Massive and Sub-massive Pulmonary Emboli

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Outline

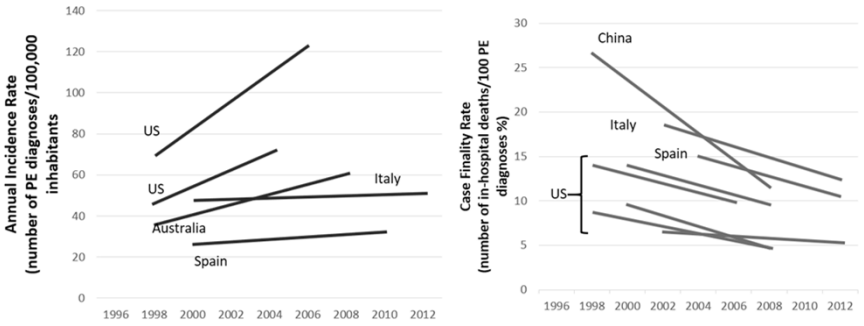
- **Incidence**
- **Risk Stratification**
- **Pharmacologic therapy**
- **Percutaneous/ Surgical therapy**
- **Case Presentations**
- **Future Direction with Chronic Thromboembolic Pulmonary Hypertension (CTEPH)**

Pulmonary Embolism- Statistics

- 300k-600k per year
  - 1-2 per 1000 people, or as high as 1 in 100 if > 80 years old
- 3rd leading cause of cardiovascular death behind myocardial infarction and stroke
- Most commonly from lower extremity DVT
  - Evidence of DVT in > 50%

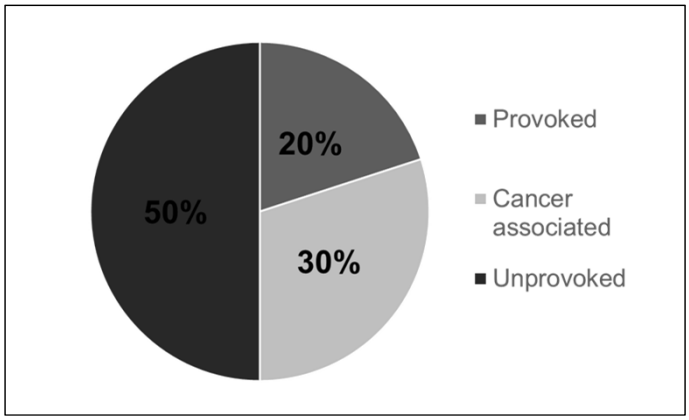
cdc.gov; Agency for Healthcare Research and Quality

Trends in Annual Incidence Rates and Case Fatality Rates of Pulmonary Embolism



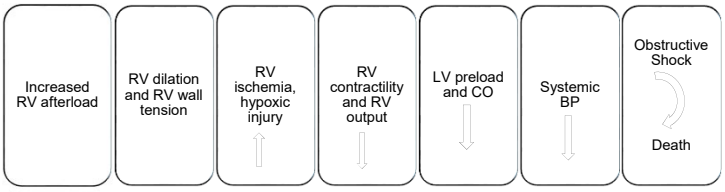
Konstantinides, SV et al. European Heart Journal 2019 00, 1-61.

