Advances in the Treatment of Pulmonary Emboli in the Emergency Department

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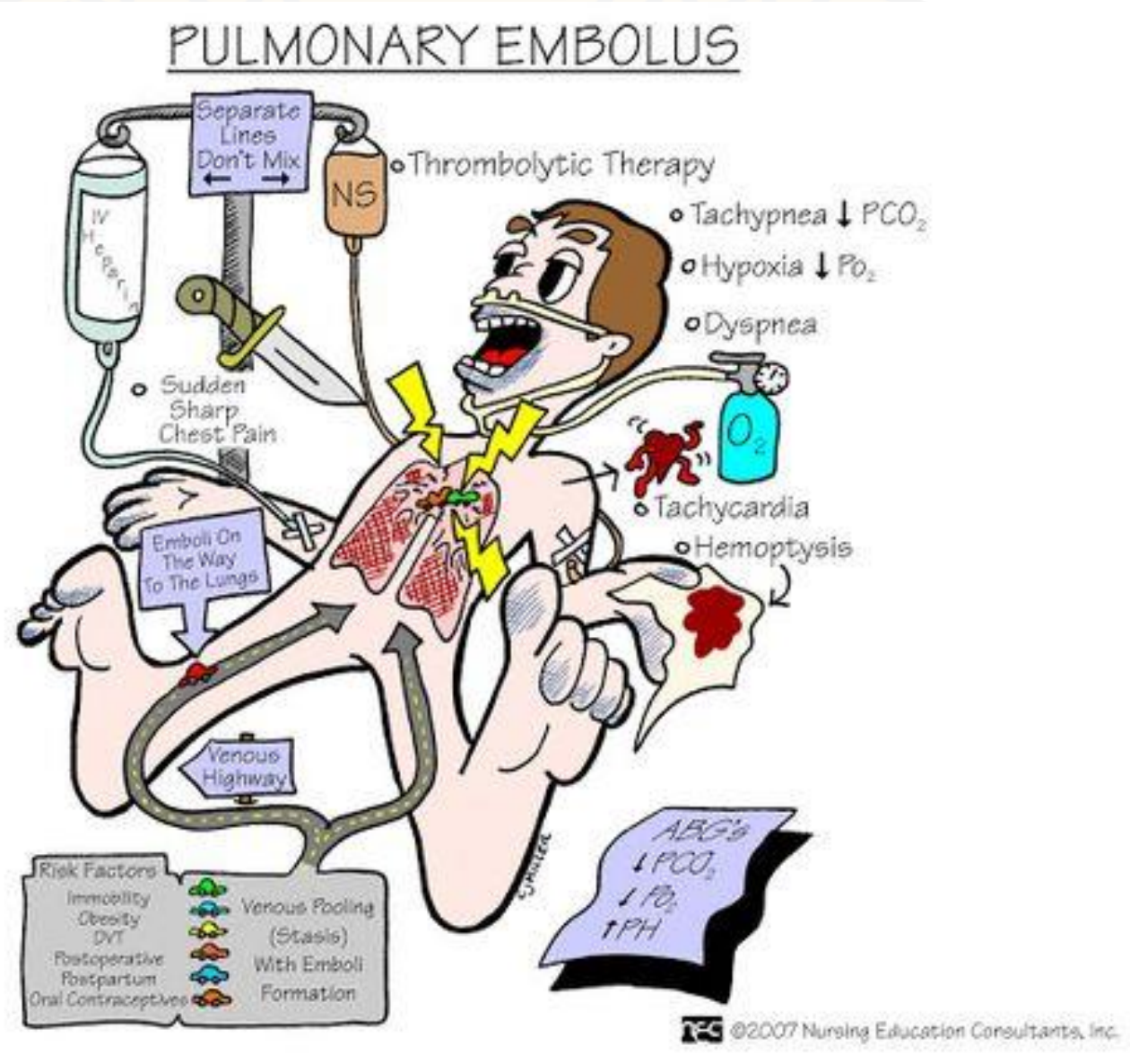
Disclosure

- I have no actual or potential conflict of interest in relation to this program/presentation.
- I have no relevant financial or nonfinancial relationships in the products or services described, reviewed, evaluated or compared in this presentation.
- I do not endorse specifically any test, treatment, or procedure mentioned on this presentation.

Objectives

- Review the pathophysiology of pulmonary emboli and its presentation
- Identify the presence of massive pulmonary emboli and when it can cause pulseless electrical activity
- Discuss the different treatment options available for simple and massive pulmonary emboli in the Emergency Department


PULMONARY EMBOLUS
Separate Lines Don't Mix
NS
IV Heparin
Thrombolytic Therapy
Tachypnea ↓ PCO_2
Hypoxia ↓ Po_2
Dyspnea
Sudden Sharp Chest Pain
O_2
Tachycardia
Hemoptysis
Emboli On The Way To The Lungs
Venous Highway
ABG's
↓ PCO_2
↓ Po_2
↑ PH
Risk Factors
Immobility
Obesity
DVT
Postoperative
Postpartum
Oral Contraceptives
Venous Pooling (Stasis) With Emboli Formation
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Acute Pulmonary Embolism

- Pathophysiology
  - Blockage of a pulmonary artery by
    - Emboli may be of air, thrombus, fat, or amniotic fluid.
    - Foreign bodies may also cause an embolus.
    - DVT's
  - The area served by the pulmonary artery fails.

Pulmonary Embolism

- Signs and Symptoms
  - Dependent upon size and location of the blockage.
  - Onset of severe, unexplained dyspnea, CP, tachycardia, tachypnea.
  - History of recent lengthy immobilization.

Pulmonary Embolism

- Risk Factors
  - Recent surgery, long-bone fractures (Knee > Hip> abdominal/GU); major trauma
  - Pregnant or postpartum
  - MI
  - Age > 50
  - Prior DVT
  - Oral contraceptive use, tobacco use.
  - Sedentary, long trips
  - History of PE, Hypercoagulopathy State (Protein S, C Deficiency, Anticardiolipin Ab, Antiphospholipids Ab, lupus anticoagulant)
  - Chronic Illness, Cancer (adenocarcinoma), nephrotic syndrome
  - Acute paralysis, immobilization

Risks

- Virchow triad
  - Venous stasis
  - Hypercoagulopathy
  - Endothelial damages

DVT

- Risks:
  - Same as PE
- Calf DVT embolized to the popliteal vein, and then to the lungs
- Test:
  - Duplex US

Wells score for prediction of PE

- A total score >6 indicates a high probability of a PE, a score of 2−6 moderate probability and a score <2 low probability.[1]

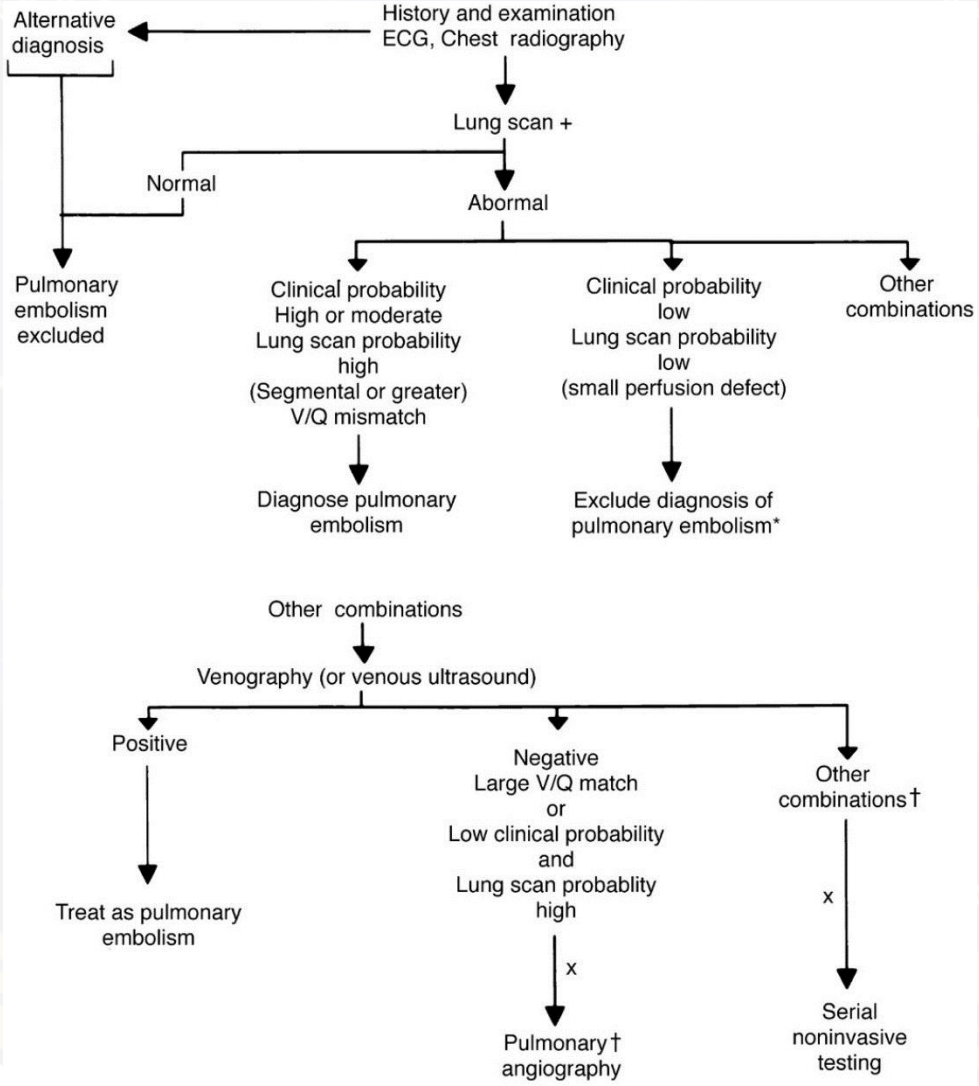
Parameter	Score
Clinically suspected DVT	3
Alternative diagnosis less likely than PE	3
Rapid heart rate	1.5
Immobilization within past 4 weeks	1.5
History of DVT	1.5
Haemoptysis	1
Malignancy	1

DVT, deep vein thrombosis; PE, pulmonary embolism.

PERC = Pulmonary Embolism Rule-out Criteria

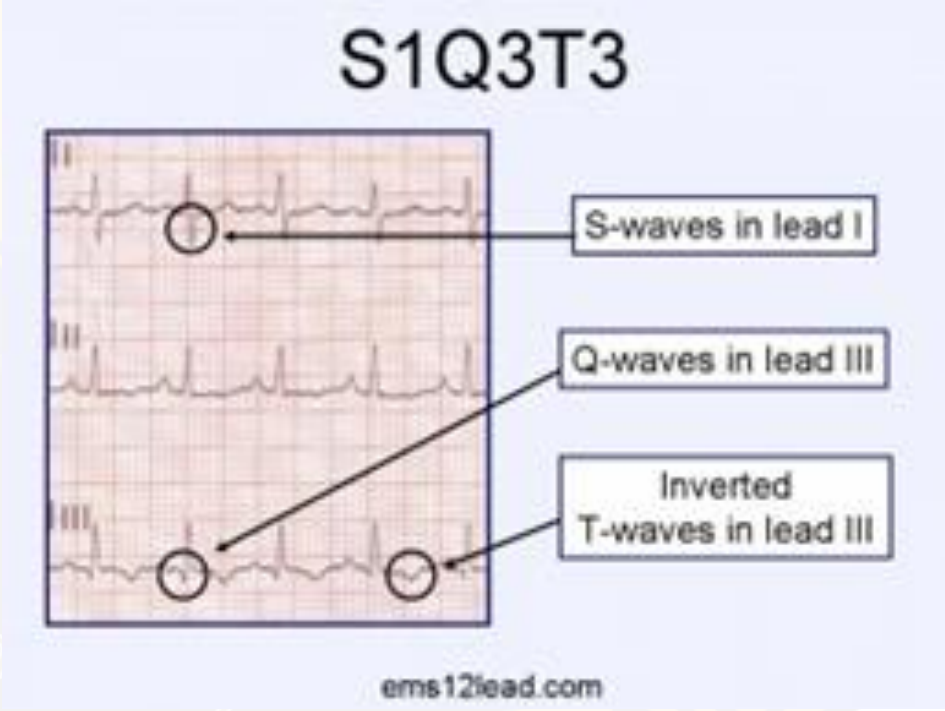
- Pulmonary embolism can be ruled out clinically if none of the 8 PERC criteria are present in a patient with a low pretest probability of PE (e.g. Wells PE CPG score of <3) that is consistent with the 'gestalt' of an experienced physician:
  - age < 50 years
  - pulse < 100 beats min
  - SaO2 >or= 95%
  - no hemoptysis
  - no estrogen use
  - no surgery/trauma requiring hospitalization within 4 weeks
  - no prior venous thromboembolism (VTE)
  - no unilateral leg swelling

Diagnostic approach when pulmonary embolism is suspected. *Can be followed with serial venous ultrasound. +Pulmonary angiography may be preferable in a patient whose condition is unstable. xBilateral venograms could be performed initially and proceed only if results are negative. †Other combinations include low clinical probability and intermediate or indeterminant lung scans and intermediate clinical probability and low-probability lung scans.

