

Dyspnea in the oncology patient: a pulmonologist's approach

JAMES BROWN MD

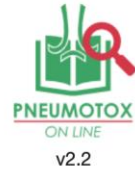
PULMONARY AND CRITICAL CARE MEDICINE

LAKELAND REGIONAL HEALTH

History – High yield

- ▶ Severity and Urgency
- ▶ Acute versus chronic complaint
- ▶ Associated complaints
 - ▶ Wheezing
 - ▶ Cough
 - ▶ Bleeding
 - ▶ jaundice
 - ▶ Swelling and weight gain
 - ▶ Palpitations
 - ▶ Aspiration
 - ▶ Ascites
 - ▶ Orthopnea (CHF, diaphragm failure, effusion)
 - ▶ Platypnea (AVMS, liver disease)
- ▶ Other medical history
 - ▶ Prior VTE
 - ▶ Port
 - ▶ Smoking
 - ▶ CTD
 - ▶ Cardiac history
 - ▶ Recent BMT
 - ▶ Recent procedures
- ▶ Medications
- ▶ Radiation

Medications



[BROWSE](#)

[DIAGNOSING DIRD](#)

[NEWS](#)

[CONTACT](#)



The Drug-Induced Respiratory Disease Website

Philippe Camus, M.D.
Dijon, France



Browse by »

DRUGS

PATTERNS

[Imatinib](#) ★ 3

Last update 22/08/2012

I - Interstitial/parenchymal lung disease

I.a	Pneumonitis (ILD), acute and/or severe (may cause ARDS)	★ 1
I.b	Pneumonitis (ILD)	★ 2
I.c	Eosinophilic pneumonia (pulmonary infiltrates and eosinophilia)	★ 1
I.d	Organizing pneumonia pattern (an area or areas of consolidation on imaging)	★ 1
I.m	ILD with a granulomatous component	★ 1
I.n	Pulmonary alveolar proteinosis (PAP)	★ 1
I.y	Progression, acceleration or exacerbation of preexisting ILD/fibrosis	★ 1

II - Pulmonary edema - Acute lung injury - ARDS

II.b	ARDS - Acute lung injury	★ 1
II.d	Pulmonary edema, cardiogenic	★ 1

SEARCH

Search by keyword



[Advanced search](#)

[Identify causative drugs](#)

[DIAGNOSING DIRD](#)

SEE ALSO UNDER

[Bosutinib](#) ★ 2

[Dasatinib](#) ★ 4

[Nilotinib](#) ★ 2

Physical exam

▶ Vitals

- ▶ Fever or hypothermia
- ▶ BP
 - ▶ Hypertension
 - ▶ Multi-kinase inhibitors
 - ▶ VEGF agents, Proteasome inhibitors
 - ▶ Hypotension
 - ▶ Sepsis
 - ▶ PE
 - ▶ Heart failure or tamponade
 - ▶ Dehydration from diarrhea, vomiting, FTT
 - ▶ Adrenal insufficiency

▶ Tachypnea

- ▶ Compensation for metabolic acidosis
- ▶ Hypermetabolic state
- ▶ Diaphragm failure

▶ SpO₂%

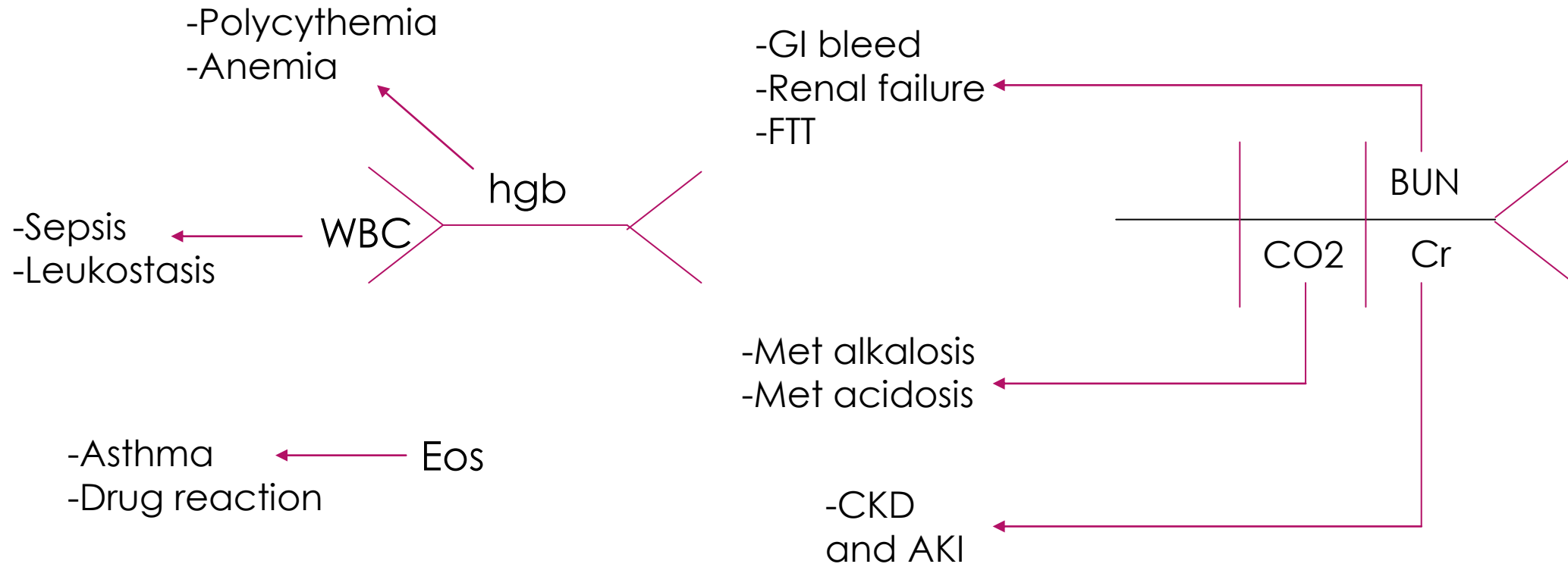
- ▶ Up to 10% differences in saturation estimates in darker-skinned patients and worse at lower saturations (Feiner 2007)
- ▶ Methemoglobinemia
 - ▶ SpO₂% usually in the mid 80s
 - ▶ Rasburicase (Alessa 2015)
 - ▶ Ifosfamide (Hadjiliadis 2000)
 - ▶ Cyclophosphamide (Sangera 2015)

