intercostal artery positioned near the center of the intercostal space.

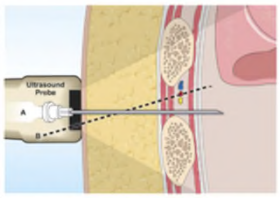


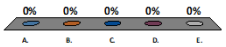
Figure 3 – Illustration demonstrating appropriate and inappropriate needle angulation (pathway A and B, respectively) from the same needle insertion site. (Reprinted with permission of the Mayo Foundation for Medical Education and Research.)

Kanai and Sekiguchi. *Chest.* 2015;147(1):e5-e7

Case Presentation #3

Thoracentesis is performed without complication. Pleural fluid analysis is consistent with an exudate, but cytology does not demonstrate malignant cells. What do you recommend next?

A. Repeat thoracentesis
B. Closed needle pleural biopsy
C. CT guided FNA of the pleura
D. Thoracoscopic pleural biopsy
E. Navigation bronchoscopy and linear EBUS TBNA



Pleural Fluid for Diagnosis of MPE

- Pleural fluid sensitivity: 62-90%
- Utility of repeat thoracentesis decreases – diminishing returns
  - 1st sample: 65%
  - 2nd sample: 27%
  - 3rd sample: 5%
- At least 50-60 mL of fluid increases diagnostic yield, but ideal minimum volume for diagnosis is unclear
  - Swiderek: 60 mL and 150 mL outperformed 10 mL
  - Abouzgheib: 50 mL similar to "large volume" (mean 890 ± 375 mL)

Antony, et al. *Eur Resp J* 2001;18:402-419
Garcia, et al. *Mod Pathol* 1994;7:665-668
Swiderek, et al. *Chest* 2010;137(1):68-73
Abouzgheib, et al. *Chest* 2009;135(4):999-1001

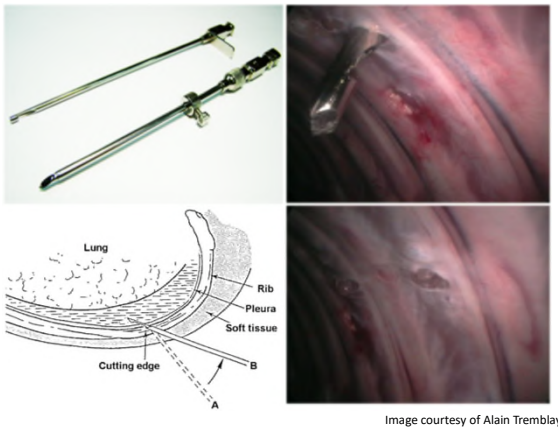
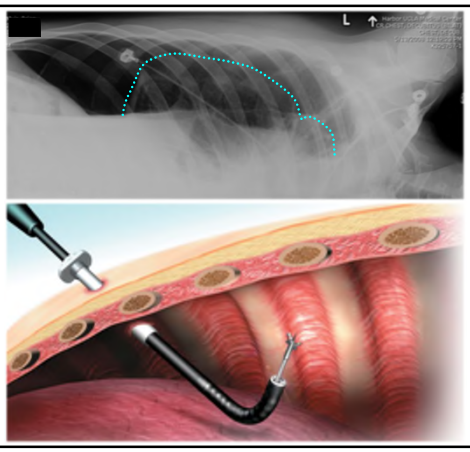
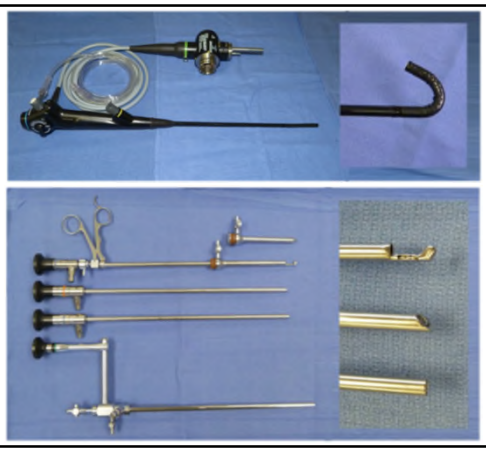