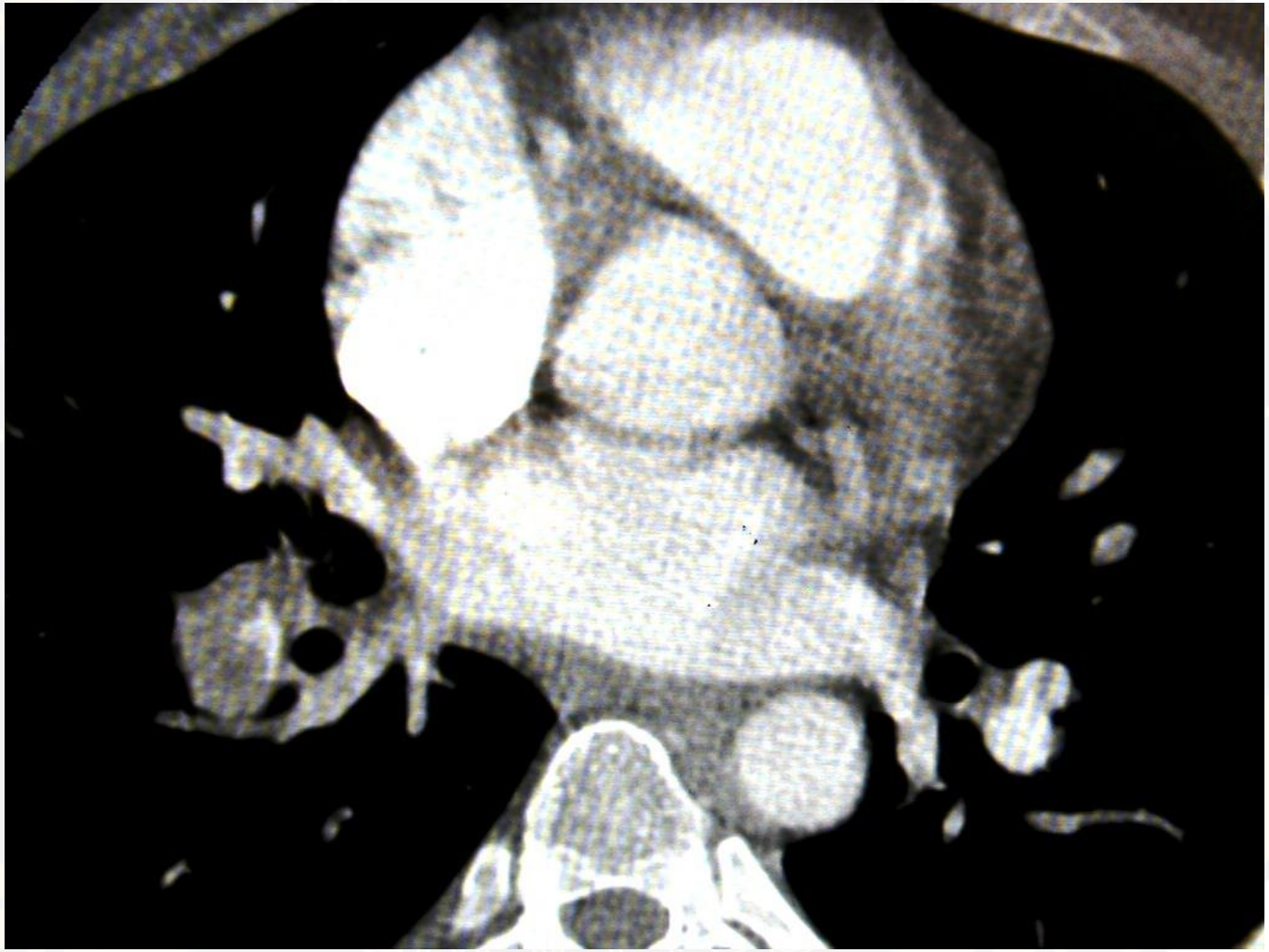


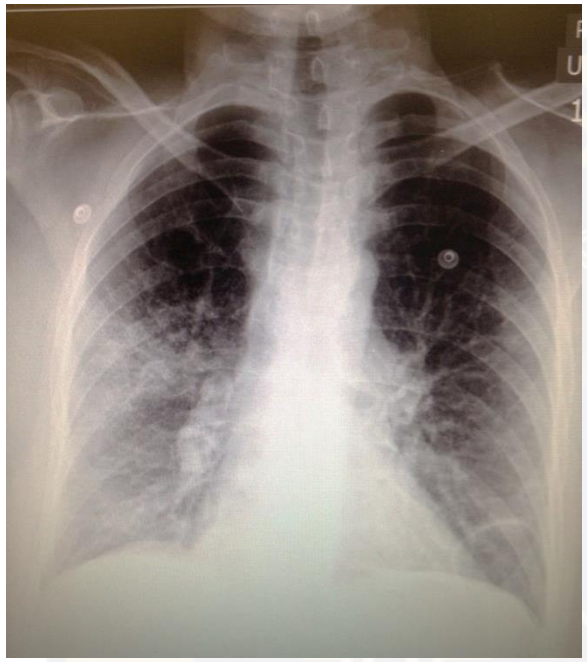
EKG

- Most common findings:
  - Sinus tachycardia and/or non-specific ST-T waves changes
- S1Q3T3
- LAD, RBBB, AFib

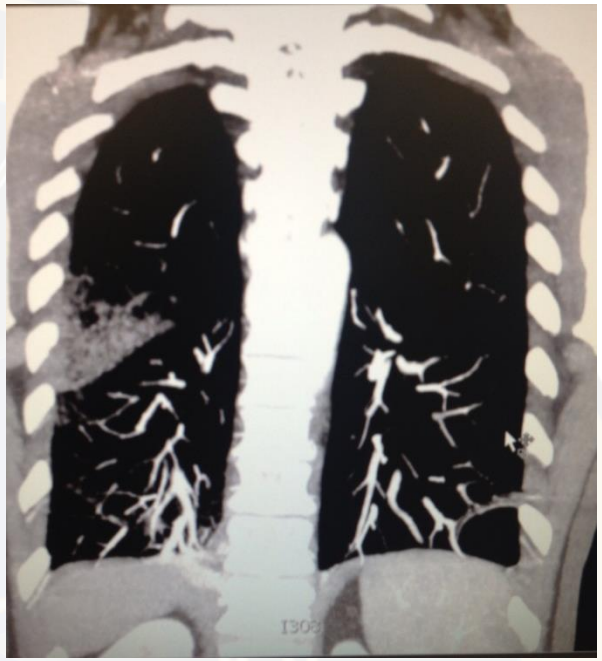


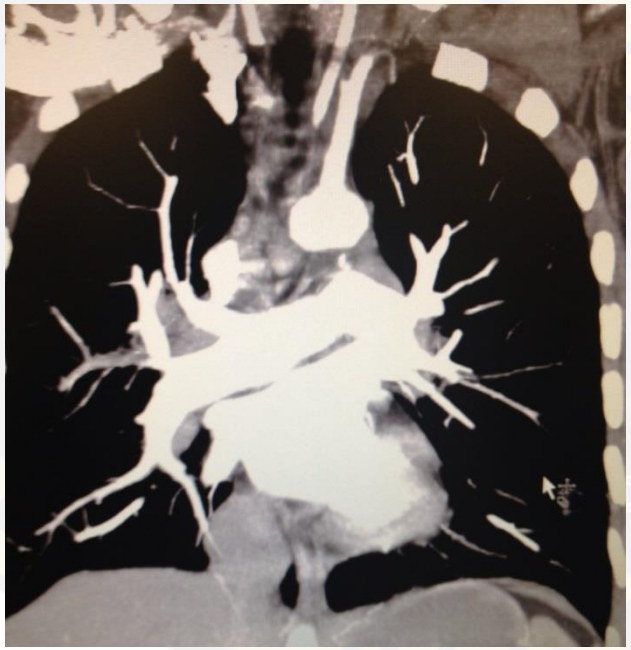
CTA SCAN

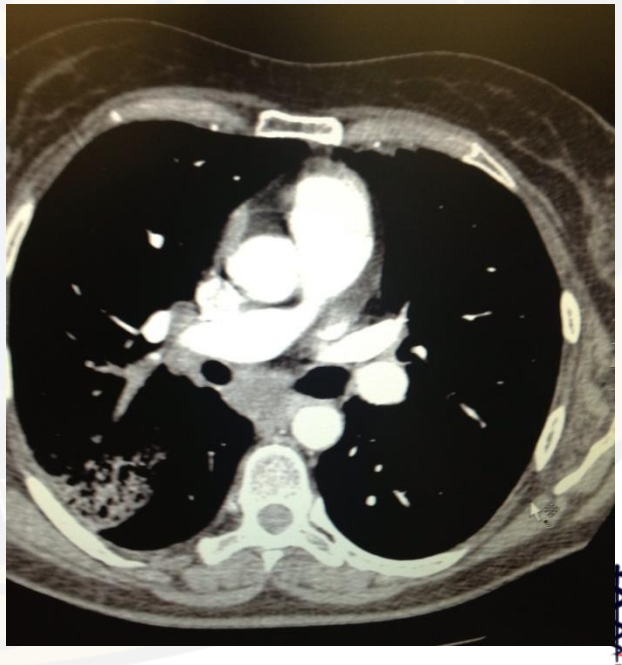


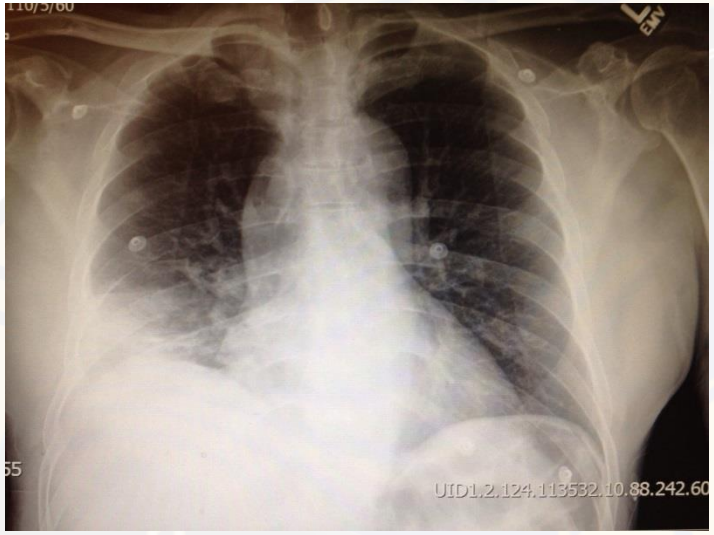


Hampton's hump





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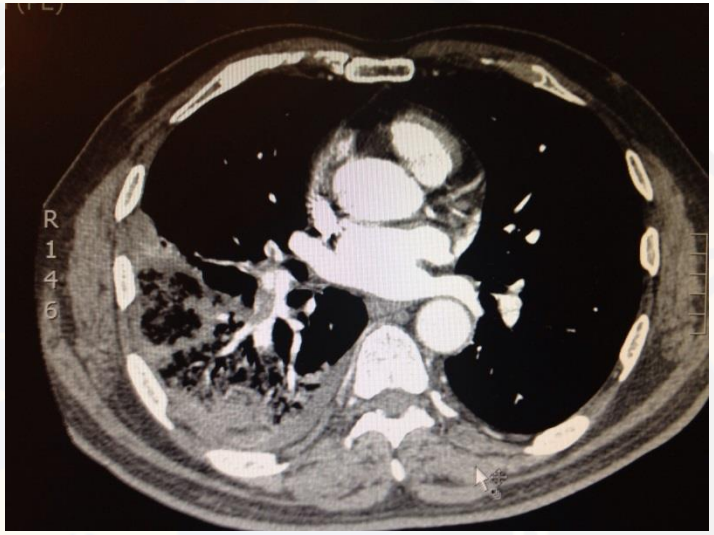
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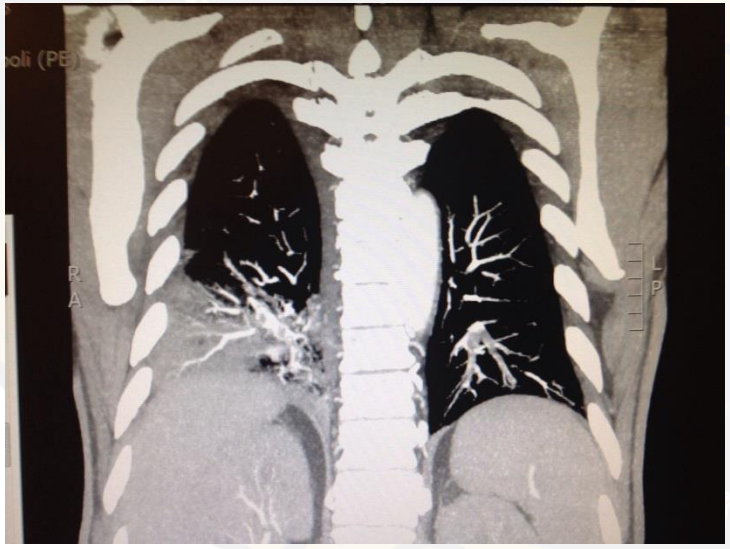
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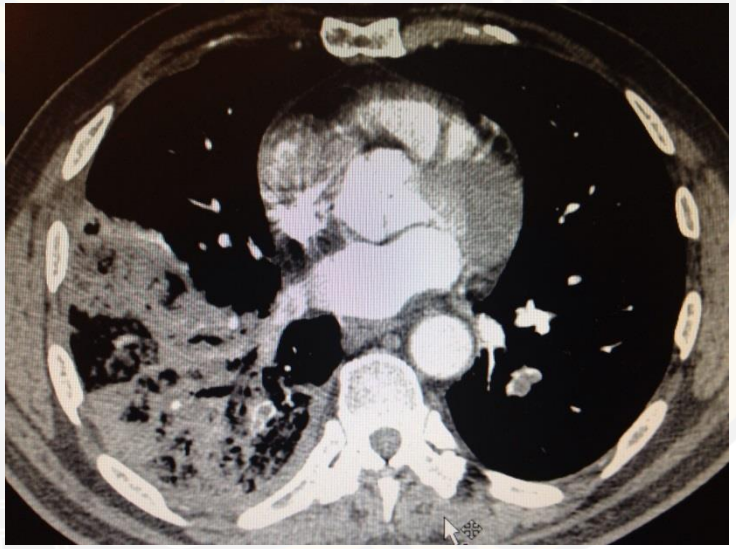
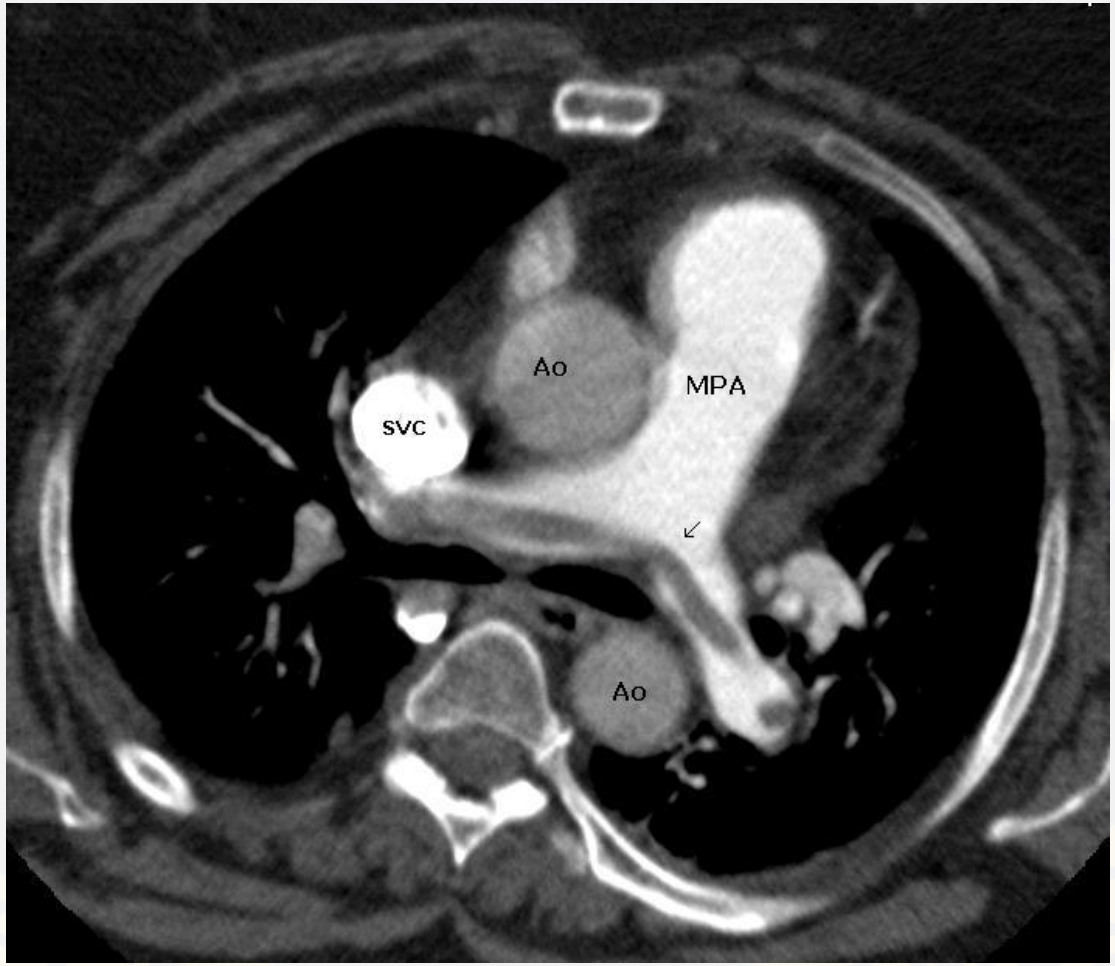