Physical Exam

- high yield head to toe

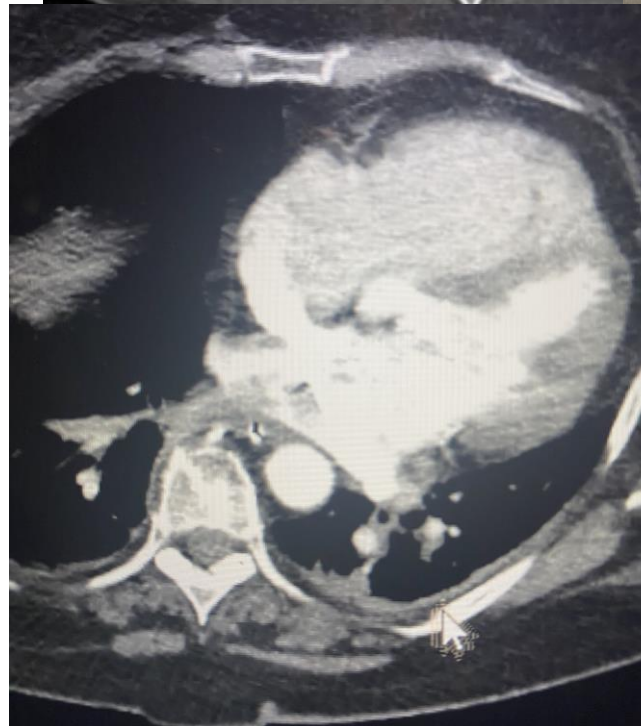
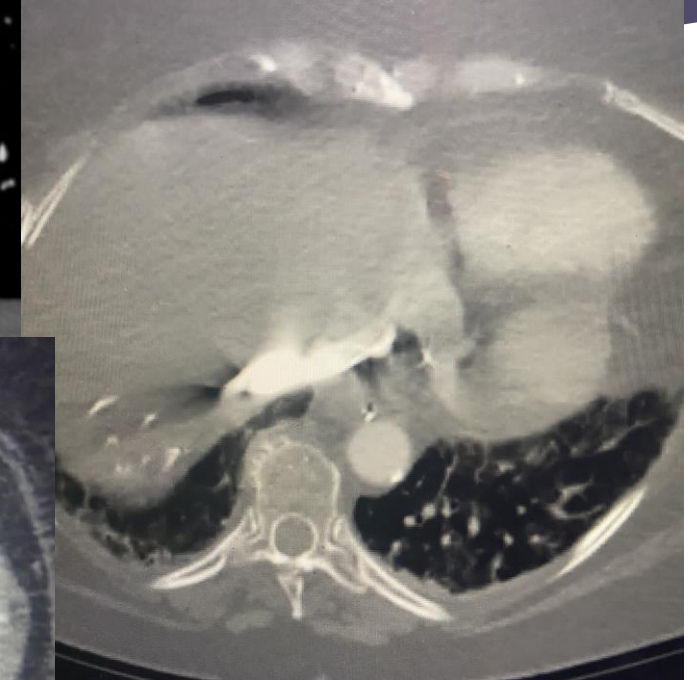
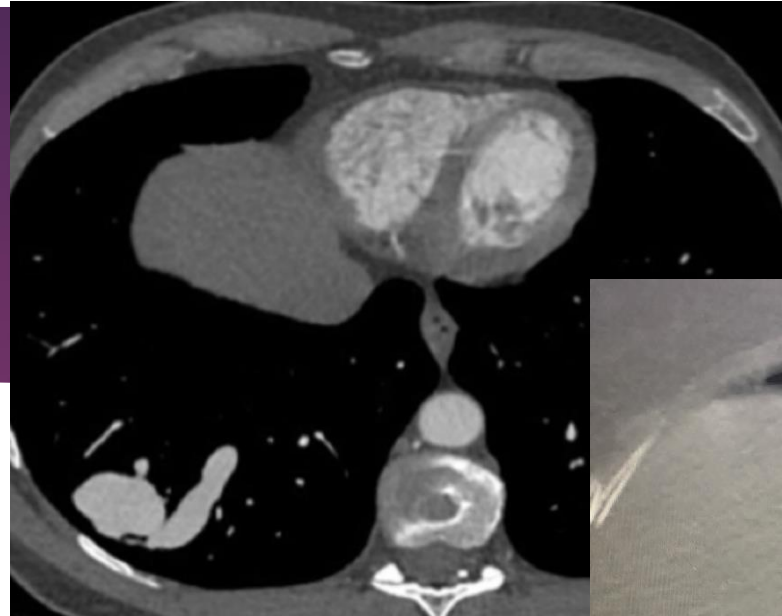
- ▶ Icterus
 - ▶ PLS after BMT?
 - ▶ Biliary obstruction?
- ▶ JVD
 - ▶ CHF
 - ▶ Tamponade
 - ▶ Valvulopathy
- ▶ Accessory muscle use
- ▶ Murmurs
- ▶ Wheezing, crackles, percussion
- ▶ Abdominal distension
- ▶ Extremities
 - ▶ Clubbing
 - ▶ Edema
 - ▶ Temperature
 - ▶ Capillary refill

Labs – Basic labs



Imaging – CT chest

- ▶ With contrast
 - ▶ Creates more ground glass
 - ▶ More difficult to assess lung parenchyma
 - ▶ CTA timing
 - ▶ PA
 - ▶ AVM (shunting)
 - ▶ PE
 - ▶ Clues for RV overload (contrast reflux)
 - ▶ Clues for intracardiac shunt (contrast in LA)
 - ▶ Aortic/bronchial artery
 - ▶ Dissection
 - ▶ Hemoptysis (Mass, mycetoma, bronchiectasis)



Bronchial artery

- ▶ Bronchial circulation is the source of massive hemoptysis in 90% of cases
 - ▶ Goal is to guide IR for bronchial artery embolization
 - ▶ → CT angio/aortogram

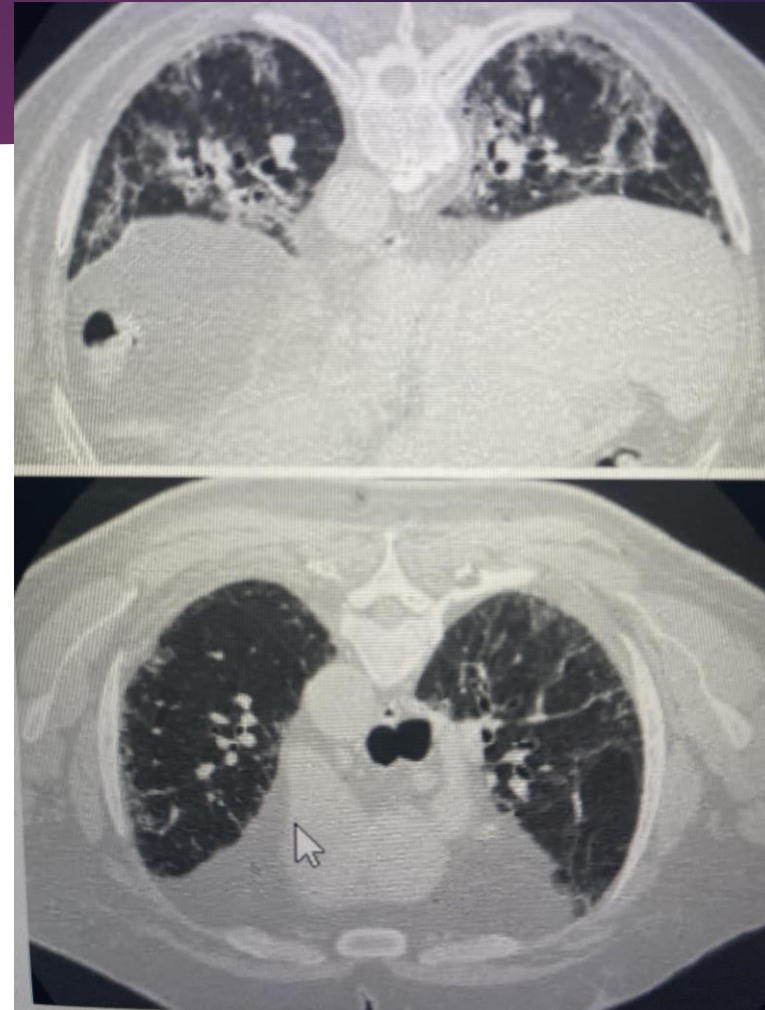


What about the kidneys?

- ▶ Contrast nephropathy from CAT scans is of questionable existence as an independent risk factor for AKI
- ▶ Concerns are based on very flawed and outdated data
- ▶ If the test will be helpful, get the test
- ▶ I routinely follow up abnormal VQ scans with CTAs that are negative
- ▶ Make a dot phrase for justification and list references
- ▶ Aycock et al 2018, Hinson et al 2019 , Ehrman et al 2017
- ▶ McDonald et al 2015
 - ▶ Mayo Clin Proc
 - ▶ Retrospective propensity score-adjusted analysis
 - ▶ A total of 6902 patients (4496 CKD stage III, matched: 1220 contrast and 1220 noncontrast; 2086 CKD stage IV-V, matched: 491 contrast and 491 noncontrast)
 - ▶ rates of AKI, emergent dialysis, and mortality were not significantly higher in the contrast group than in the noncontrast group in either CKD subgroup (CKD stage III: OR, 0.65-1.00; $P<.001-.99$ and CKD stage IV-V: OR, 0.93-2.33; $P=.22-.99$).