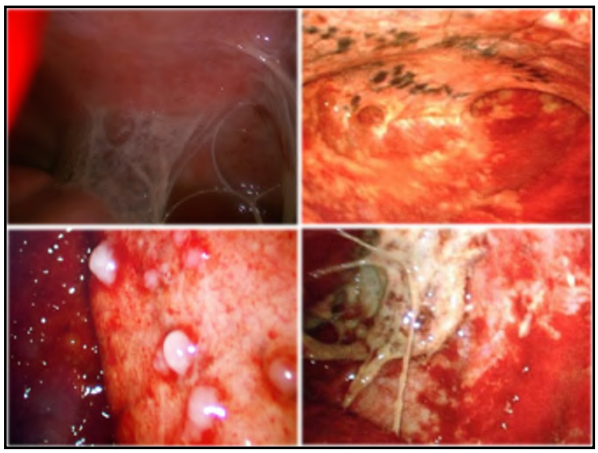
Image courtesy of Alain Tremblay



Thoracoscopes

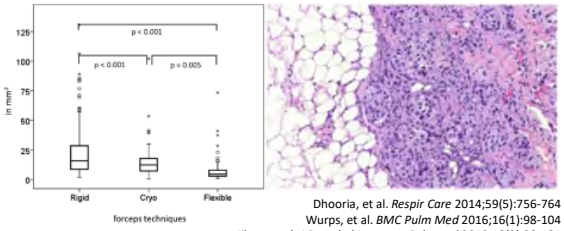
Rigid	Flex-Rigid
• Richard Wolf, Karl Storz	• Olympus
• 7 mm diameter trocar sleeve	• 5 mm diameter trocar sleeve
• 3 mm biopsy forceps	• 2 mm biopsy forceps
• Increased optical resolution	• Increased maneuverability
• Larger biopsies	• Smaller chest wall incision
	• Grip same as bronchoscope





Rigid vs. Semi-Rigid Thoracoscopes

- Larger and deeper biopsies for rigid > cryoprobe > flex-rigid
- Multiple series demonstrate similar diagnostic yields
  - Studies had few mesotheliomas (highest 30%)



Dhooria, et al. *Respir Care* 2014;59(5):756-764
Wurps, et al. *BMC Pulm Med* 2016;16(1):98-104
Khan, et al. *J Bronchol Intervent Pulmonol* 2012;19(2):98-101

Pleural Biopsy > Pleural Fluid

- Pleural Biopsy Options
  - Closed Needle Biopsy
  - Transthoracic Needle Aspiration
  - Medical Thoracoscopy
  - VATS

Disease	Pleural Fluid	Closed Needle Biopsy	Thoracoscopy
Lung Cancer	55-60%	60% (↑ w/ U/S)	90-95%
Mesothelioma	30-70%	40%	> 90%
Tuberculosis	< 50%	80%	100%

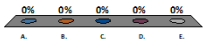
Koegelenberg and Diacon. *Respirology* 2011;16:738-746
Miyoshi, et al. *PLoS One* 2016;11(11):e0167186
McLaughlin, et al. *Lung Cancer* 2009;65(3):388-399

Case Presentation #4

Repeat thoracentesis reveals malignant cells. IHC staining is TTF (-), napsin A (-), P63 (+), and P40 (+), suggestive of squamous cell carcinoma.

Which of the following would you request?

A. Limited panel of molecular markers: EGFR, ALK, KRAS
B. Broad molecular marker profiling with NGS
C. PD-L1
D. Biomarkers have little utility in this setting
E. Refer to Oncology