Saddle PE

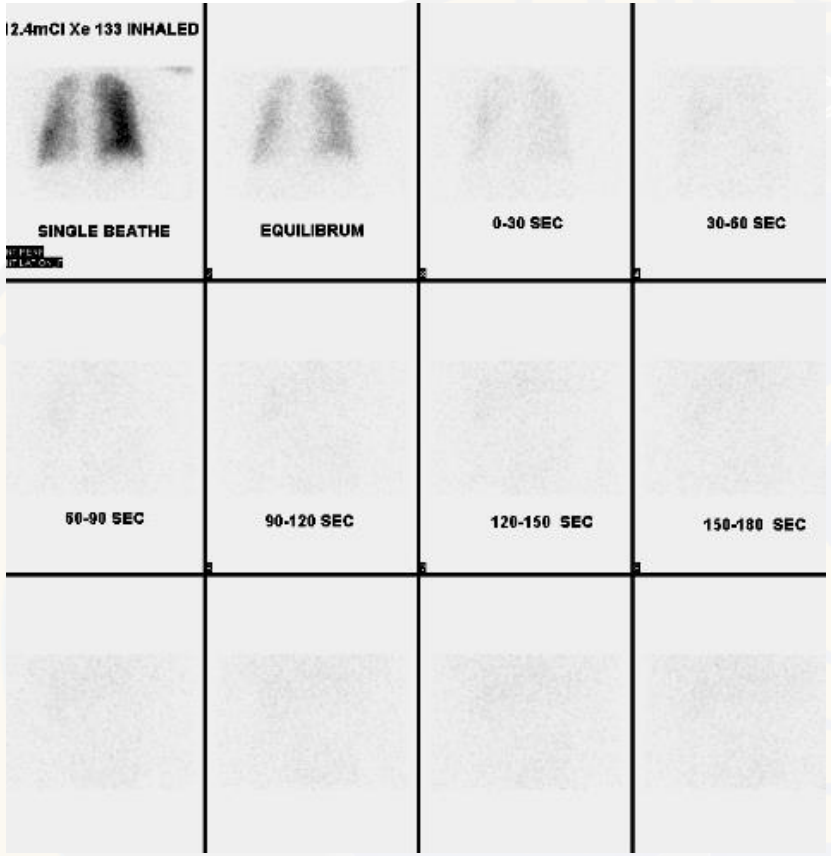


VQ Scan

- If low probability with low clinical risks
  - Bye, bye!
- If low probability with high clinical risks
  - Needs to do further tests
  - Doppler, CTA, angiogram…
  - Between 4-40% (~14%) it can still be PE

VQ Scan

- PIOPED Criteria for high probability
  - 2 large (>75% of a **segment**) V/Q mismatches
  - 1 large and 2 or more moderate mismatches
  - 4 or more moderate mismatches
- PIOPED Criteria for intermediate probability
  - 1 large V/Q mismatch with or without 1 moderate (25-75% of a **segment**) mismatch
  - 1-3 moderate mismatches
  - 1 matched defect with a normal CXR
- PIOPED Criteria for low probability
  - 1 or more perfusion defect that is smaller than the CXR defect
  - 2 or more matches with a normal CXR and some areas of normal perfusion in lung
  - 1 or more small perfusion defect (<25% of a **segment**) with a normal CXR
  - Perfusion defect cause by effusions, cardiomegaly, aortic dilatation, hila, mediastinum, and elevated hemidiaphragm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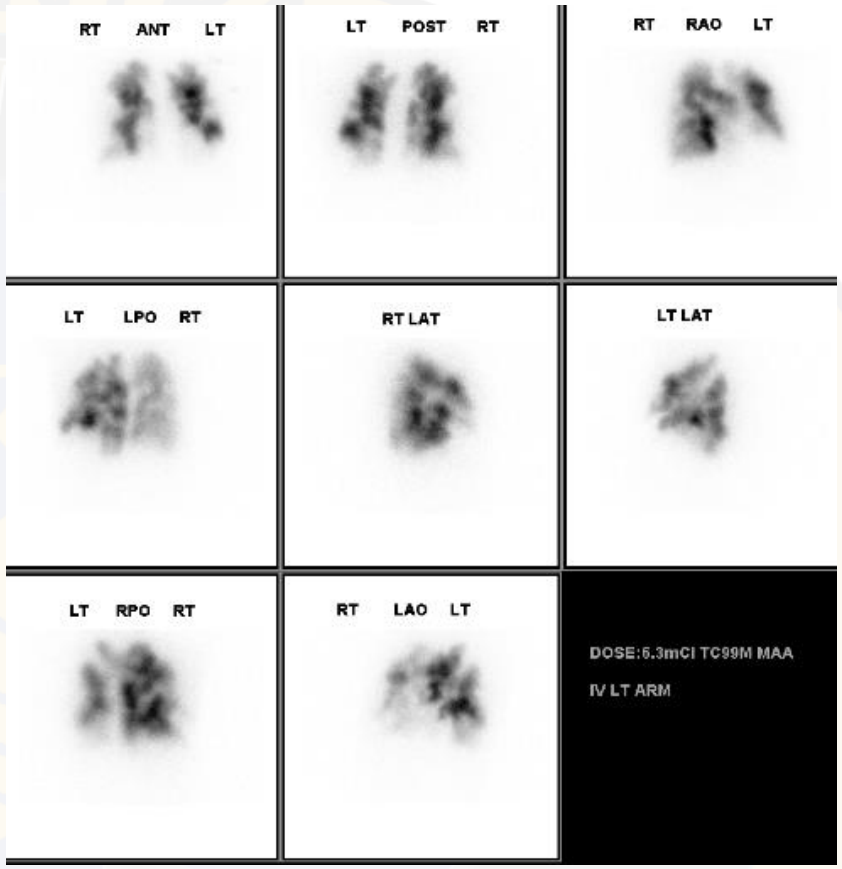
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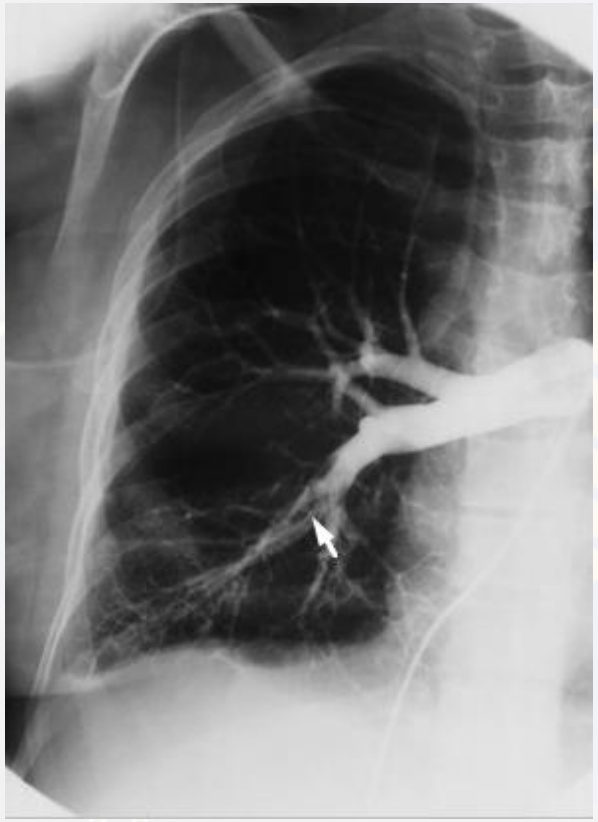
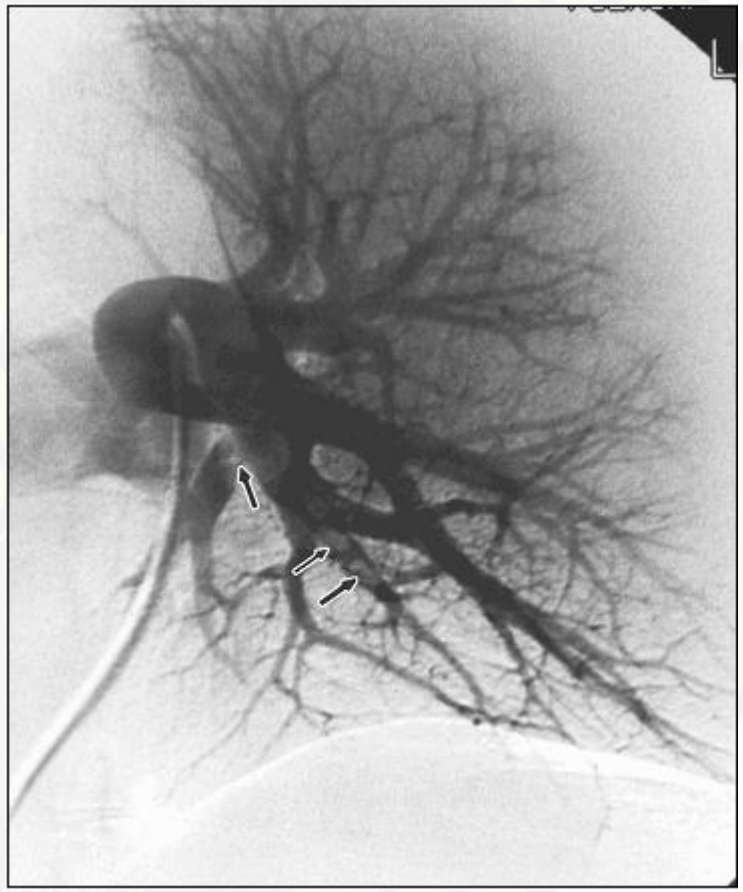
VQ SCAN