Imaging – CT chest

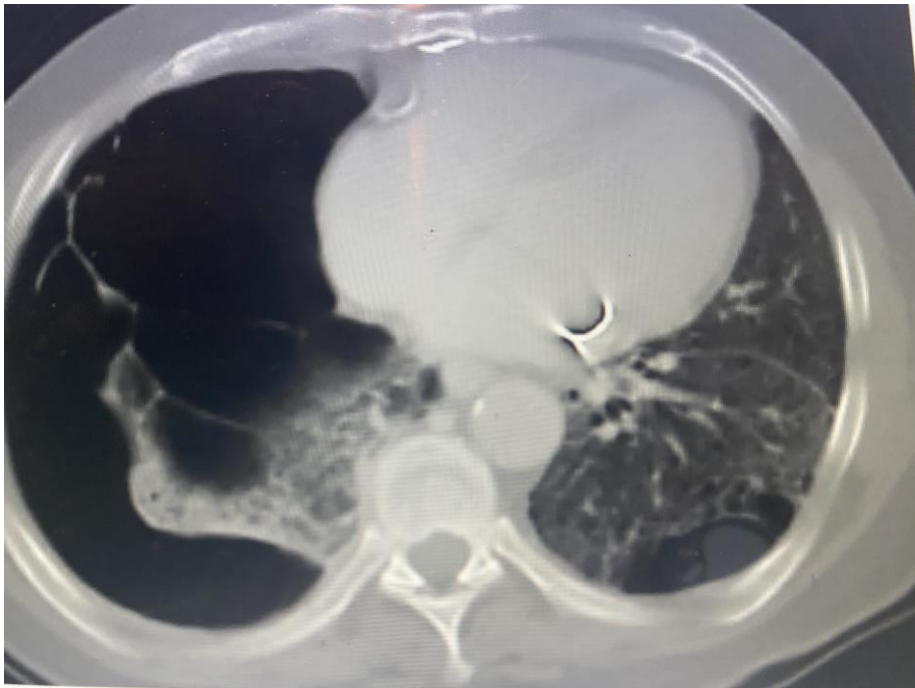
- ▶ Without contrast
 - ▶ HRCT chest
 - ▶ Can miss or mischaracterize nodules
 - ▶ Prone images with inspiration and expiration
 - ▶ Best for interstitial lung disease
 - ▶ Non con CT chest
 - ▶ Best for nodules and masses
 - ▶ Prone to artifacts at the bases



Examples

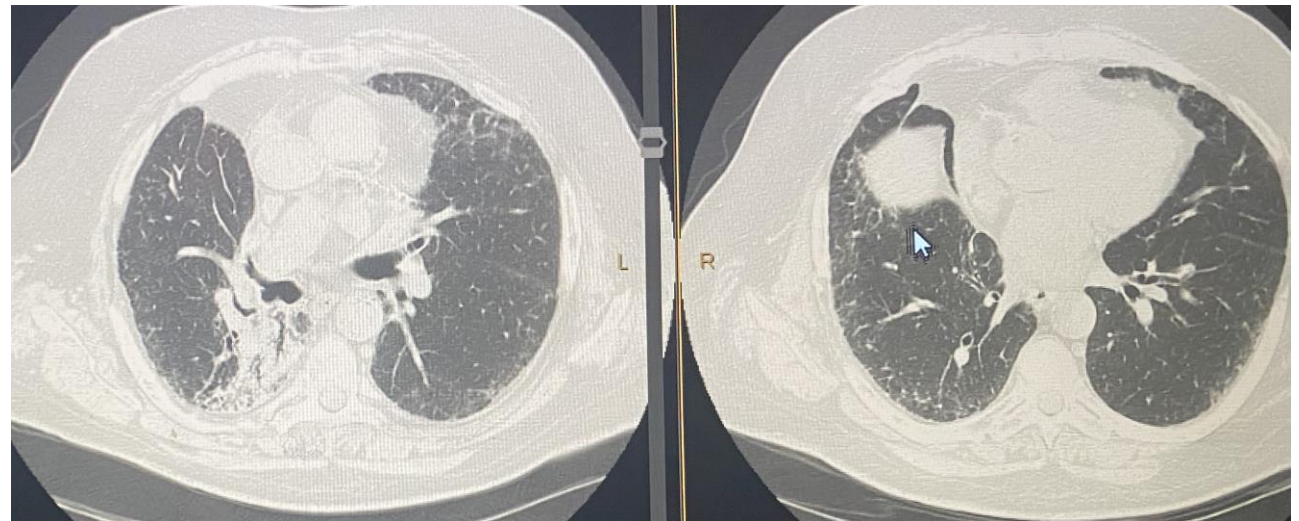
h/o small cell, severe bolus disease and dynamic hyperinflation