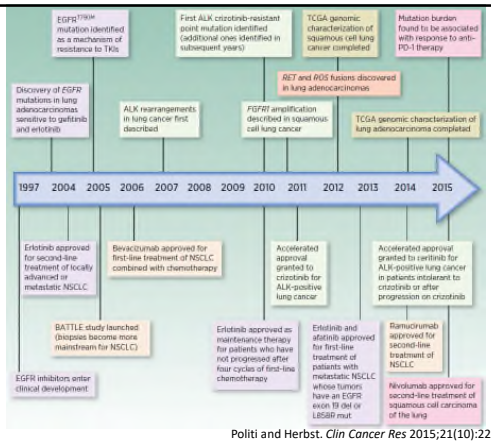
Common IHC Markers for Lung Cancers

	TTF-1[1]	Napsin A	CK7	CK20	P63	CK5/6, CK903	NE Markers[2]	Other
Non-mucinous adenoCA	85% +	+	+	-	-/+	-/+	-	
Mucinous adenoCA[3]	-/+ 10-20% +	-/+	+/-	+/-	-/+	-/+	-	May have focal CDX2
Squamous cell	-	-	-/+	-	+	+	-	
Small cell	90% +[4]	-	-/+	-	-	-	+	Punctate Cam5.2 and AE1/3 Diffuse CK903 or CK5/6 exclude SCLC
Carcinoid	50% +[4]	-	-	-	-	-	+	Ki-67 labeling index
Mesothelioma	-	-	+	-	-	+	-	WT1, Calretinin, HMBE-1, D2-40

All above entities are AE1/3+ and Cam5.2+, although reactivity is variable in NE tumors (e.g. carcinoid, small cell carcinoma)

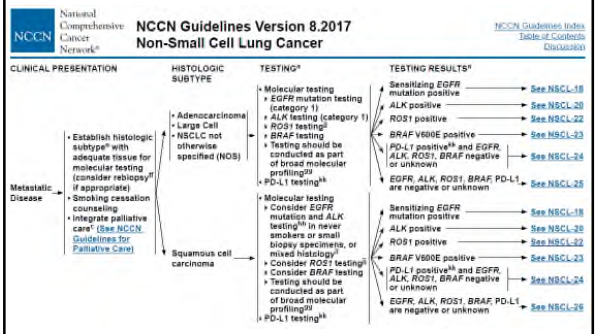
[1] Thyroid metastasis can be TTF-1+ but are distinguished by +thyroglobulin. Other adenocarcinoma metastasis are usually TTF-1–.
[2] Standard NE markers include synaptophysin, chromogranin, and CD56. These may be variably expressed in small cell carcinoma, but morphology trumps the immunophenotype in this diagnosis.
[3] Metastatic pancreatic and upper GI adenocarcinoma may be difficult to distinguish from primary lung mucinous adenocarcinoma by either morphology or immunoprofile (both may be CK7+/CK20+ and TTF-1–). DPC4 may be helpful: it is deleted in 55% of carcinomas of the pancreatic but not lung origin.
[4] TTF-1 is not specific for small cell carcinoma of the lung because >40% of extrapulmonary small cell carcinomas are also TTF-1 positive. In contrast, TTF-1 is positive in pulmonary but usually not intestinal carcinoids.

Adapted/Modified from Rekhtman and Bishop. *"Quick Reference Handbook for Surgical Pathologists"*. New York, Springer-Verlag;2011.



Politi and Herbst. *Clin Cancer Res* 2015;21(10):2213-2220

Molecular Testing for NSCLC



NCCN Clinical Practice Guidelines in Oncology. www.nccn.org/patients

Adequacy for Molecular Marker Testing

- Testing for molecular markers has a high success rate in lung parenchyma, lymph nodes, and pleural biopsies
- Some sources are less successful
  - BAL, pleural fluid: fewer malignant cells
  - Bone: secondary to the acidification required in specimen processing

Mutation	Lung	Lymph Node	Pleura	Bone
EGFR	94%	97%	96%	83%
ALK	91%	94%	97%	78%
KRAS	92%	93%	92%	86%

VanderLaan, et al. *Lung Cancer.* 2014;84(1):39-44.
Albanna, et al. *J Thorac Oncol.* 2014;1120-1125.