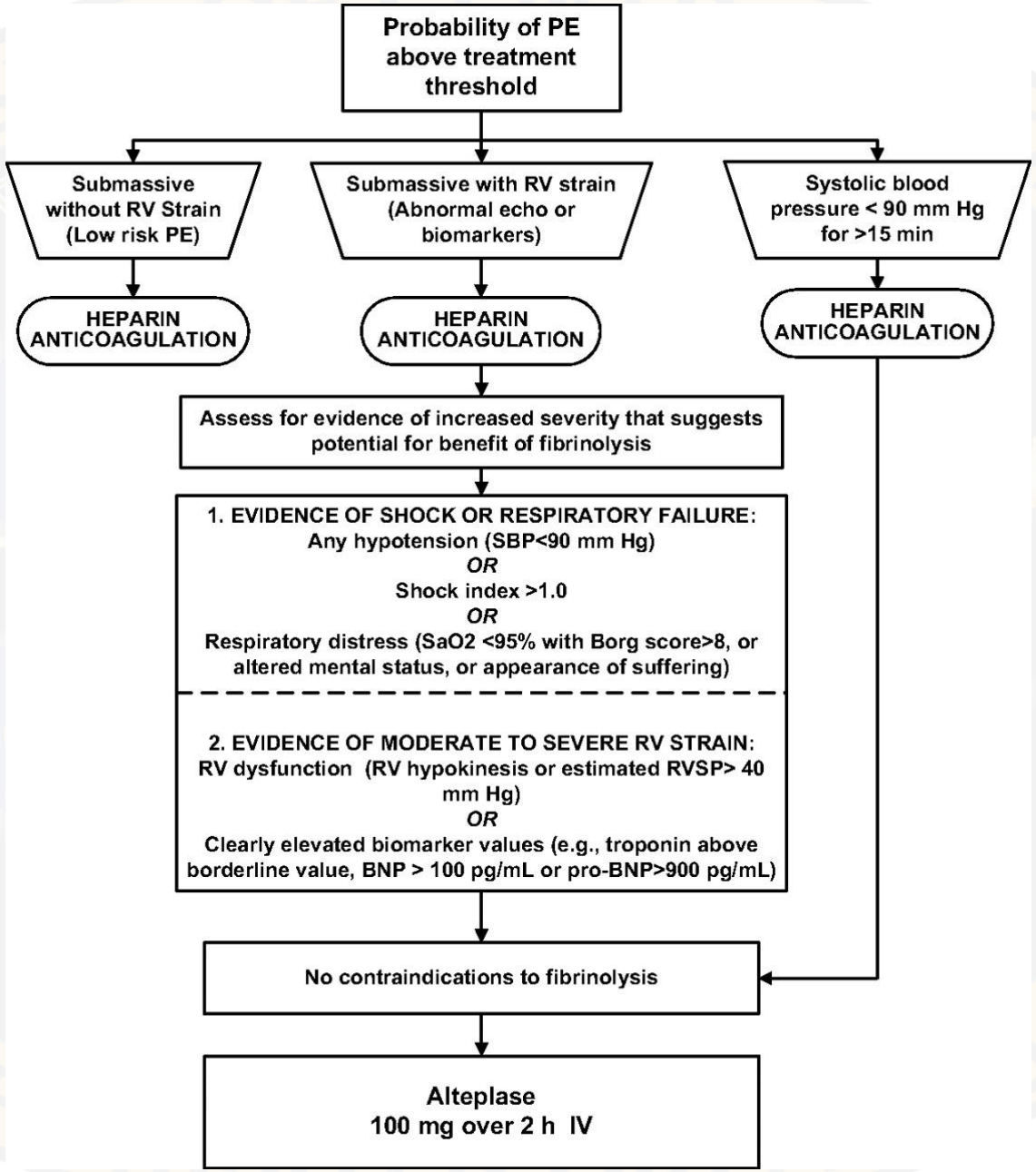
Pulmonary Angiogram



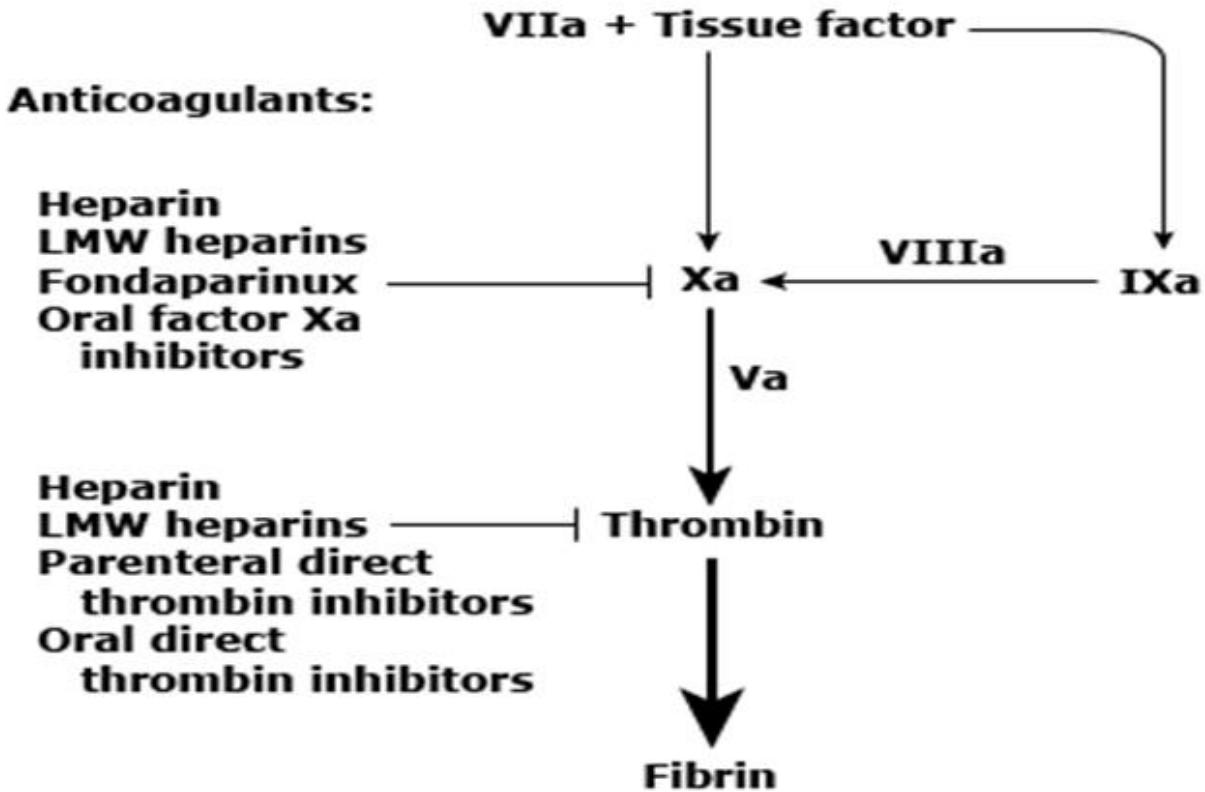


Pulmonary Embolism

- Management
  - Maintain the airway.
  - Support breathing.
    - High-flow oxygen or assist ventilations as indicated.
    - Intubation may be indicated.
  - Establish IV access
  - Monitor vital signs closely.
  - Anticoagulation
    - Heparin, Lovenox, warfarin, tPA
  - Pulmonary angiogram
  - Greenfield (IVC) filter


Probability of PE above treatment threshold
Submassive without RV Strain (Low risk PE)
Submassive with RV strain (Abnormal echo or biomarkers)
Systolic blood pressure < 90 mm Hg for >15 min
HEPARIN ANTICOAGULATION
HEPARIN ANTICOAGULATION
HEPARIN ANTICOAGULATION
Assess for evidence of increased severity that suggests potential for benefit of fibrinolysis
1. EVIDENCE OF SHOCK OR RESPIRATORY FAILURE:
Any hypotension (SBP<90 mm Hg)
OR
Shock index >1.0
OR
Respiratory distress (SaO2 <95% with Borg score>8, or altered mental status, or appearance of suffering)
2. EVIDENCE OF MODERATE TO SEVERE RV STRAIN:
RV dysfunction (RV hypokinesis or estimated RVSP> 40 mm Hg)
OR
Clearly elevated biomarker values (e.g., troponin above borderline value, BNP > 100 pg/mL or pro-BNP>900 pg/mL)
No contraindications to fibrinolysis
Alteplase
100 mg over 2 h IV

Coagulation cascade: Anticoagulant effects



Classes of anticoagulant agents

Class of agent	Specific drugs
LMWH	Enoxaparin (Lovenox), dalteparin (Fragmin), and tinzaparin (Innnohep)
Factor Xa inhibitor	Fondaparinux (Arixtra)
Oral direct factor Xa inhibitors	Apixaban (Eliquis), rivaroxaban (Xarelto), and edoxaban (Savaysa)
Parenteral direct thrombin inhibitors	Argatroban, lepirudin (Refludan), bivalirudin (Angiomax)
Oral direct thrombin inhibitors	Dabigatran (Pradaxa)

Schulman S, et al. N Engl J Med. 2009;361:2342–52
N Engl J Med. 2012;366:1287–97.
N Engl J Med. 2013;369:1406–15

Special populations

Population	Preferred agent	Comments
Pregnancy	LMWH	Cant have warfarin
Malignancy	LMWH	
Obesity	IV UFH	LMWH absorption may be poor with anasarca, massive edema, etc
Pts with need to have anticoagulation reversed	IV UFH	
Excessive clot burden	IV UFH	
Hemodynamic instability	IV UFH	
Renal failure with CrCl<30	IV UFH	

Heparin nomogram

aPTT (sec)	Dose
Initial dose	80 units/kg bolus + 18 units/kg/hr infusion
aPTT <35 sec	80 units/kg bolus + increase infusion rate by 4 units/kg/hr
aPTT 35-45 sec	40 units/kg bolus + increase infusion rate by 2 units/kg/hr
aPTT >45-60	Increase infusion rate by 2 units/kg/hr
aPTT >60-80	No change
aPTT >80-90	Decrease infusion rate by 2 units/kg/hr
aPTT >90	Hold infusion for 1 hour + decrease infusion rate by 3 units/kg/hr

Fondaparinux (Arixtra)

- Advantageous in people with HIT
- No antidote
- Monitoring: 0.5 to 1.5 mcg/mL fondaparinux level (anti factor Xa activity)

Once daily dosing:

- 5 mg (<50 kg)
- 7.5 mg (50 to 100 kg)
- 10 mg (>100 kg)
- 1.5 mg pts with CrCl 20 - 50 mL/min

Pharmacokinetics:

- 100 percent bioavailable after SQ injection,
- half-maximal and peak serum concentrations reached in 25 minutes and 1.7 hrs
- half-life 15 -17 hrs.
- Anticoagulant activity persists for about 3-5 half-lives following discontinuation of fondaparinux, or a period of 2-4 days in individuals with normal renal function.
- Not used in pregnancy or in pediatrics

Transitioning between anticoagulants

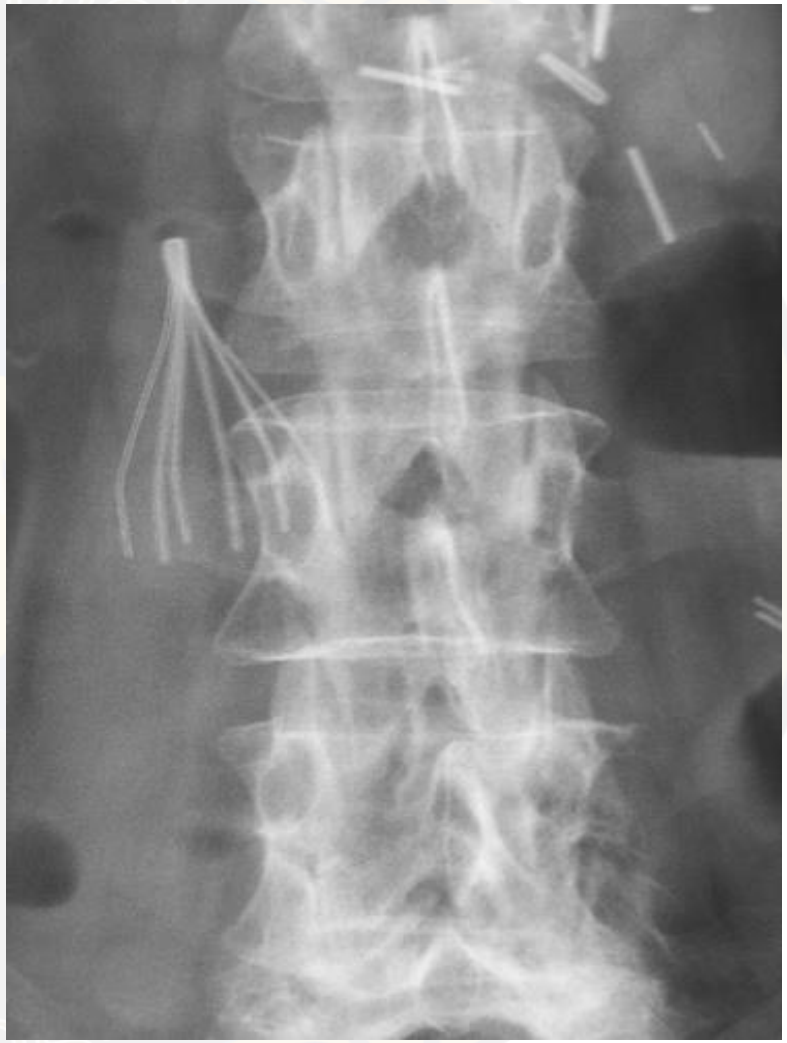
- From other anticoagulants to fondaparinux –
  - onset of action of fondaparinux is rapid, so it is generally started at the time another anticoagulant is discontinued. For patients on warfarin, it is generally started when the international normalized ratio (INR) drops below 2.

Transitioning between anticoagulants

- From fondaparinux to other agents –
  - to warfarin in the setting of acute VTE, we typically start warfarin and fondaparinux at the same time, and continue fondaparinux for at least five days and until the INR is in the therapeutic range.
  - to a direct acting oral anticoagulant (DOAC; eg, dabigatran, apixaban, edoxaban, rivaroxaban), we typically start the DOAC 24 hours after the last dose of fondaparinux.

IVC Filter

- Vena cava filters are of little help when anticoagulant treatment is not contraindicated, even in patients with PE and features of clinical severity



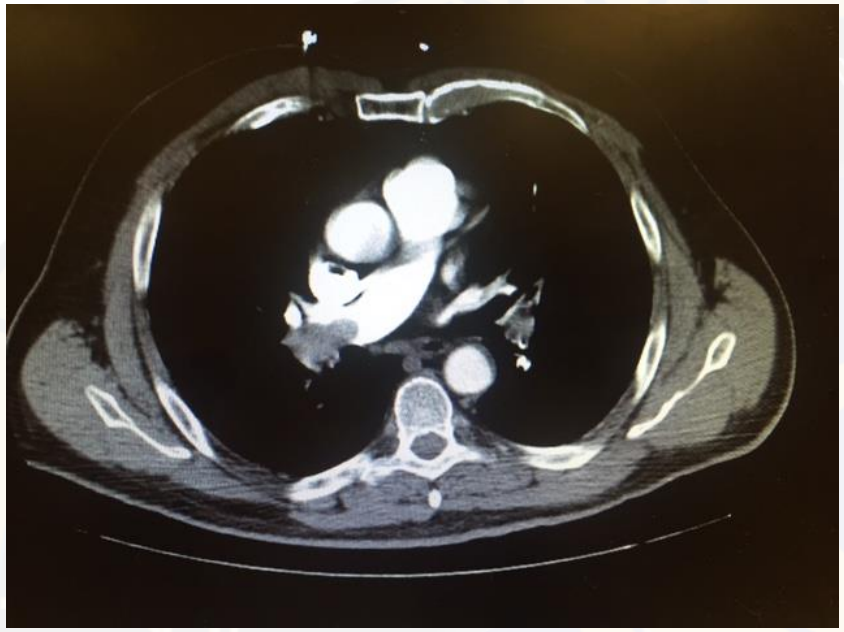
Mismetti P, et al. JAMA. 2015;313:1627–35.

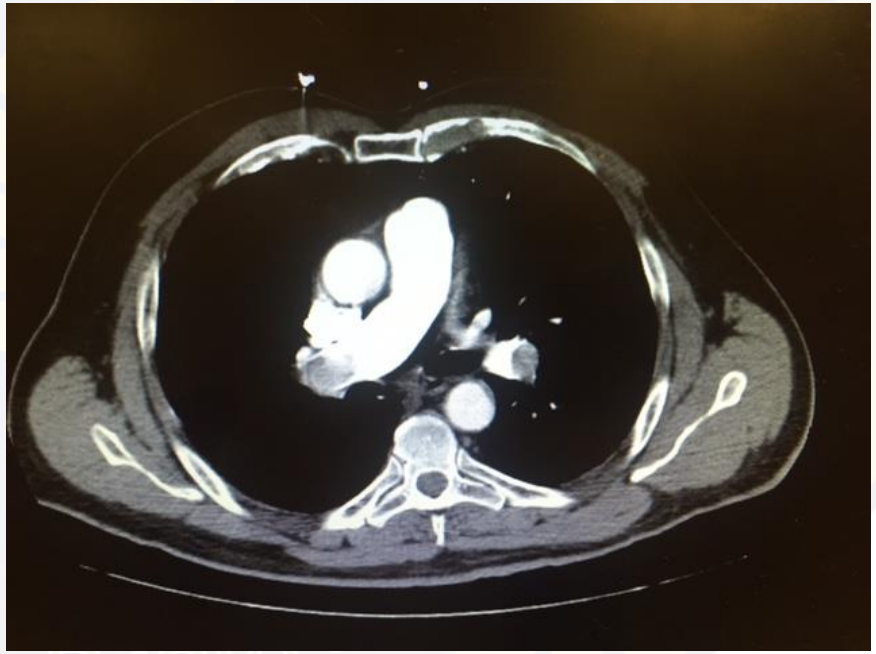
Massive PE or Unstable PE

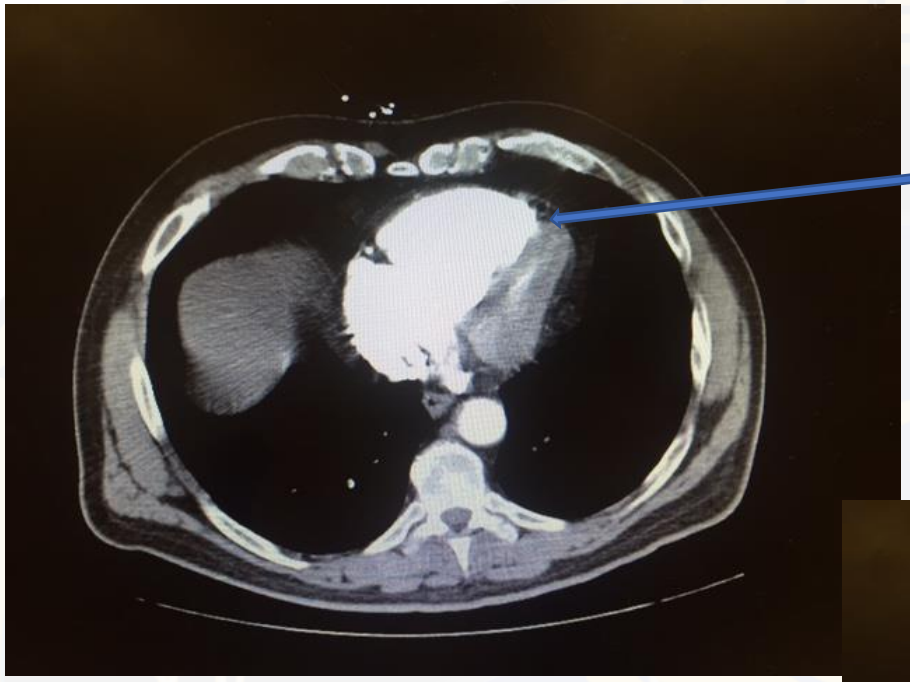
- Definitive:
  - Hemodynamic unstable
  - Causes increased PVR → RV outflow obstruction → decreased LV preload → decreased CO