Treated with liquid morphine



h/o radiation and now concomitant IPF

Treated with Esbriet and gabapentin

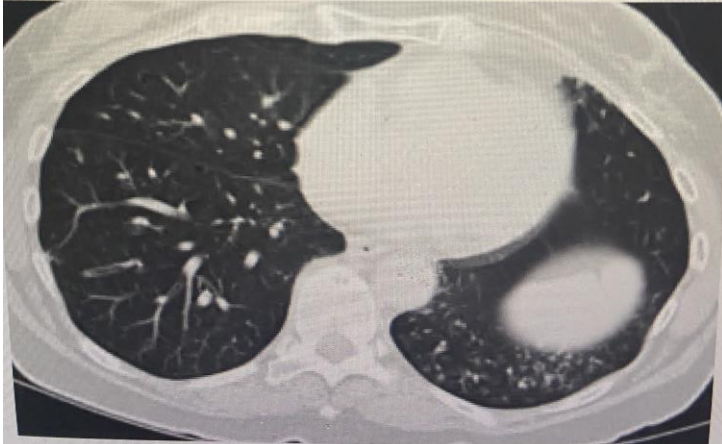


Examples - micronodules

Centrilobular nodules

-MAI, medication induced bronchiolitis, hypersensitivity pneumonitis

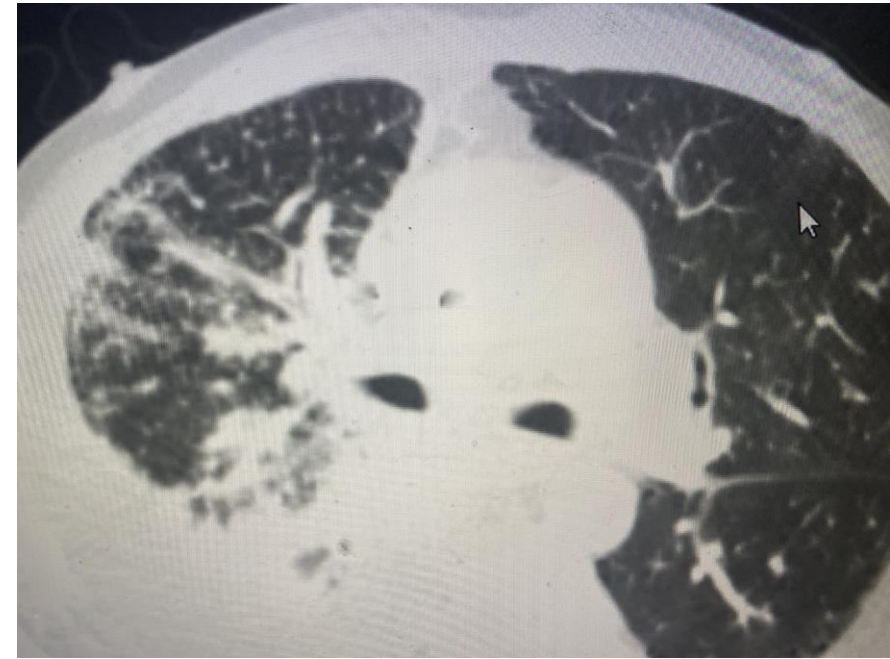
-Spare the periphery

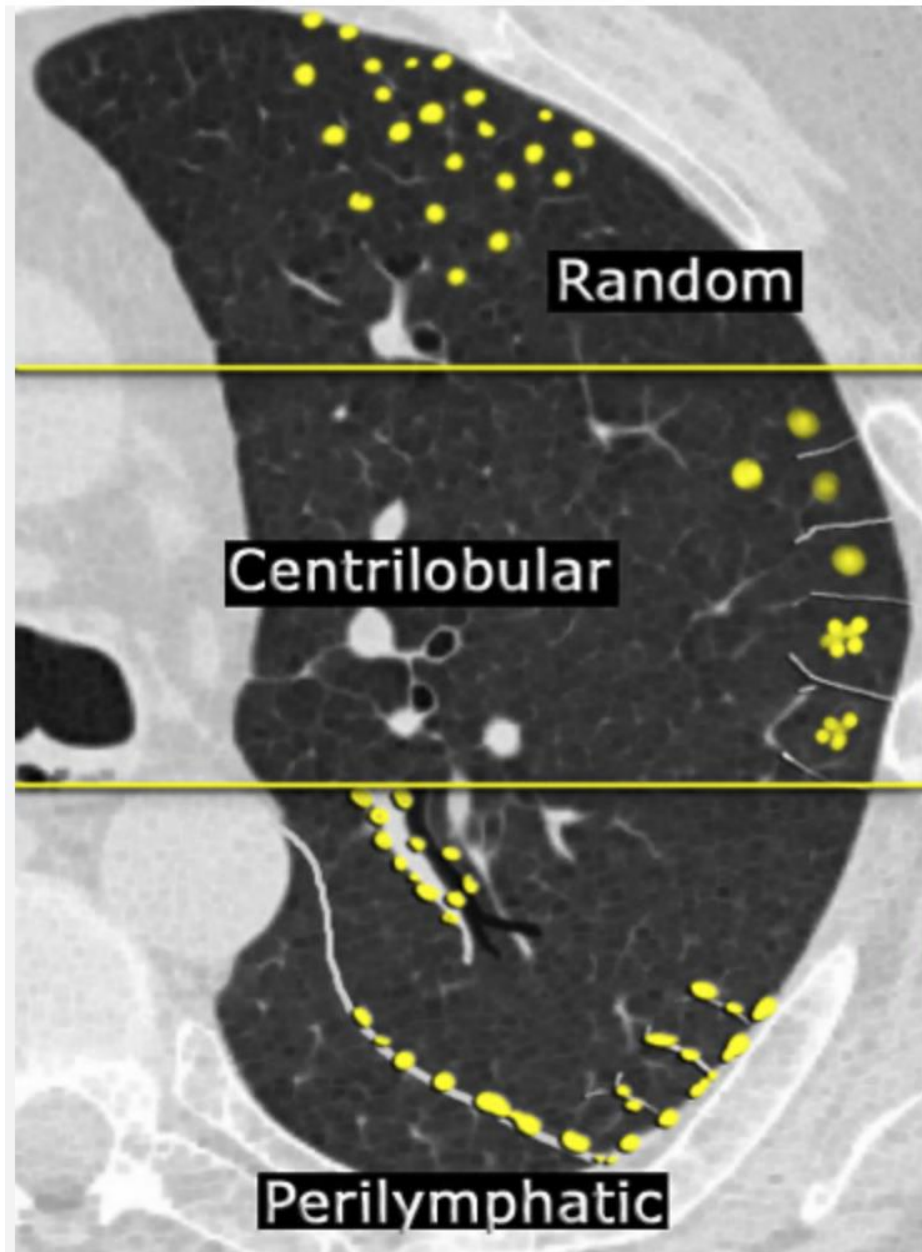


Peri lymphatic

-lymphangitic spread, sarcoidosis

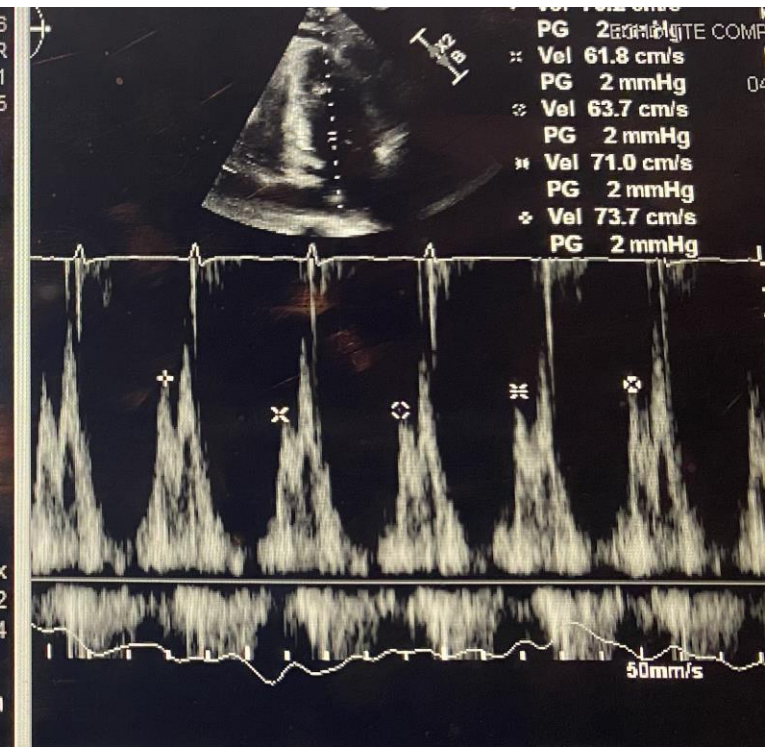
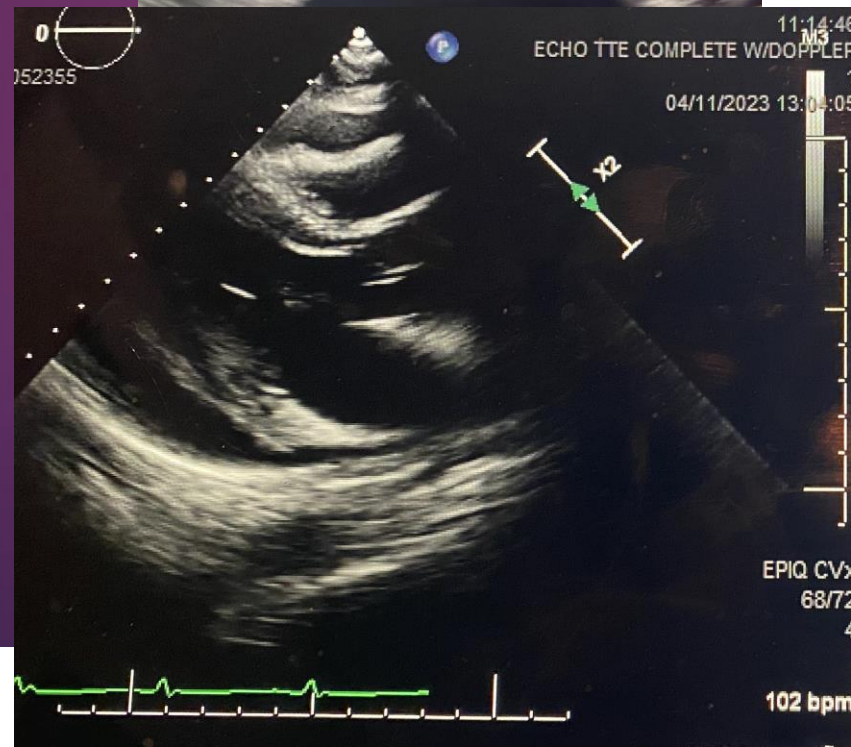
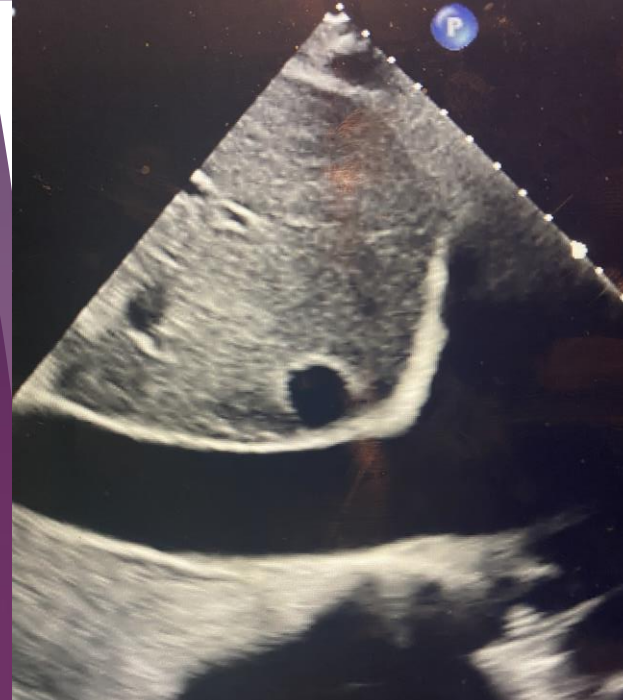
-bronchovascular and subpleural