Next Generation Sequencing for EGFR

- NGS (aka massively parallel sequencing) can simultaneously detect multiple point mutations but are not consistently recommended in practice guidelines. (recommended by NCCN)
  - Ex) 48 BAL and pleural fluid samples from EGFR+ patients confirmed by resection

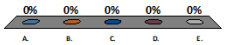
	Sanger Sequencing	NGS
36 cases with 0.3% to 9% neoplastic cells	16%	81%
12 cases without evidence of tumor	0%	42%

Buttitta, et al. *Clin Cancer Res* 2012;19(3):691-698.

Case Presentation #5

IHC testing confirms lung primary adenocarcinoma, EGFR(+) with exon 19 mutation. The patient has ECOG 2 performance status. There is initial reduction in tumor size with erlotinib therapy. The patient remains symptomatic from the pleural effusion. What palliative intervention would you recommend?

A. Repeat thoracentesis
B. Tunneled indwelling pleural catheter
C. Chest tube with talc pleurodesis
D. Thoracoscopy with talc pleurodesis
E. Refer to Palliative Care for hospice



Palliation Options

- Noninvasive palliation
- Recurrent thoracentesis
- Tunneled indwelling pleural catheter
- Pleurodesis
  - Chest Tube Slurry
  - Poudrage / Insufflation


THORACOSCOPIC INSUFFLATION


SLURRY THROUGH CHEST TUBE


Image courtesy of Alain Tremblay

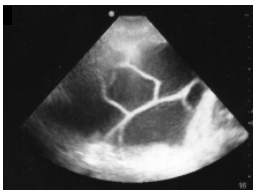
Natural History of MPE

- Asymptomatic effusions often stay small
  - No progression in small, asymptomatic effusions (n=14)
  - Median radiographic follow-up: 98 days
  - Median survival: 128 days
- Symptomatic effusions usually rapidly recur
  - 94 patients with symptomatic MPE treated with thoracentesis drainage
  - 90 (95.7%) had a recurrence < 30 days
  - Mean time to symptomatic recurrence: 4.2 days

Tremblay, et al. *J Bronchol* 2007;14:98-100
Anderson, et al. *Cancer* 1974;33:916-922

Predicting Prognosis for Patients with MPE

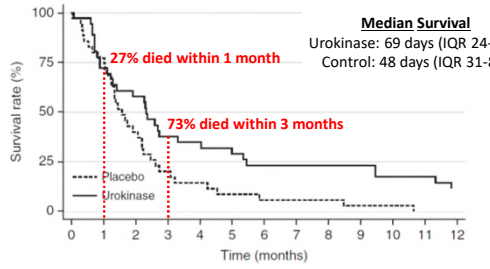
- TIME3: intrapleural urokinase prior to pleurodesis for septated MPE
  - Prospective, double-blind, 1:1 RCT
  - 71 subjects: 36 urokinase, 35 placebo
- Exclusion: expected survival < 4 weeks
- No difference in co-primary outcomes:
  - Dyspnea
  - Time to pleurodesis failure



Mishra, et al. *Am J Resp Crit Care Med* 2018;197(4):502-508

Predicting Prognosis for Patients with MPE

- 93% of subjects died within the 12 month follow-up period

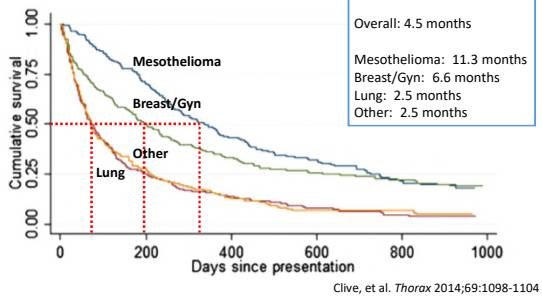


Median Survival
Urokinase: 69 days (IQR 24-123)
Control: 48 days (IQR 31-80)

Mishra, et al. *Am J Resp Crit Care Med* 2018;197(4):502-508

Poor Prognosis for MPE

- 789 patients from 3 international cohorts



Median Survival

Overall: 4.5 months

Mesothelioma: 11.3 months
Breast/Gyn: 6.6 months
Lung: 2.5 months
Other: 2.5 months