Massive PE or Unstable PE

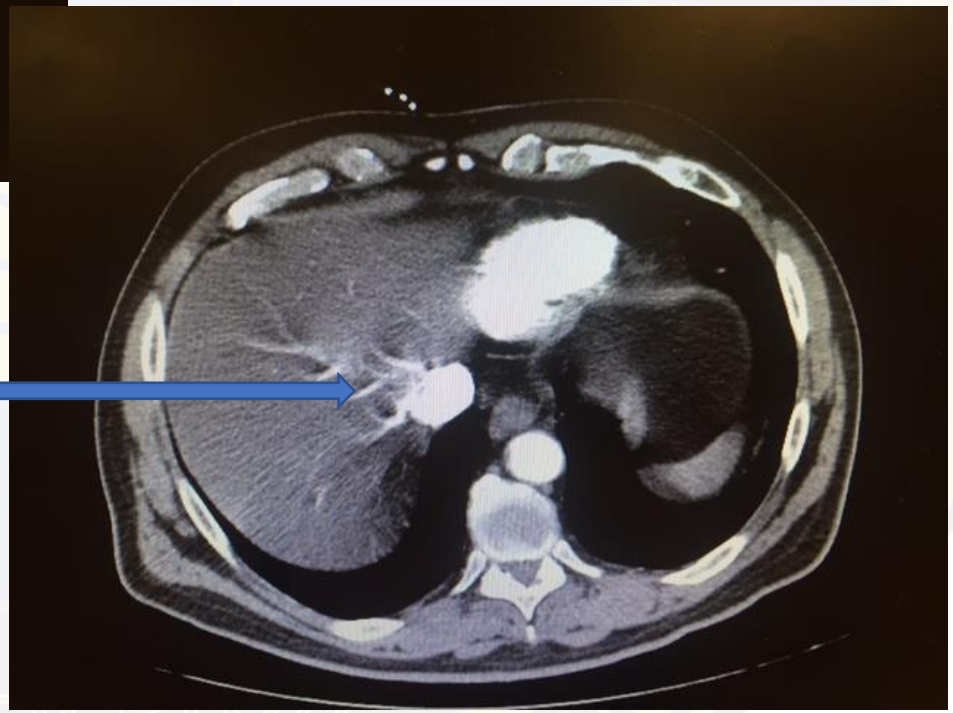
- Presentation:
  - 40% or more of pulmonary vessels involved
  - Complete obstruction of blood flow to one or more lobes
  - Severe hypoxia
  - Right side heart failure
    - JVD, **Hypotension**, high PCWP
    - Right heart stranding
  - RV thrombosis



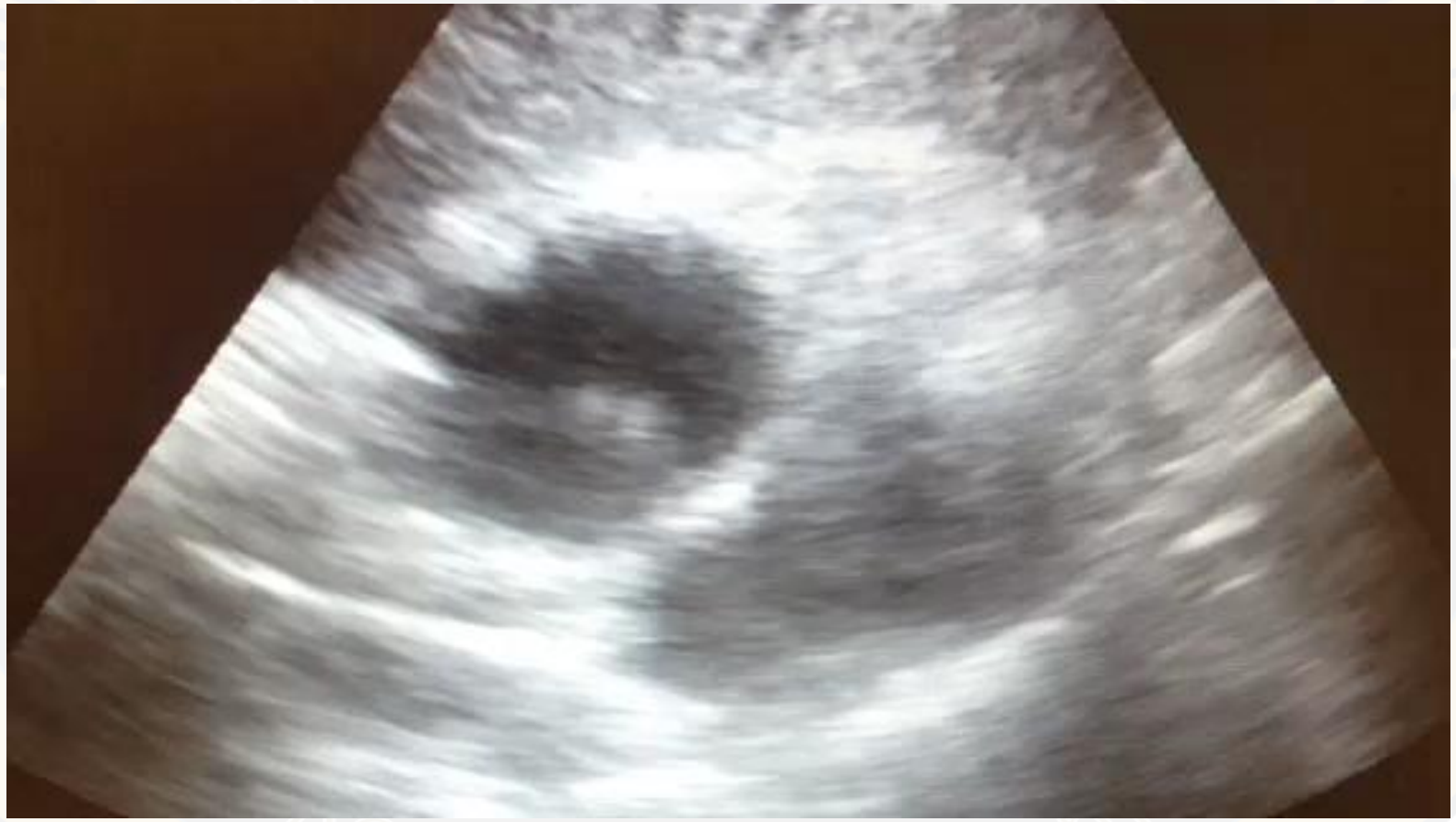


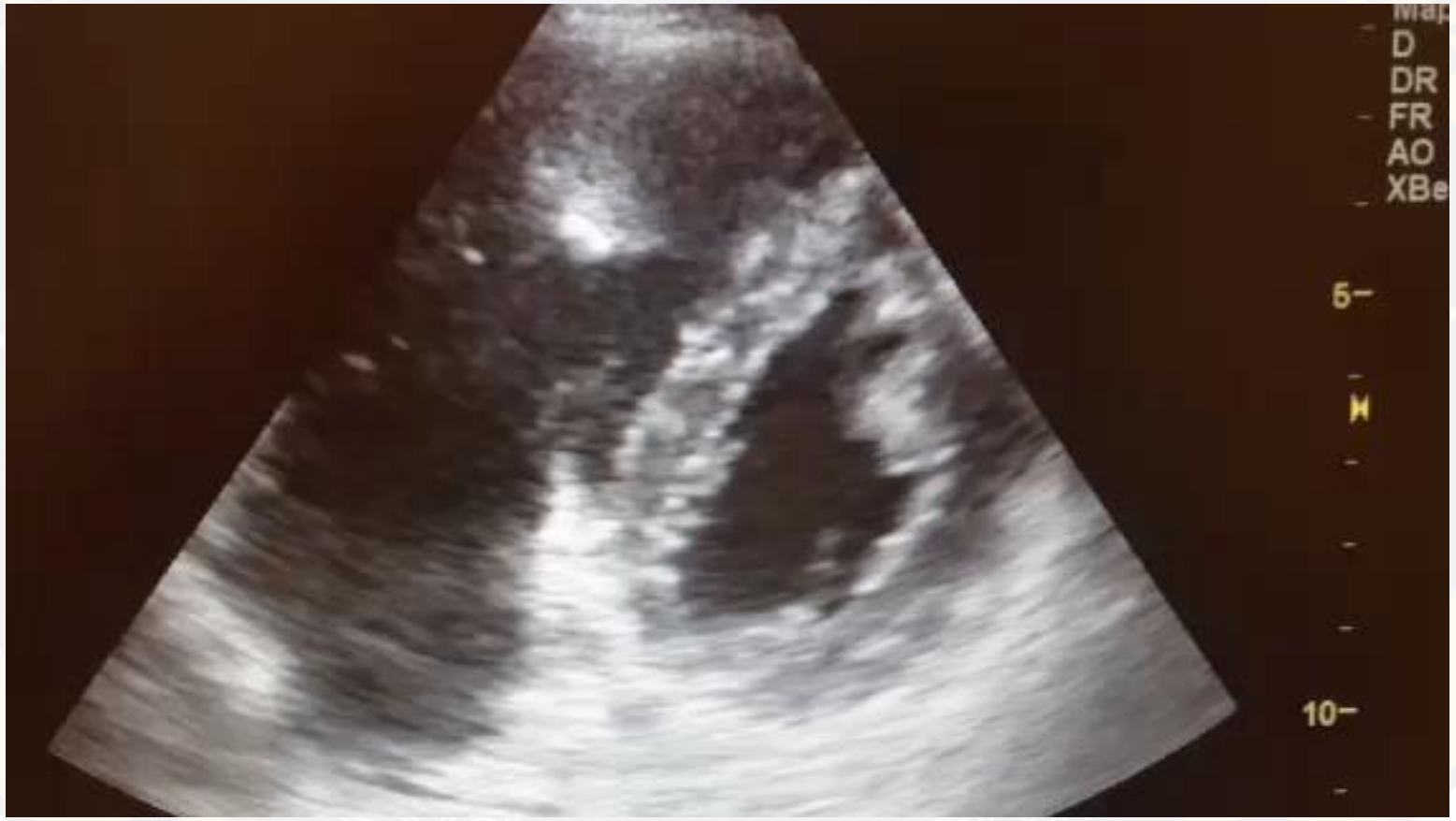


RV Dilatation and larger that the LV



IVC and Portal vein congestion

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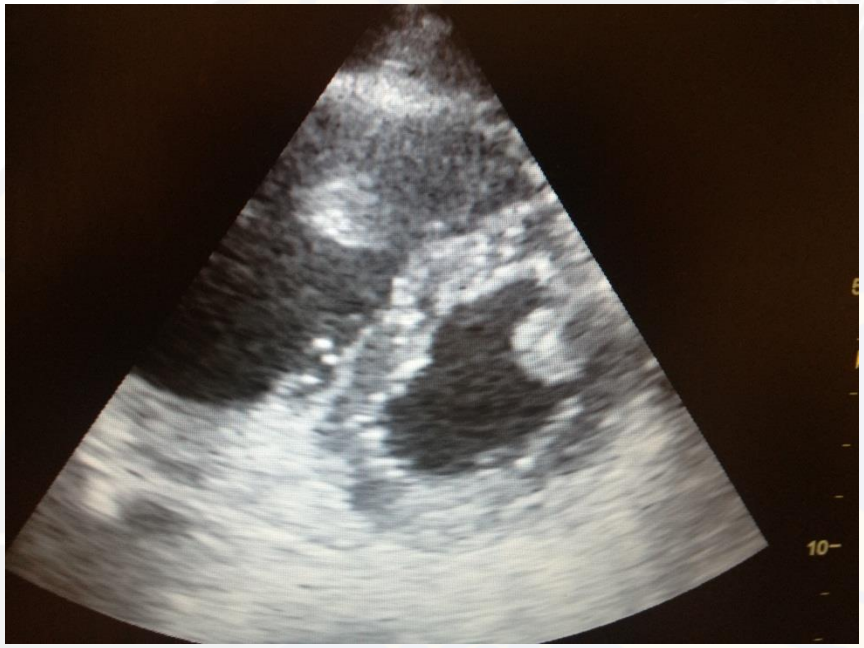
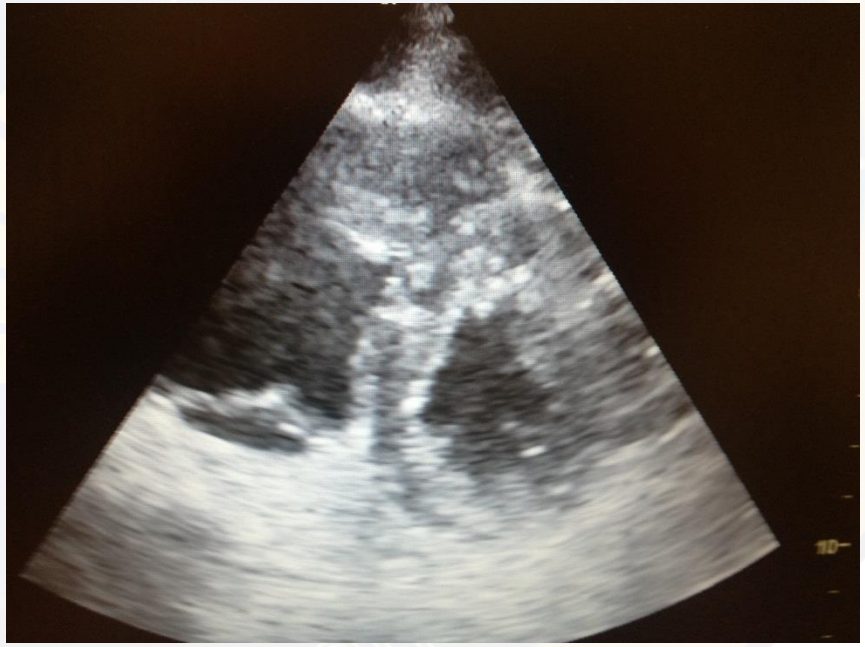




Thrombolytics

- The role of thrombolytic therapy has been accurately defined for low-risk and high-risk patients with PE.
- In normotensive patients without signs of right ventricular dysfunction or damage, the risk of mortality and of PE-related complication is low and the use of thrombolytic treatment is not indicated, in part because of its associated bleeding risk

Konstantinides SV, et al. Eur Heart J. 2014;35:3033–69
N Engl J Med. 2002;347:1143–50
N Engl J Med. 2014;370:1402–11.
Am J Cardiol. 2013;111:273–7

Thrombolytics

- Patients with high-risk PE have a high mortality risk when receiving anticoagulant treatment alone.
  - In this setting, the hemodynamic effects of thrombolytic treatment far outweigh its bleeding risk and the only contraindication to thrombolytic therapy in these patients is active uncontrollable bleeding.
  - In these patients, thrombolysis is associated with a reduction in mortality or recurrent PE

Konstantinides SV, et al. Eur Heart J. 2014;35:3033–69
N Engl J Med. 2002;347:1143–50
N Engl J Med. 2014;370:1402–11.
Am J Cardiol. 2013;111:273–7

Thrombolytics

- Thrombolytic therapy is associated with a reduction in the combined endpoint of mortality and hemodynamic decompensation in patients with intermediate-risk PE, but
  - This is obtained without a decrease in overall mortality and with a significant increase in major extracranial and intracranial bleeding.
- In patients with high-intermediate-risk PE, thrombolytic therapy should be given in case of hemodynamic worsening.