Echo and POCUS

- IVC gives clues for RV pressures
- volume status
- tamponade
- RV failure from PE or MI



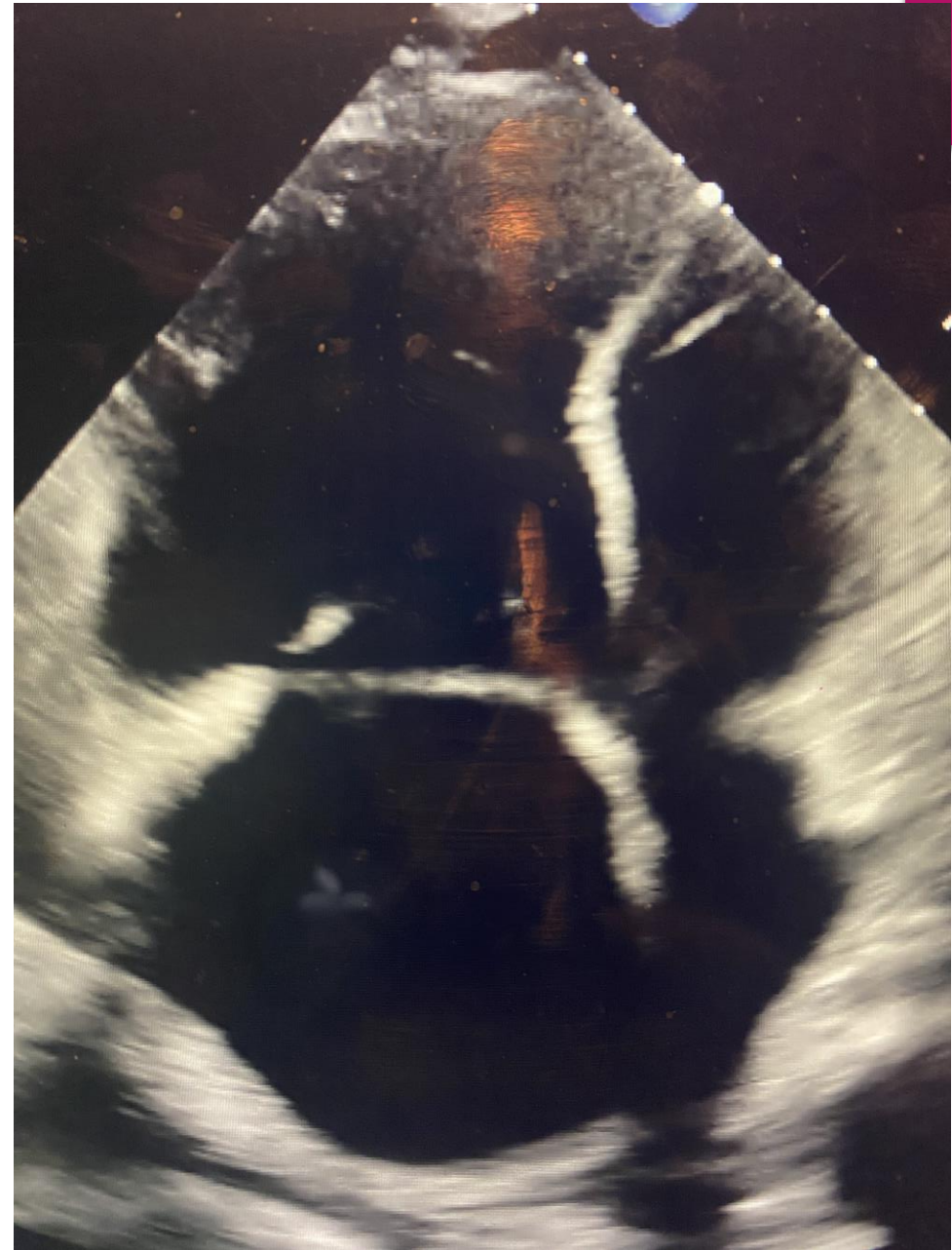
RV failure

-PE?

-Tumor or medication
induced pulmonary
hypertension?

-Malignancy-induced PVOD?
(McHugh 2021)

-CTEPH



Bubble study

R → L shunt



Specific Situations

Anemia

-IV iron, pulmonary rocket rocket fuel

[BMC Pulm Med.](#) 2015; 15: 58. Published online 2015 May 8. doi: [10.1186/s12890-015-0050-y](https://doi.org/10.1186/s12890-015-0050-y)

PMCID: PMC4426177 | PMID: [25952923](https://pubmed.ncbi.nlm.nih.gov/25952923/)

Anemia and hemoglobin serum levels are associated with exercise capacity and quality of life in chronic obstructive pulmonary disease