Clive, et al. *Thorax* 2014;69:1098-1104

L-E-N-T Prediction Score

- Factors independently associated with survival:
  - **L DH (pleural fluid)**
  - **E COG performance status**
  - **N eutrophil : Lymphocyte (serum)**
  - **T umor cell type**
  - Effusion size
  - Serum NT-proBNP

Variable	Score
LDH level in pleural fluid (IU/L)	
<1500	0
>1500	1
ECOG PS	
0	0
1	1
2	2
3–4	3
NLR	
<9	0
>9	1
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

Clive, et al. *Thorax* 2014;69:1098-1104

Predicting Survival

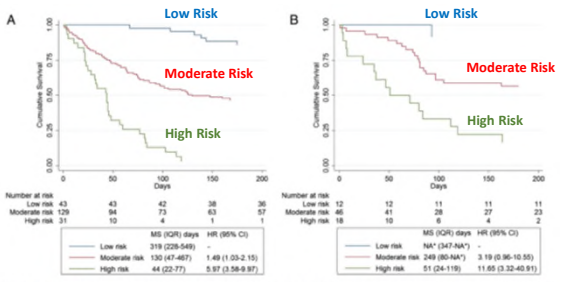
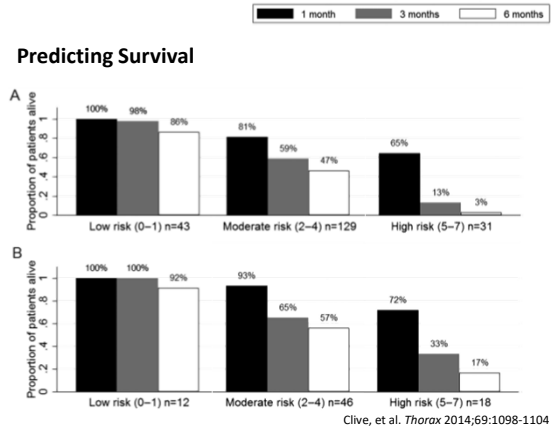


Figure 2 Survival curves according to the LENT score. (A) 'UK Cohort 1' and (B) 'UK Cohort 2'. MS, median survival; IQR, interquartile range; HR, hazard ratio; 95% CI, 95% confidence interval; NA*, Unable to provide data as insufficient patients have died.

Clive, et al. *Thorax* 2014;69:1098-1104

Predicting Survival



Clive, et al. *Thorax* 2014;69:1098-1104

BTS guidelines

Management of a malignant pleural effusion: British Thoracic Society pleural disease guideline 2010

Mark E Roberts,[1] Edmund Neville,[2] Richard G Berrisford,[3] George Antunes,[4] Nabeel J Ali[1], on behalf of the BTS Pleural Disease Guideline Group

Recurrent Thoracentesis

- Pleural effusions treated by aspiration alone are associated with a high rate of recurrence of effusion at 1 month so **aspiration is not recommended if life expectancy is > 1 month**

Definitive Palliative Therapies

- Other than in patients with a very short life expectancy, **small-bore chest tubes followed by pleurodesis** are preferable to recurrent aspiration.
- In patients with good performance status, **thoracoscopy** is recommended for diagnosis of suspected malignant pleural effusion and for drainage and **pleurodesis** of a known malignant pleural effusion.
- Ambulatory **indwelling pleural catheters** are effective in controlling recurrent and symptomatic malignant effusions in selected patients.

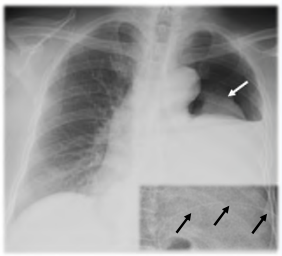
Roberts, et al. *Thorax* 2010;65(Suppl 2):ii32-ii40

Case Presentation #6

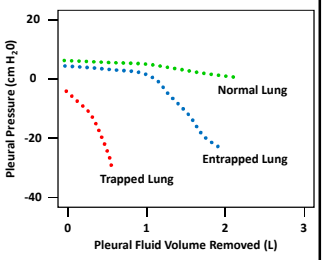
A TPC is placed without difficulty. While draining fluid after TPC insertion, the patient complains of chest pain. Post procedure CXR is performed.