Thrombolytics

- Direct oral anticoagulants have been shown to be as effective as and safer than the combination of (low molecular weight) heparin and VKA in patients with VTE and low- to intermediate-risk PE.

Altepase

- 100 mg over 2 hours
- During cardiac arrest and with PEA
  - 50 mg IVP
  - CPR x 10 minutes
  - Repeat 50 mg IVP

EKOS

- The use of thrombolytic agents has become routine medical practice in the treatment of embolic and thrombotic vascular occlusions.
- Thrombolytic therapy has been established as an important therapeutic tool in the treatment of native peripheral artery occlusive disease and thrombosed arterial bypass grafts.
- The therapeutic success in the treatment of stroke and myocardial infarction relies greatly on the speed the thrombolytic agent can reestablish flow within the affected cerebral or coronary circulation.

Ultrasound-Enhanced Thrombolysis: EKOS EndoWave Infusion Catheter System
Charles A. Owens; Semin Intervent Radiol. 2008 Mar; 25(1): 37–41.

EKOS

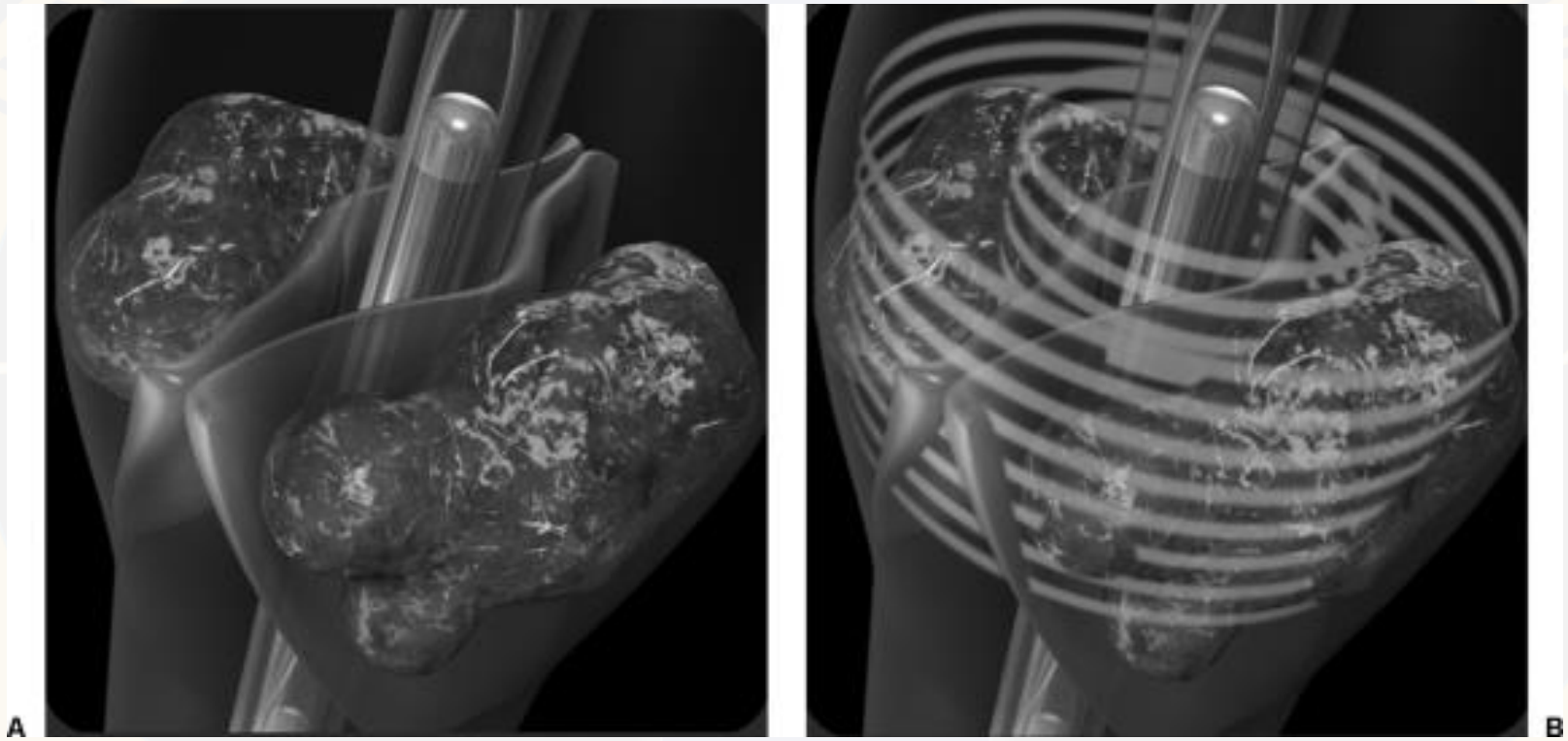
- In the area of venous thromboembolic disease, catheter-directed thrombolysis with or without assisted mechanical thrombolysis is becoming the standard of medical care in the treatment of acute and subacute deep vein thrombosis (DVT).
- Anticoagulation therapy is ineffective at removing thrombus of the deep venous system, and when extensive, DVT carries a high risk of developing post-thrombotic syndrome (PTS) and venous status ulcers.
- To avoid the development of PTS, aggressive therapy to remove the venous thrombus/venous obstruction must be undertaken before irreversible valvular damage occurs.

Ultrasound-Enhanced Thrombolysis: EKOS EndoWave Infusion Catheter System
Charles A. Owens; Semin Intervent Radiol. 2008 Mar; 25(1): 37–41.

EKOS

- The EKOS EndoWave Infusion Catheter System (EKOS Corporation, Bothell, WA) enhances catheter-directed thrombolysis by accelerating the fibrinolytic process via the application of ultrasound.
- Improving the efficiency of the thrombolytic process reduces the treatment time and total lytic dose delivered.
- The overall cost of therapy and the risk of an associated bleeding complication thus are reduced.

Ultrasound-Enhanced Thrombolysis: EKOS EndoWave Infusion Catheter System
Charles A. Owens; Semin Intervent Radiol. 2008 Mar; 25(1): 37–41.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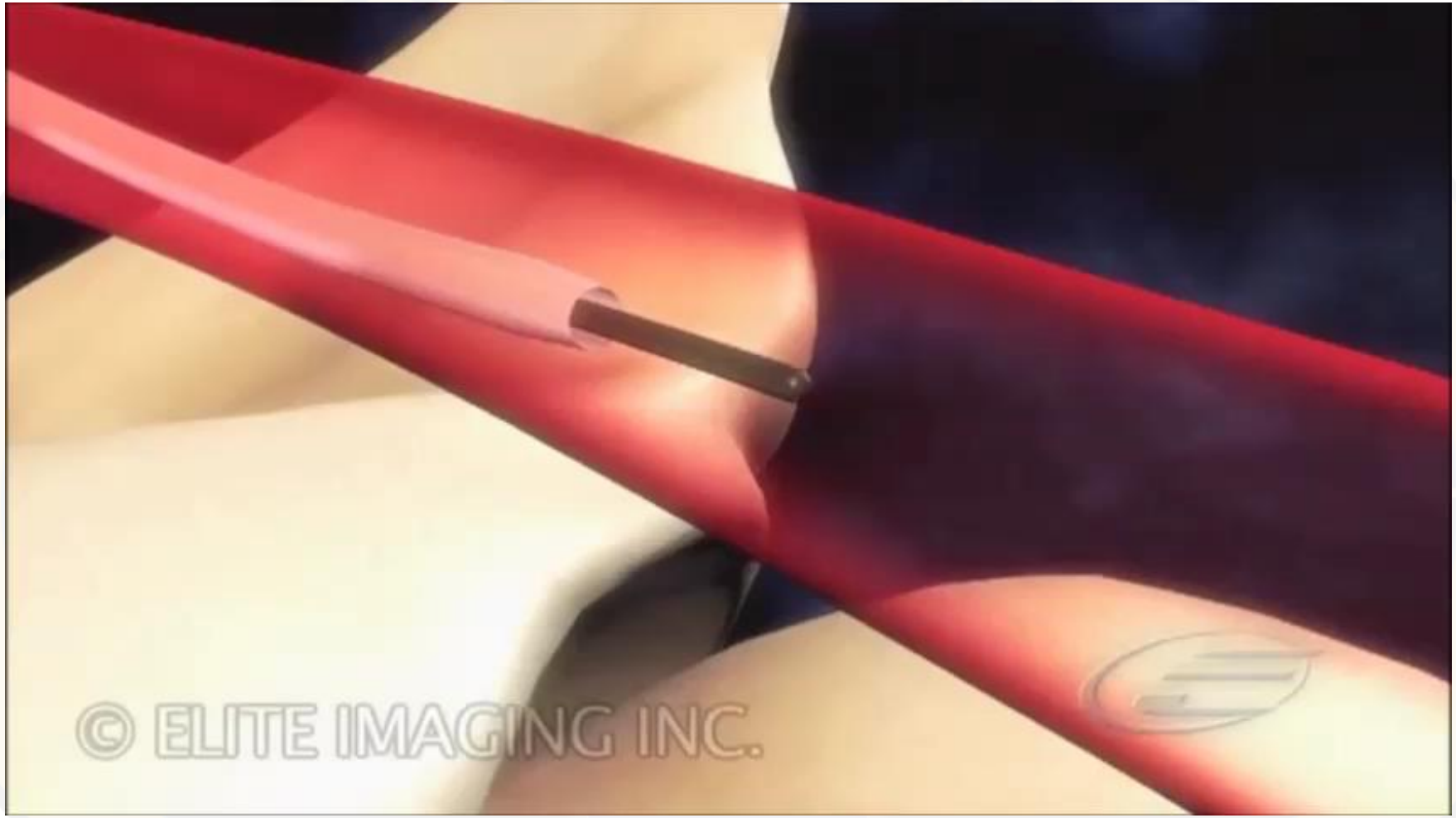
B