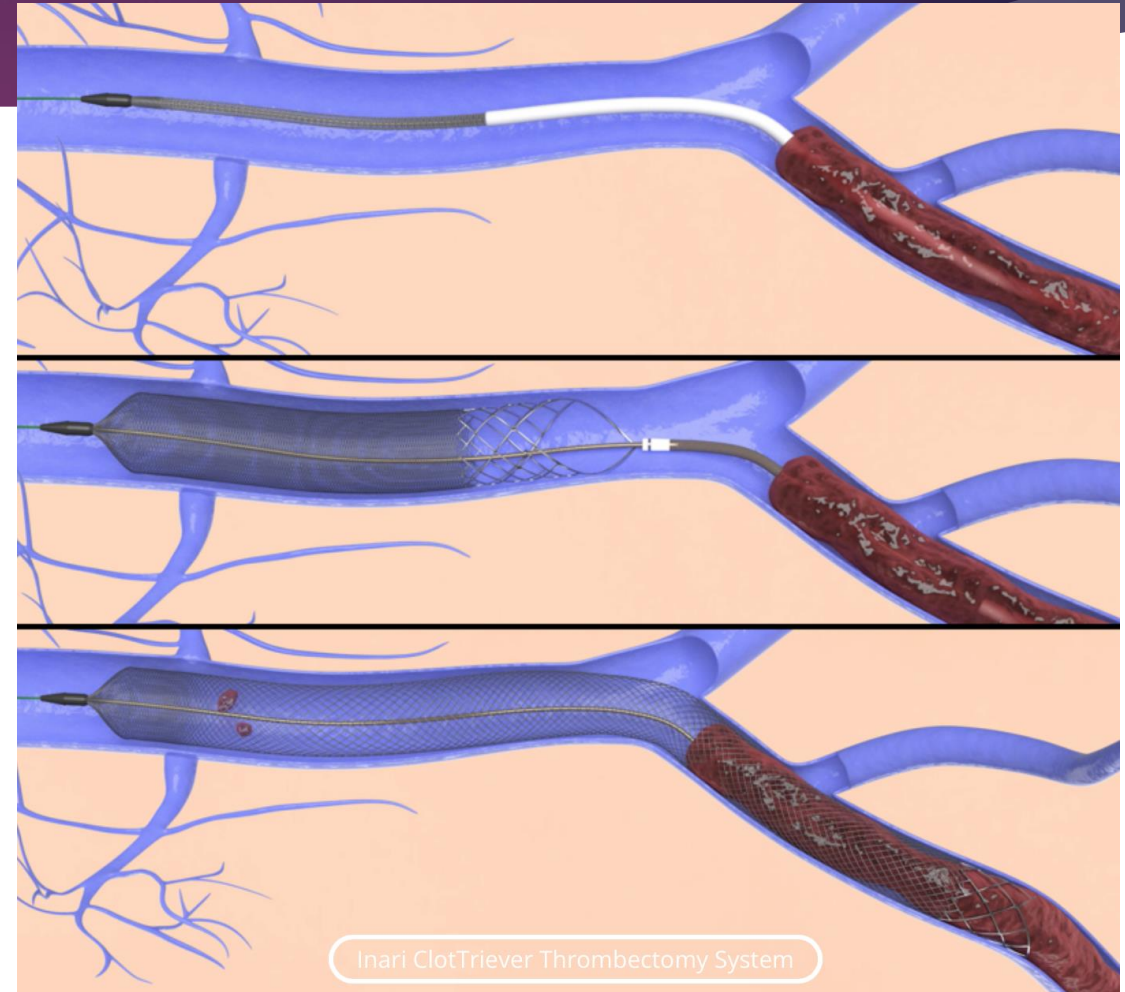
[Marcello Ferrari](#), [Lorenzo Manea](#), [Kamel Anton](#), [Paola Bruzzone](#), [Mara Meneghello](#), [Francesco Zamboni](#), [Luigi Purgato](#), [Lucia Cazzoletti](#), [Pietro Ferrari](#), and [Renato Testi](#)

- ▶ 105 COPD patients
- ▶ Anemic vs non Anemic
- ▶ Anemic patients
 - ▶ Higher medical research council dyspnea scale (MRCs)
 - ▶ Lower 6MWD
 - ▶ Lower VO₂max
 - ▶ Worse quality of life
 - ▶ No difference in muscle strength
 - ▶ Were not that anemic (hgb 11.5)

Pulmonary Emboli

PEERLESS Trial

- ▶ FlowTrieversystem versus catheter-directed thrombolysis (CDT)
- ▶ Enrolling in multicenter RCT
- ▶ Patients with intermediate-high risk pulmonary embolism (PE)
- ▶ Potential for immediate relief without the risk of lytics
- ▶ May be able to offer interventions to higher risk patients in lower risk PEs
- ▶ <https://clinicaltrials.gov/ct2/show/NCT05111613>



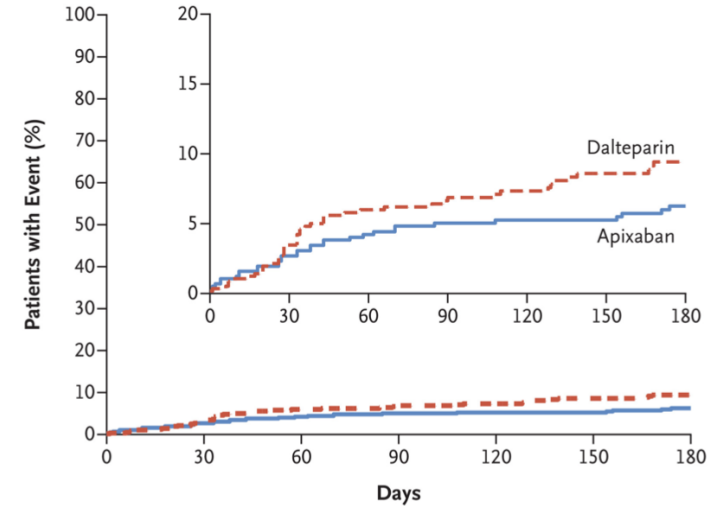
IVC filters

- ▶ 8,255 IVC filter lawsuits as of May 2022 (Miller 2023)
- ▶ Jury awards as high as \$34 million
- ▶ Lack of evidence to support the use of IVC filters in any situation other than an absolute contraindication to anticoagulation
- ▶ In 2014, the FDA updated recommendations:
 - ▶ Risks > benefits between 29 and 54 days
 - ▶ Rarely retrieved that soon in real life
- ▶ American College of Chest Physicians in 2021 – strong recommendation against the use of IVC filters in addition to anticoagulants
- ▶ Society of interventional radiology clinical practice guidelines from 2020 – moderate recommendation stating “In patients with acute VTE who are being treated with therapeutic anticoagulation, we recommend against routine placement of an IVC filter”
- ▶ PREPIC2 trial, Randomized, open-label, blinded end point trial: “Among hospitalized patients with severe acute PE, the use of a retrievable inferior vena cava filter plus anticoagulation compared to anticoagulation alone did not reduce the risk of symptomatic recurrent PE at 3 months. These findings do not support the use of this type of filter in patients who can be treated with anticoagulation”

Apixaban and VTE in oncology patients

- ▶ Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer. [April 23, 2020](#)
N Engl J Med 2020; 382:1599-1607
 - ▶ multinational, randomized, investigator-initiated, open-label, noninferiority trial with blinded central outcome adjudication
 - ▶ Patients with cancer and VTE to receive apixaban or dalteparin for 6 months
 - ▶ Oral apixaban was noninferior to subcutaneous dalteparin for the treatment of cancer-associated venous thromboembolism without an increased risk of major bleeding