What would you recommend?

A. Additional TPC drainage now
B. Attach TPC to suction via pleural drainage system
C. D/C patient and continue symptomatic drainage PRN

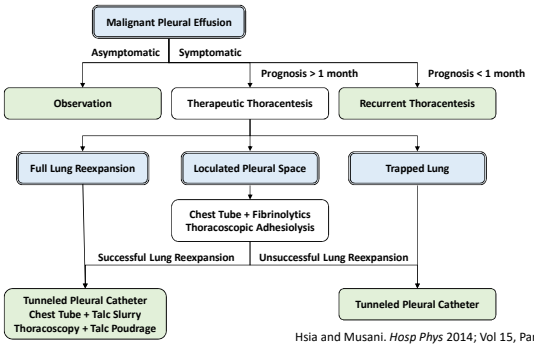


Bronchopleural Fistula vs. Pneumothorax *ex vacuo*



Hsia and Musani. *Hosp Phys* 2014; Vol 15, Part 1

Malignant Pleural Effusion Management Algorithm



Hsia and Musani. *Hosp Phys* 2014; Vol 15, Part 1

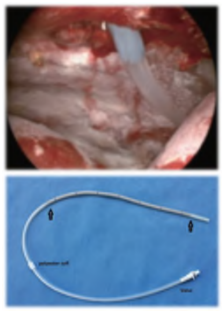
TIME2: Definitive Palliation Options

	Talc Pleurodesis	Tunneled Pleural Catheter
Hospitalization	2-6 days	None
Procedure Success	70%	100%
Dyspnea Improvement	No Difference	
Quality of Life		
Cost Benefit	No Difference (TPC Favored if Survival < 14 weeks)	
Complications	Fever / SIRS	Cellulitis (<10%)
	Hypoxemia / ARDS	Pleural Infection (5%)
Other Considerations	TPC for Procedure Failures	Requires Self-Care of TPC
	N/A for Trapped Lung	Spontaneous Pleurodesis

Davies, et al. *JAMA* 2012;307(22):2383-2389
Penz, et al. *Chest* 2014;146(4):991-1000
Fysh, et al. *Chest* 2013;144(5):1597-1602

Emerging Palliation Strategies

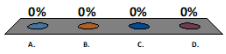
- Rapid Pleurodesis Protocol
  - Reddy, et al. *Chest* 2011;139(6):1419-1423
  - Krochmal, et al. *J Thorac Dis* 2016;8(9):2538-2543
  - OPTIMUM: Sivakumar, et al. *BMJ Open* 2016;6(10):e012795
- Silver Nitrate ($AgNO_3$) Coated IPC
  - Tremblay, et al. *Exp Lung Res* 2017;43(9-10)
  - SEAL-MPE: Bhatnagar, et al. *Am J Resp Crit Care Med* 2016;193:A7813
  - SWIFT: www.clinicaltrials.gov



Case Presentation #7

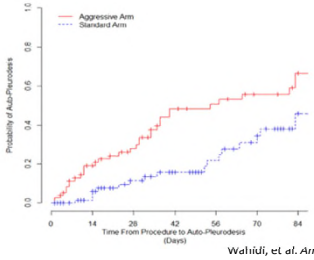
The patient has evidence of trapped lung but otherwise has relief of dyspnea with TPC drainage. How often do you recommend drainage?

A. Scheduled daily
B. Scheduled but not daily (e.g. q2 or q3 days)
C. PRN symptoms
D. Adjusted based on drainage volume



Drainage Frequency

- ASAP Trial: multicenter, RCT of TPC drainage frequency
  - Aggressive QD vs. standard QOD drainage
  - Primary outcome: incidence of autopleurodesis



Aggressive drainage:
- more frequent pleurodesis
  - 47% vs. 24%, p=0.003
- shorter time to pleurodesis
  - 54 vs. 90 days, p=0.005

Wahidi, et al. *Am J Respir Crit Care Med* 2017;195(8):1050-1057

Big Picture: Are We Doing a Good Job?