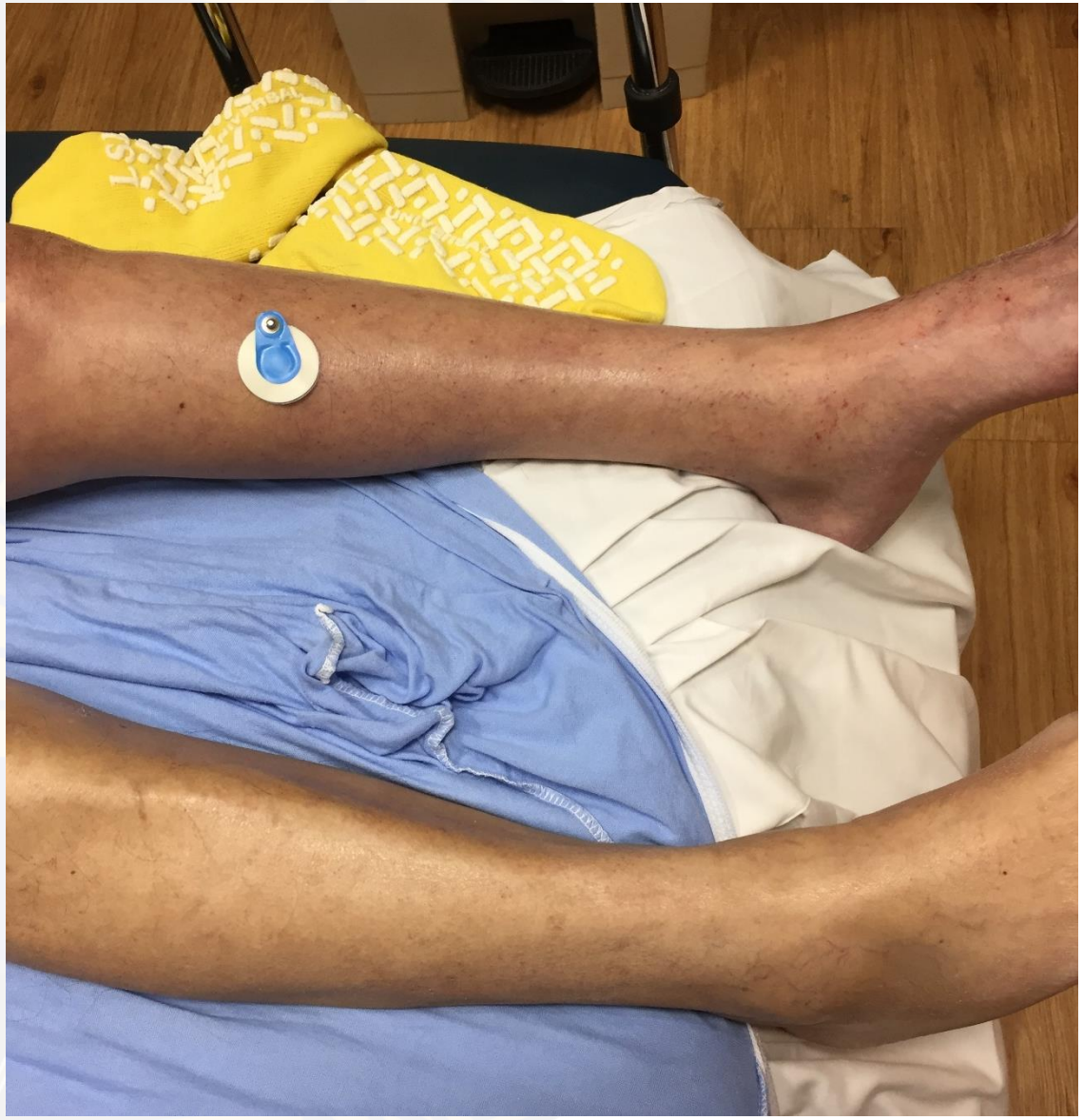


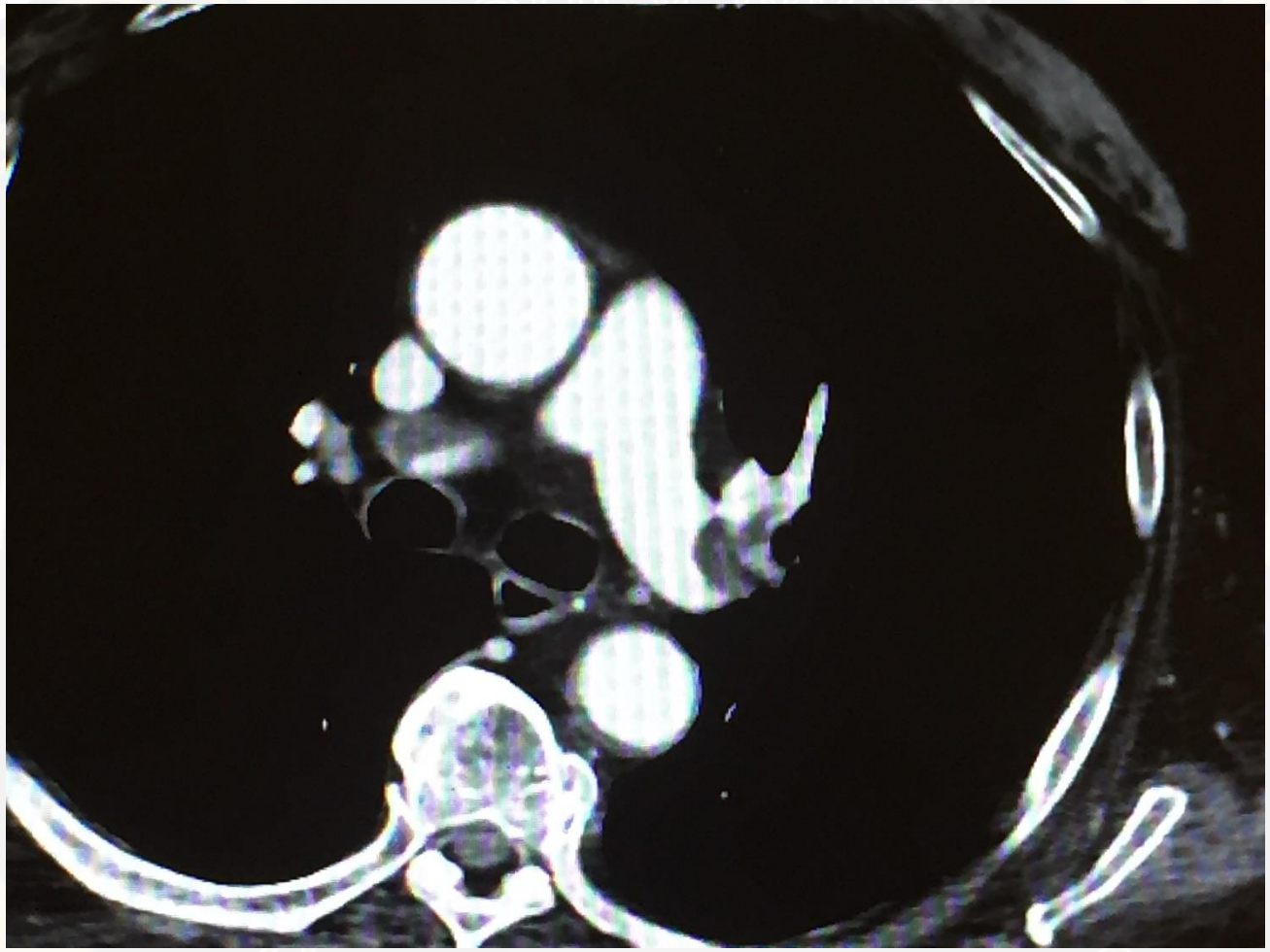
Possible complications with EKOS

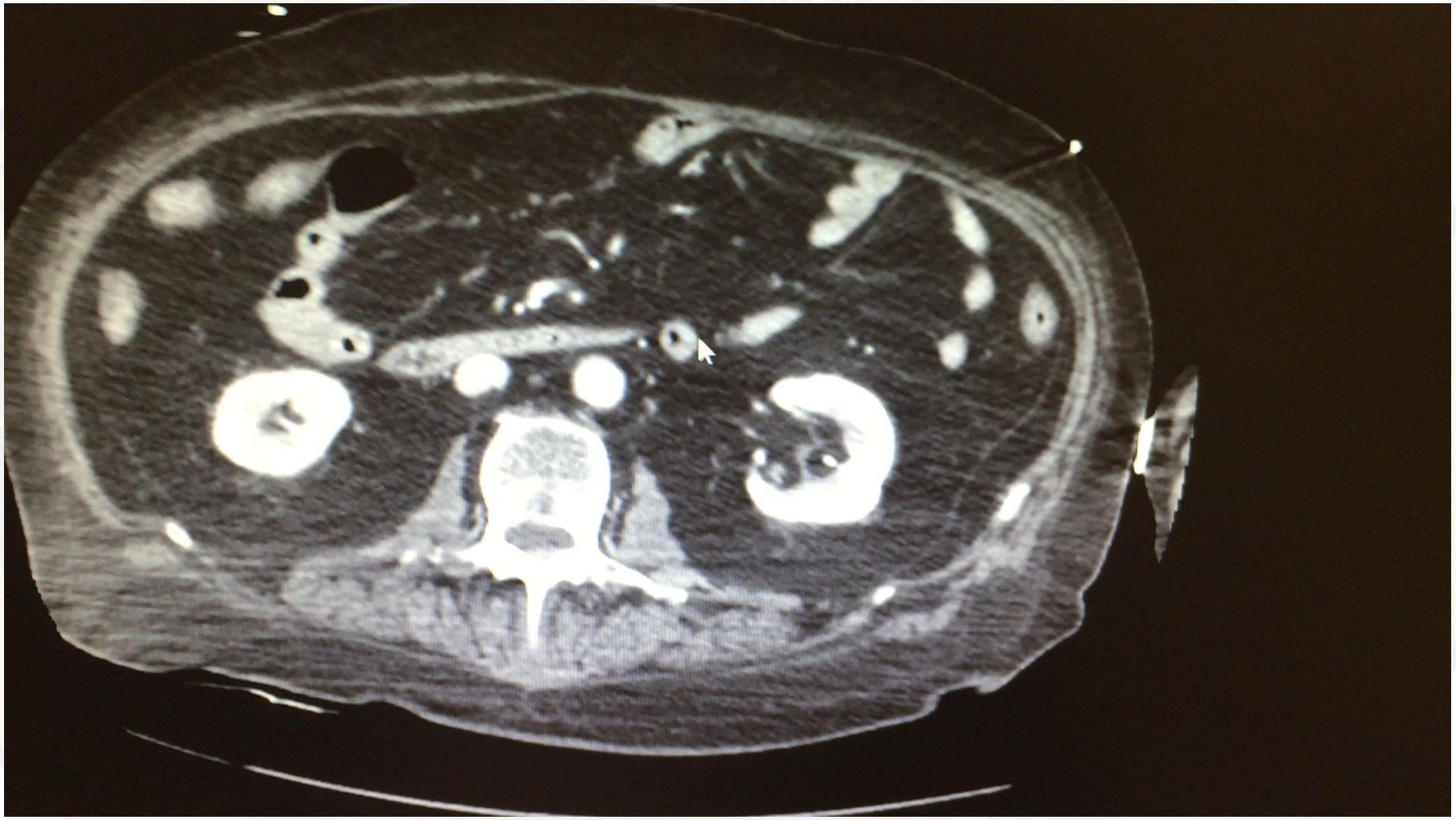
- Death from worsening RV failure
- Distal embolization
- Pulmonary artery perforation with lung hemorrhage
- Systemic bleeding complications
- Pericardial tamponade
- Heart block or bradycardia
- Hemolysis
- Contrast-induced nephropathy
- Puncture-related complications

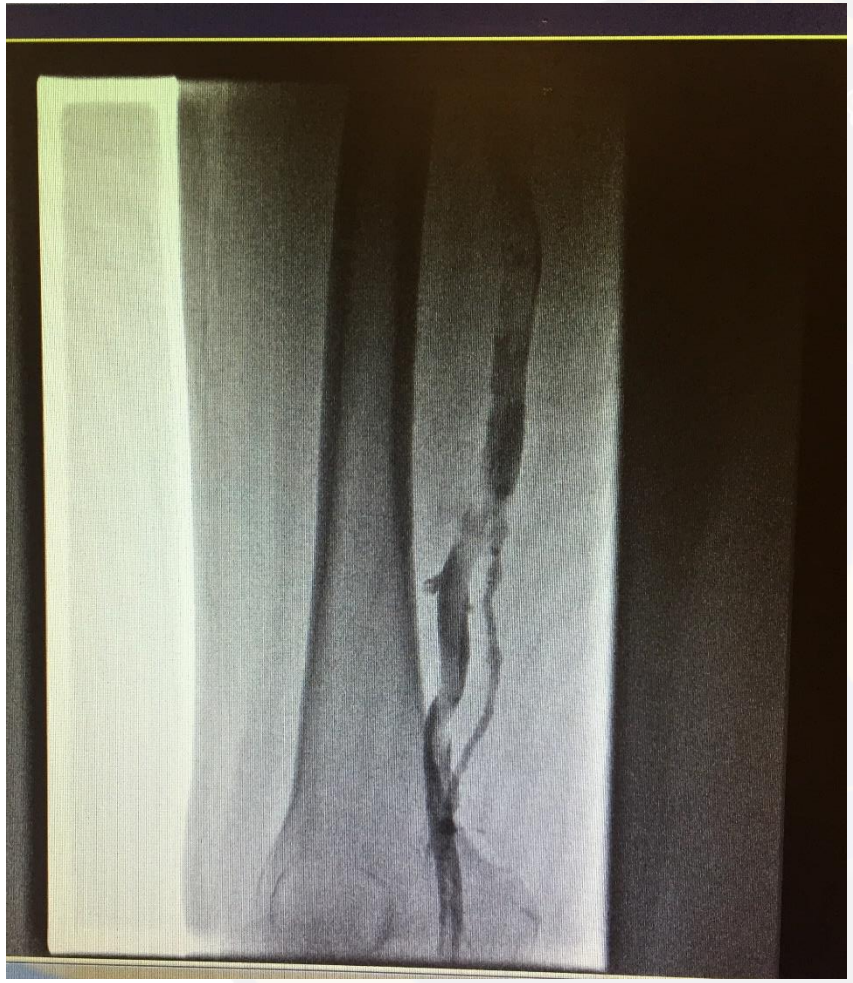
J Vasc Interv Radiol. 2009;20:1431–40.