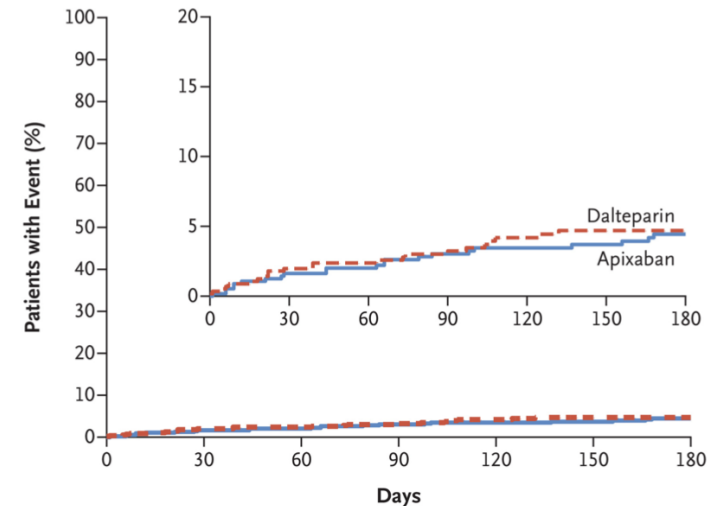
A Recurrent Venous Thromboembolism



No. at Risk

Dalteparin	579	507	462	417	383	352	217
Apixaban	575	522	481	453	424	399	241

B Major Bleeding

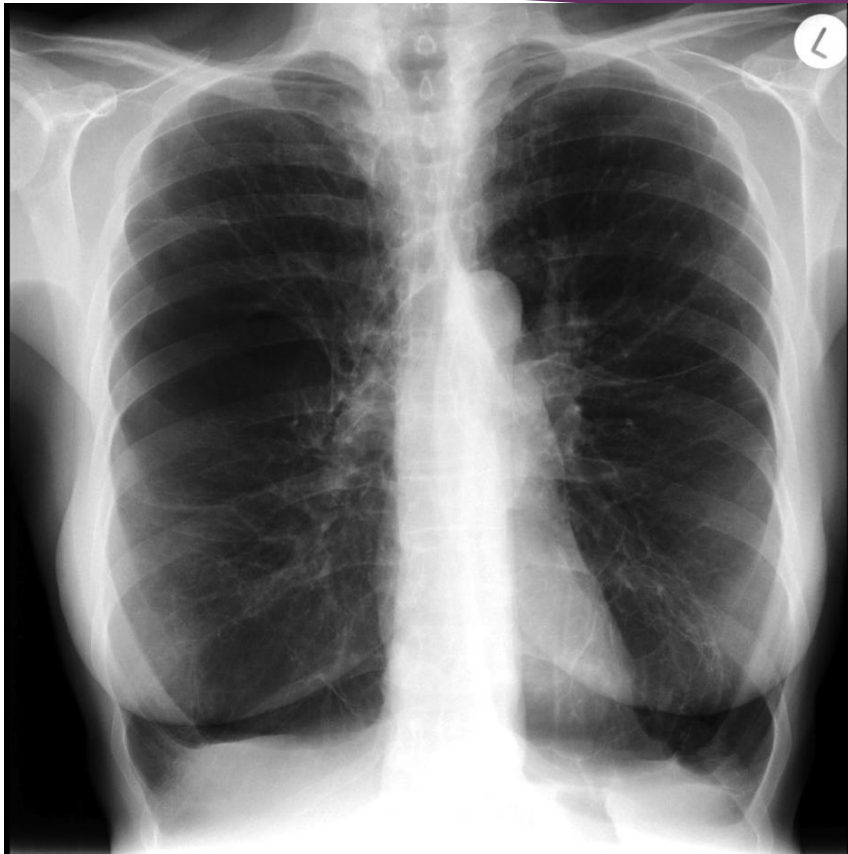


No. at Risk

Dalteparin	579	510	473	430	387	355	222
Apixaban	575	527	490	458	427	402	238

Advanced Emphysema

Advanced emphysema



- ▶ More hyperinflation = less PIFR
 - ▶ Correlates with age (older = worse PIFR)
 - ▶ Lower IC = worse PIFR
 - ▶ Being female has been associated with reduced PIFR
 - ▶ Hyperinflation (worsened during exacerbation) reduced PIFR
- ▶ → bad obstruction and hyperinflation = may not benefit from an inhaler

Advanced emphysema

Internal Resistances of Bronchodilator DPI

Bronchodilator DPI	Resistance (kPa \cdot s/L [L/min])
Aerolizer	0.019
Diskhaler	0.021
Breezhaler/Neohaler	0.022
Accuhaler/Diskus	0.027
Ellipta	0.029
Genuair/PressAir	0.031
Turbuhaler	0.036
HandiHaler	0.051

Mahler. Ann ATS 2017;14:1105

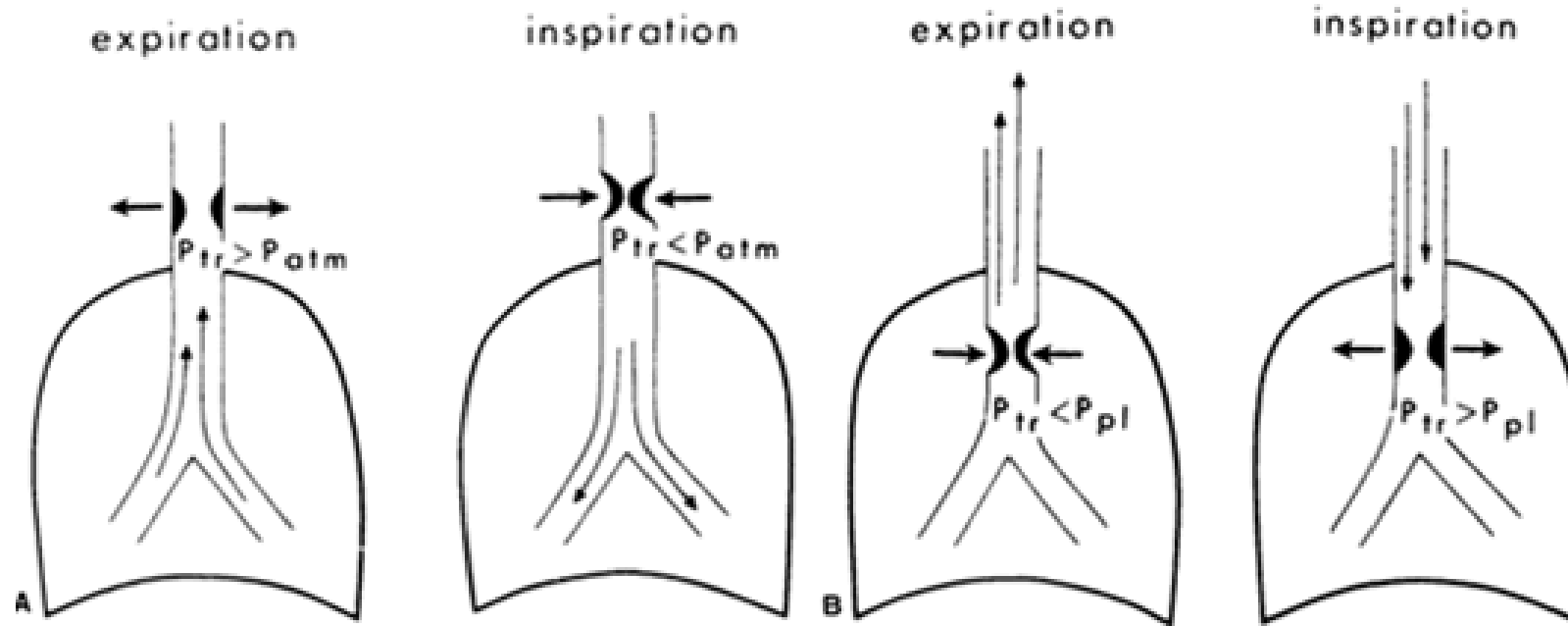
Pharmacology literature indicates patients must generate 60 L/min to receive optimal dose
More resistance = more difficult to generate flow
→ DPIs require hard and fast inhalation