Goals of Palliation for MPE

- Relieve Symptoms → How does our practice compare to guideline recommendations?
- Minimize Hospitalization → How well do we avoid readmissions?

Epidemiology

- 126,825 admissions for MPE in the United States in 2012
  - Heathcare Cost and Untilization Project-Nationwide Inpatient Sample (HCUP-NIS)
- Mean age = 68.0 years (IQR 58.4-77.2)
- 55.8% female

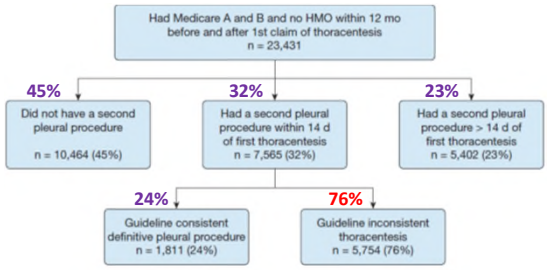
Primary Malignancy	Total
Lung	37.8%
Breast	15.2%
GI	11.0%
Gynecologic	9.0%
Hematologic	11.2%
Other	22.2%
Unknown	11.2%

- **Median LOS: 5.5 days**
  - **2.7-10.1 days (IQR)**
- **Inpatient Mortality: 11.6%**
- **Hospital Charges: $42,376**
  - **$21,618 - $84,679 (IQR)**

Taghizadeh, et al. *Chest* 2017;151(4):845-854

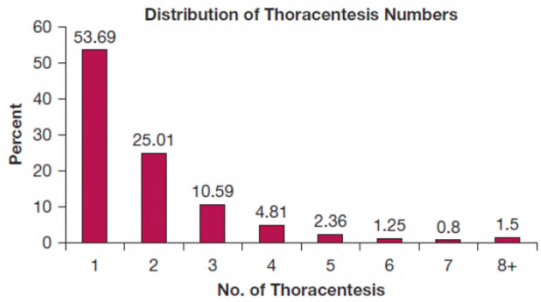
Overuse of Repeat Thoracentesis?

- SEER-Medicare patient database



Ost, et al. *Chest* 2017. epub ahead of print

Overuse of Repeat Thoracentesis?



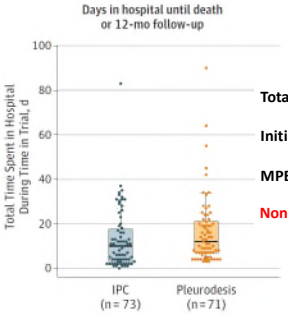
Ost, et al. *Chest* 2017. epub ahead of print

AMPLE: Hospitalization for TPC vs. Pleurodesis

- Multi-center, international trial of TPC vs. Pleurodesis
  - 74 TPC
  - 72 Pleurodesis (talc slurry)
  - Exclusion: expected life expectancy < 3 months
- Primary outcome: total hospitalization days until death or 1 year

Thomas, et al. *JAMA* 2017;318(19):1903-1912

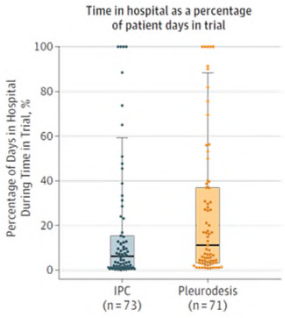
AMPLE: Hospitalization for TPC vs. Pleurodesis



	Median Days (IQR) TPC	Pleurodesis
Total Hosp. Days	10 (3-17)	12 (7-21)
Initial Hosp. Days	1 (1-2)	3 (3-4)
MPE-Related Days	1 (1-3)	4 (3-6)
Non-MPE Days	5 (1-13)	7 (2-15)

Thomas, et al. *JAMA* 2017;318(19):1903-1912

AMPLE: Hospitalization for TPC vs. Pleurodesis

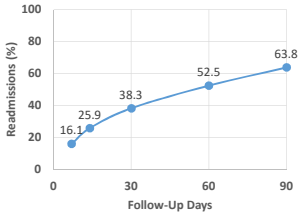


- Hospitalization days represented **7.1%** of total trial days (median, IQR 1.9-28.3%)