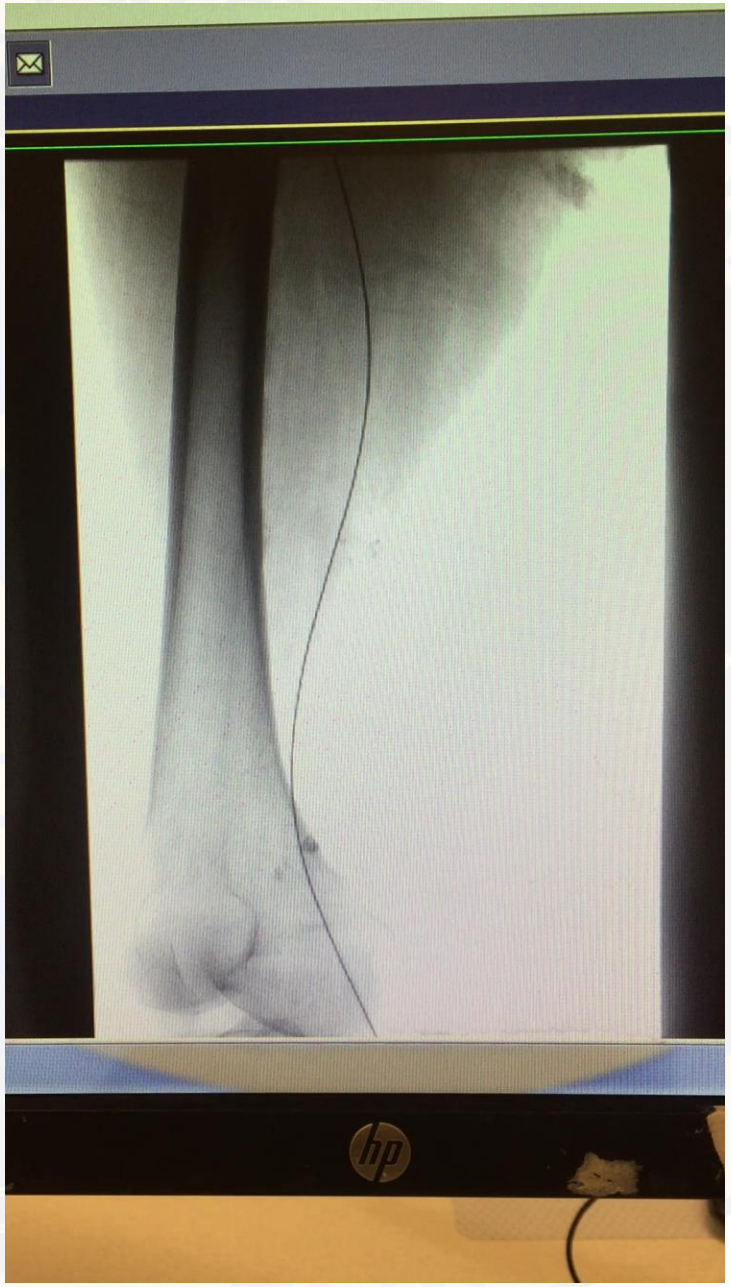

FC
173
100
36
(10)
40
44
11
33.6

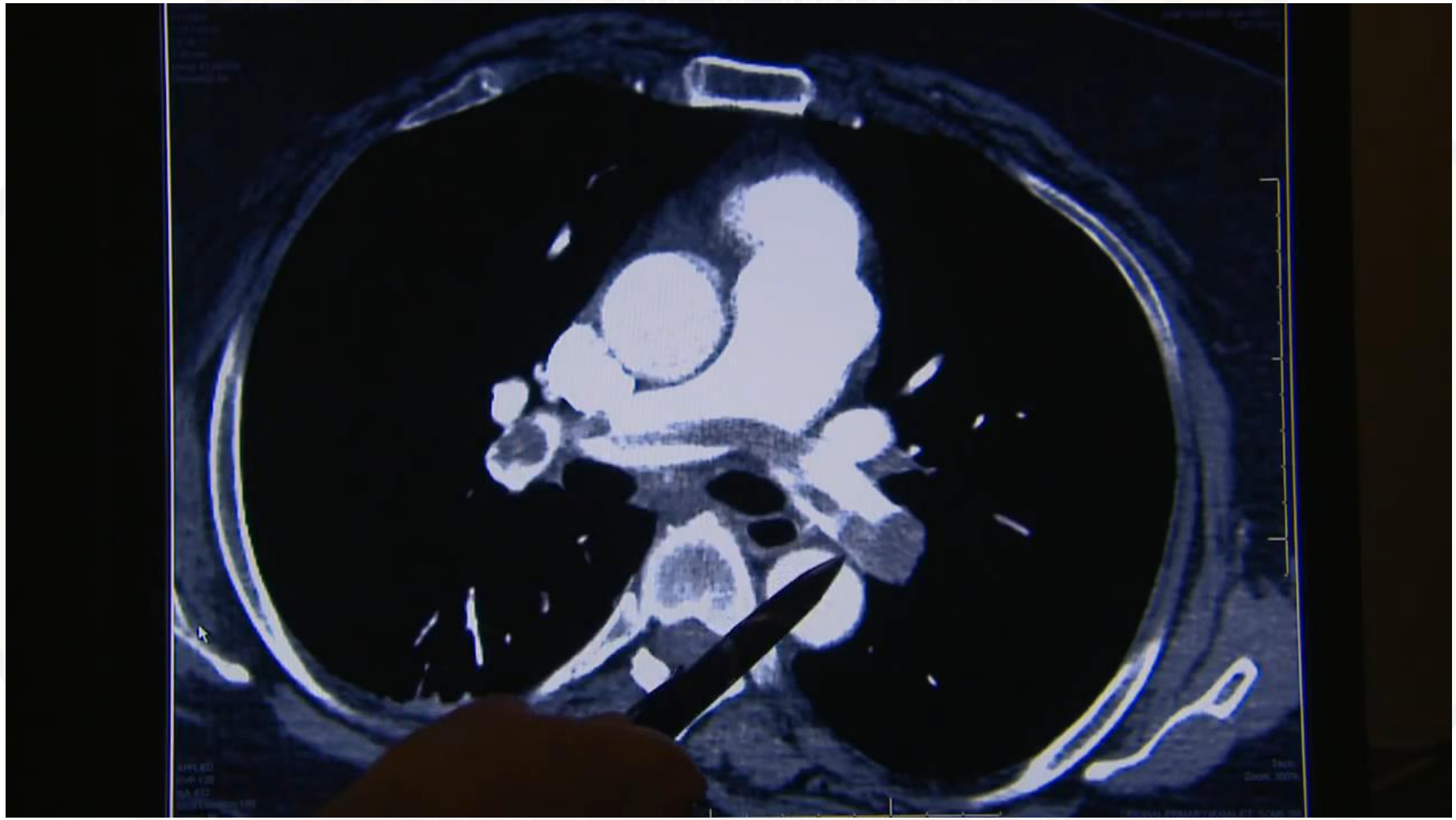


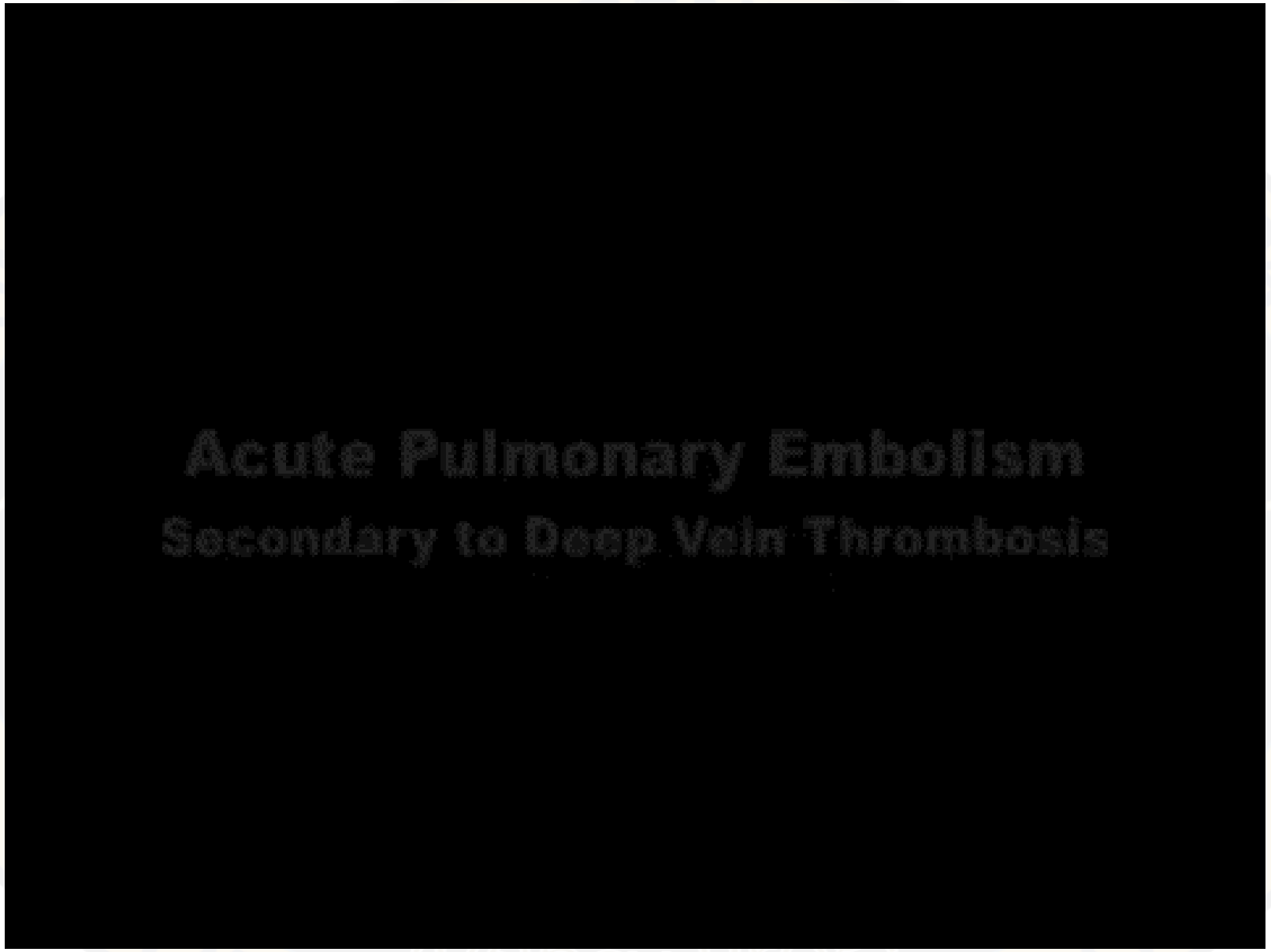






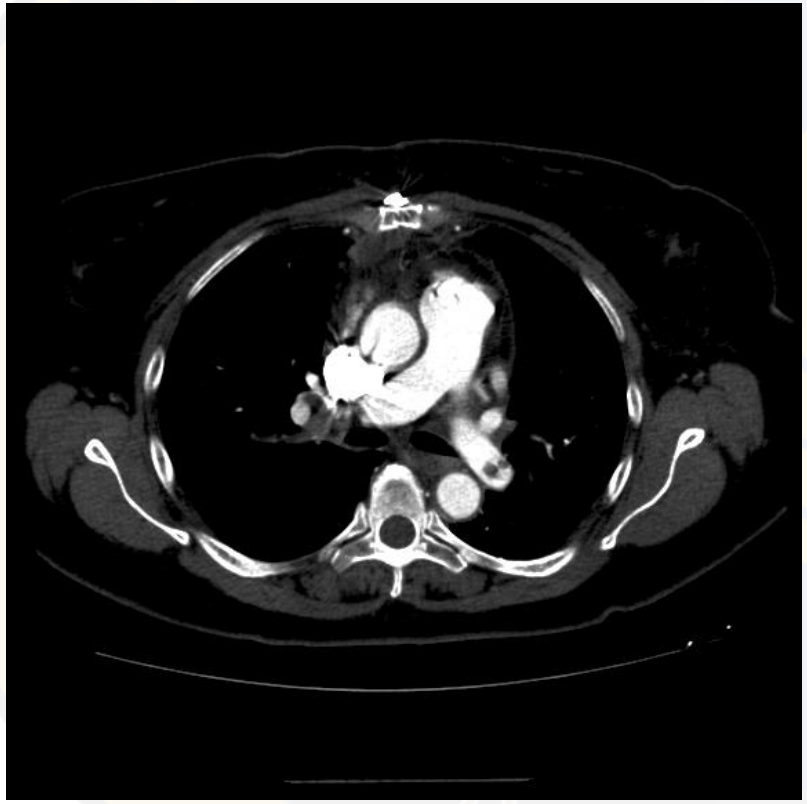


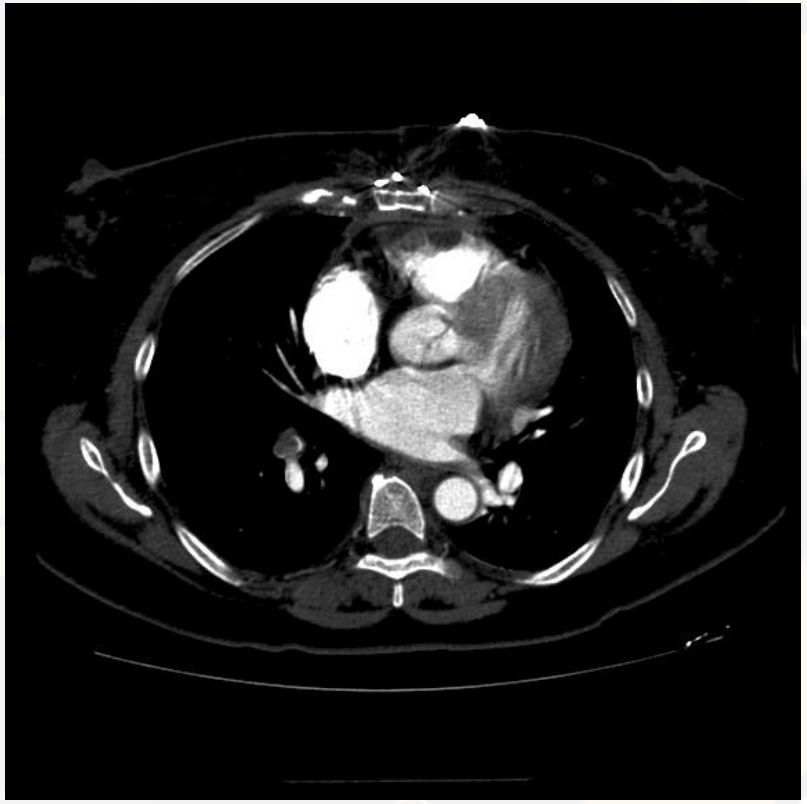




Ann Thorac Surg. 2011;91:728–32

- 67 y/o male c/o CP, SOB, etc.
- s/p CABG three weeks previous
- VS
  - HR 120/min RR 24/min BP 100/50 O2sat 92%
- PE
  - Taq; basilar rales L>R

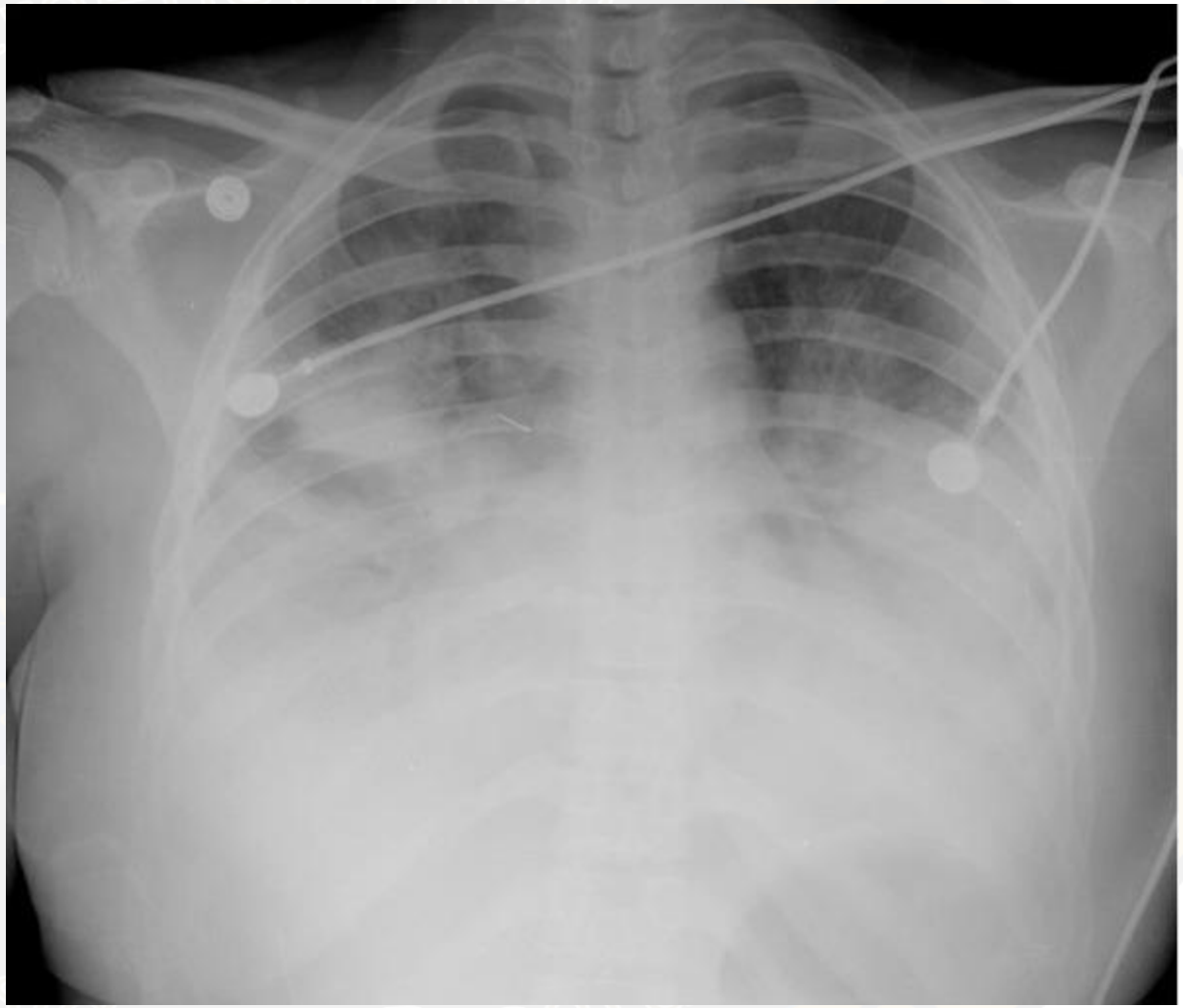




- Hyperviscocity p/ CABG
- No anticoagulants
- Theory:
  - Some of the patients who “die suddenly” within 30 days of CABG succumb to PE without any clear warning signs and without the diagnosis of PE being established. DVT is also difficult to detect clinically because leg discomfort and swelling may be attributed to trauma from the vein harvest site, excessive hydration during cardiopulmonary bypass, or muscle cramping due to perioperative immobility. Rarely is DVT suspected in the contralateral leg after vein harvest for CABG.

Amniotic Fluid Embolism

- Dyspnea and hypotension during labor or abortion
- Decreased O2 saturation
- Can have cardiac arrest, DIC
- Treatment
  - supportive



Amniotic Fluid Embolism

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In Summary…..

- We reviewed the pathophysiology and possible presentations for pulmonary emboli
- We reviewed the presentation for massive pulmonary emboli and the need for immediate diagnosis and aggressive treatment
- We identified the mechanisms that the different anticoagulants work as the alternative managements

Questions?