Advanced emphysema

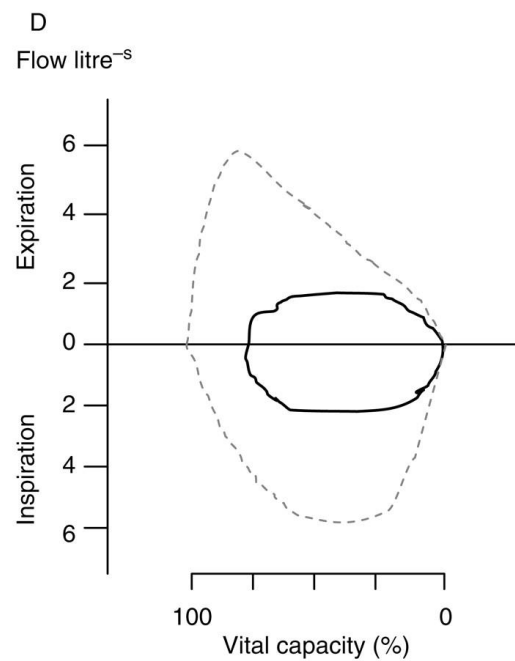
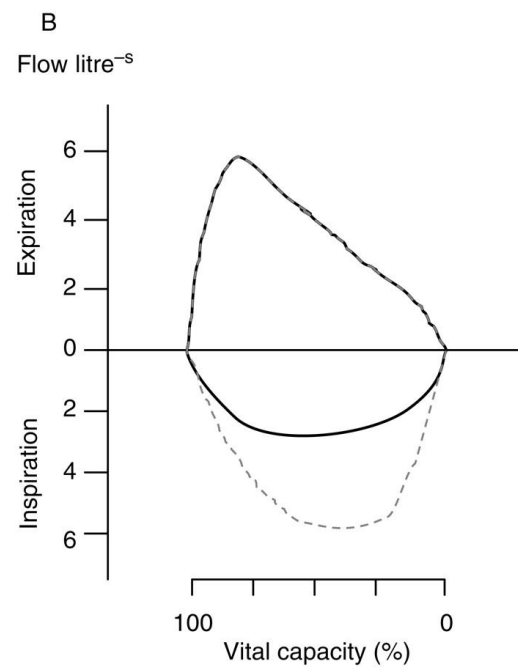
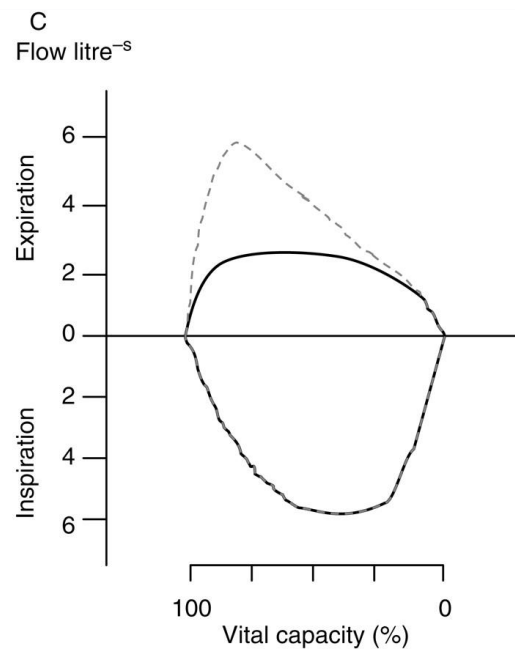
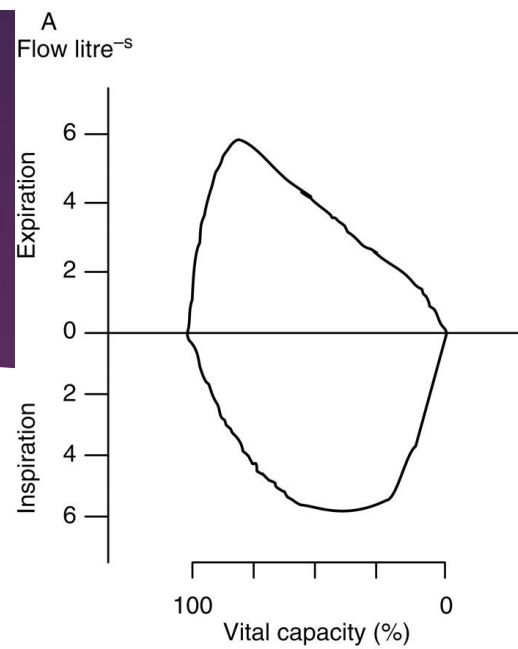
My go-to regimen

- ▶ All nebulizer meds
 - ▶ Revfenacin
 - ▶ Formoterol
 - ▶ Budesonide
- ▶ Prevent exacerbations
 - ▶ Azithromycin TIW
 - ▶ Mepolizumab or Tezepelumab
- ▶ Hypercapnic → Home non-invasive ventilator
- ▶ Severe dynamic hyperinflation → Liquid morphine

Endobronchial tumor



FVLs



Checkpoint inhibitor pneumonitis

- ▶ Patient risk factors
 - ▶ Lung cancer
 - ▶ Renal cell cancer
 - ▶ h/o ILD
 - ▶ Prior chest radiation
 - ▶ Smoking
 - ▶ Age > 70
- ▶ Usually around 6 months of therapy but range is broad 1.5 to 127 weeks
- ▶ Almost always with elevated CRP and ESR

CPI pneumonitis

Table 2: National Cancer Institute CTCAE Pneumonitis Grading System

Table 2: National Cancer Institute CTCAE Pneumonitis Grading System

Grade	Symptom
1	Asymptomatic; clinical or diagnostic observations only; intervention not indicated
2	Symptomatic; medical intervention indicated; limiting instrumental ADL
3	Severe symptoms; limiting self-care ADL; oxygen indicated
4	Life-threatening respiratory compromise; urgent intervention indicated (ie, tracheostomy or intubation)
5	Death

Source.—Reference 26.

Note.—ADL = activities of daily living.

-Sarcoid like reaction



Thank You

- ▶ Feiner JR, Severinghaus JW, Bickler PE. Dark skin decreases the accuracy of pulse oximeters at low oxygen saturation: the effects of oximeter probe type and gender. *Anesth Analg*. 2007 Dec;105(6 Suppl):S18-S23. doi: 10.1213/01.ane.0000285988.35174.d9. PMID: 18048893.
- ▶ Alessa MA, Craig AK, Cunningham JM. Rasburicase-Induced Methemoglobinemia in a Patient with Aggressive Non-Hodgkin's Lymphoma. *Am J Case Rep*. 2015 Sep 3;16:590-3. doi: 10.12659/AJCR.894088. PMID: 26334783; PMCID: PMC4562617.
- ▶ Hadjiliadis D, Govert JA. Methemoglobinemia after infusion of ifosfamide chemotherapy: first report of a potentially serious adverse reaction related to ifosfamide. *Chest*. 2000 Oct;118(4):1208-10. doi: 10.1378/chest.118.4.1208. PMID: 11035699.
- ▶ Sangera, R., & Johnson, B. (2015). Feeling blue? cyclophosphamide induced methemoglobinemia. *Chest*, 148(4). <https://doi.org/10.1378/chest.2224540>
- ▶ McDonald JS, McDonald RJ, Lieske JC, Carter RE, Katzberg RW, Williamson EE, Kallmes DF. Risk of Acute Kidney Injury, Dialysis, and Mortality in Patients With Chronic Kidney Disease After Intravenous Contrast Material Exposure. *Mayo Clin Proc*. 2015 Aug;90(8):1046-53. doi: 10.1016/j.mayocp.2015.05.016. Erratum in: *Mayo Clin Proc*. 2015 Oct;90(10):1457. Kallmes, David E [Corrected to Kallmes, David F]. PMID: 26250726; PMCID: PMC4550308.
- ▶ McHugh, S., Vanchiere, C., Oliveros, E., Islam, S., Luceno, S., Vaidya, A., & Forfia, P. (2021). Malignancy-related pulmonary hypertension presenting as a pulmonary veno-occlusive-like syndrome: A single-center case series. *JACC. Case Reports*, 3(7), 1044–1050. <https://doi.org/10.1016/j.jaccas.2021.04.008>
- ▶ Ferrari, M., Manea, L., Anton, K., Bruzzone, P., Meneghello, M., Zamboni, F., Purgato, L., Cazzoletti, L., Ferrari, P., & Testi, R. (2015). Anemia and hemoglobin serum levels are associated with exercise capacity and quality of life in chronic obstructive pulmonary disease. In *BMC Pulmonary Medicine* (Vol. 15, Issue 1). Springer Science and Business Media LLC. <https://doi.org/10.1186/s12890-015-0050-y>
- ▶ Miller, R. V., Jr. (2023, January 9). *Cordis and Cook IVC filter lawsuit settlement update*. Lawsuit Information Center. https://www.lawsuit-information-center.com/bard_ivc_lawsuits.html
- ▶ Agnelli, G., Becattini, C., Meyer, G., Muñoz, A., Huisman, M. V., Connors, J. M., Cohen, A., Bauersachs, R., Brenner, B., Torbicki, A., Sueiro, M. R., Lambert, C., Gussoni, G., Campanini, M., Fontanella, A., Vescovo, G., Verso, M., & Caravaggio Investigators. (2020). Apixaban for the treatment of venous thromboembolism associated with cancer. *The New England Journal of Medicine*, 382(17), 1599–1607. <https://doi.org/10.1056/NEJMoa1915103>
- ▶ Kalisz, K. R., Ramaiya, N. H., Laukamp, K. R., & Gupta, A. (2019). Immune checkpoint inhibitor therapy-related pneumonitis: Patterns and management. *Radiographics: A Review Publication of the Radiological Society of North America, Inc*, 39(7), 1923–1937. <https://doi.org/10.1148/rg.2019190036>