Thomas, et al. *JAMA* 2017;318(19):1903-1912

Readmissions for MPE

- 7,965 hospitalizations in California for MPE from 2009-2011
  - Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project (HCUP) State Inpatient Database (SID)
  - ICD-9 codes used to track readmissions in patients with an index admission for MPE

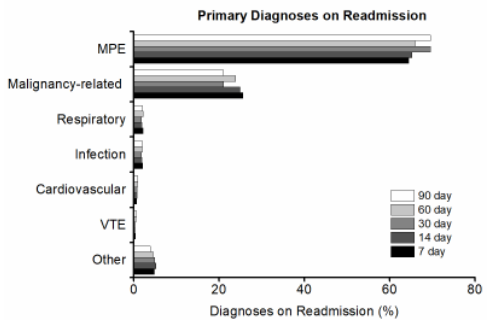


Disposition

Home - Routine	59.9%
Home Health Care	26.5%
SNF	11.3%
DNR	15.7%

Yang, et al. Submitted for publication.

Readmissions for MPE



Yang, et al. Submitted for publication.

Readmissions for MPE

	Index Hospitalizations	7-Day Readmissions	14-Day Readmissions	30-Day Readmissions	60-Day Readmissions	90-Day Readmissions
Index Hospitalizations	NA	5,957	5,957	5,957	5,526	4,982
Readmissions	NA	961	1,545	2,279	2,899	3,180
Readmission rate (%)	NA	16.1%	25.9%	38.3%	52.5%	63.8%
Length of stay (Days)						
Mean (SD)	**6.4 (5.8)**	**6.8 (6.9)**	**6.8 (6.8)**	**6.8 (6.5)**	**6.8 (6.4)**	**6.7 (6.2)**
Median (IQR)	**5 (3 - 8)**	**5 (3 - 9)**	**5 (3 - 9)**	**5 (3 - 9)**	**5 (3 - 9)**	**5 (3 - 9)**
Hospital Mortality (%)	NA	0.30	0.20	0.10	0.10	<0.01
Costs per Hospitalization (US $)						
Mean (SD)	19,378 (18,951)	19,774 (19,033)	20,289 (21,668)	20,189 (20,666)	20,278 (20,088)	20,113 (19,649)
Median (IQR)	14,317 (7,645 - 23,469)	13,088 (7,677 - 23,436)	13,721 (7,689 - 23,511)	13,798 (7,769 - 23,818)	14,116 (7,881 - 23,867)	14,031 (8,091 - 23,940)

Yang, et al. Submitted for publication.

Factors Associated with Readmissions

Patient Factors
- Age
- Gender
- Race
- Charlson Comorbidity Index
- Cancer Type
- Median Income
- Urbanicity
- Payer Category
- DNR Status
- Disposition
- Length of Stay

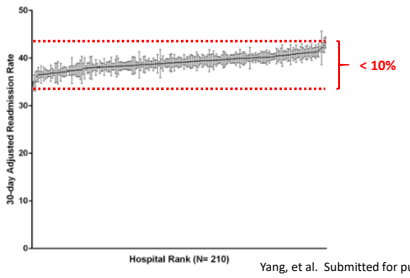
Hospital Factors
- Hospital Size
- Teaching Hospital
- Proportion of Minorities
- Hospital Type

Factor	OR (95% CI)
Female Gender	0.78 (0.63-0.95)
Charlson Comorbidity Index	1.51 (1.15-1.99)
DNR Status	1.37 (1.03-1.84)

Yang, et al. Submitted for publication.

Hospital Variability in 30-Day Readmission Rates

- 313 Hospitals
  - Excluded hospitals with < 5 MPE admissions/year



Yang, et al. Submitted for publication.

Thank you for your attention!

Conclusions

- MPE represents advanced disease with (generally) poor prognosis
- Palliative options are effective and should be selected based on the patient's status and wishes
- Patients with MPE are frequently readmitted – this (probably) extends beyond use, selection, or failure of palliation methods and needs to be identified and prevented