Risk Factors for Persistent VTE Incidence: Trends in VTE Risk Factor Prevalence

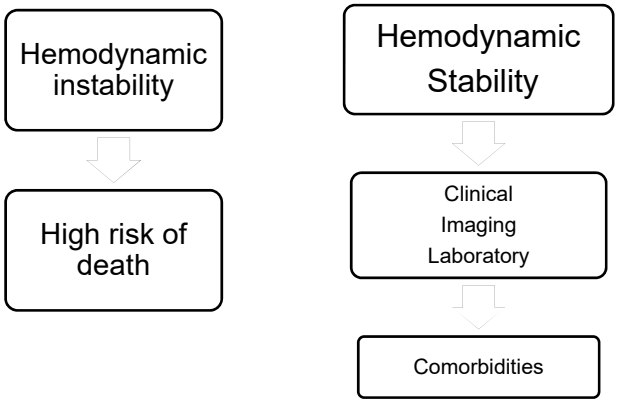


Benjamin E, et al. Circulation 2017; 135:e146-e603

Pathophysiology of Massive Pulmonary Embolism



Pulmonary Embolism- Risk Stratification



Pulmonary Embolism- Risk Stratification

High risk (massive PE)	Intermediate risk (submassive PE) (high or low)	Low risk PE
Hemodynamic instability	Hemodynamic stability	
• SBP < 100 mmHg for >15 minutes (secondary to PE) or requiring pressors • Decrease in SBP > 40 mmHg from baseline • Cardiac arrest	• Systemically normotensive • RV dysfunction (strain) on TTE or CTPE • Myocardial necrosis- elevated troponin and BNP	• Systemically normotensive • No RV dysfunction • No myocardial necrosis

Pulmonary Embolism- Risk Stratification

Simplified PESI Score

Patient Characteristic	Points
Age >80	1
History of Cancer	1
History of Cardiopulmonary Disease	1
HR ≥ 110	1
SBP < 100	1
Oxygen Saturation < 90%	1

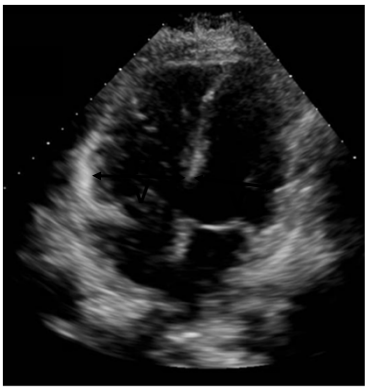
≥ 1 point(s)= 30 day mortality risk 10.9% (95% CI 8.5-13.2%)

Jimenez D et al. Arch Int Med 2010; 170:1383-1389.

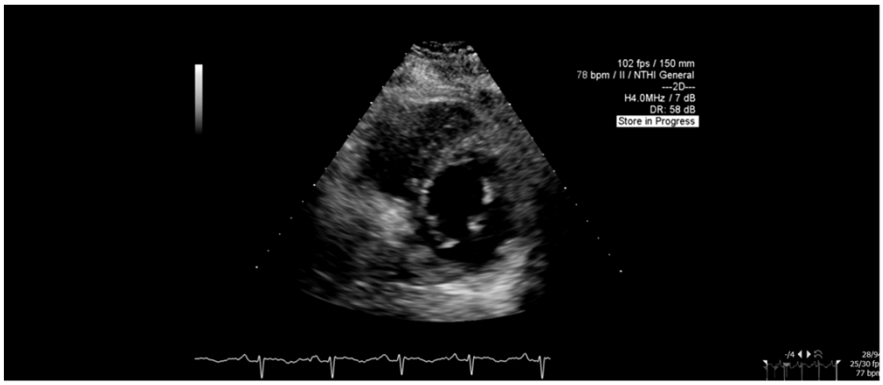
Imaging Evidence of RV Strain

Echocardiographic

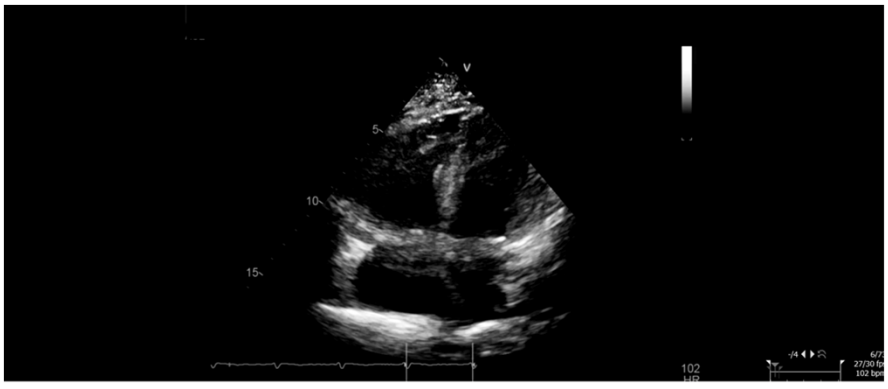
- **Enlarged RV with RV/LV ratio > 1 in the apical 4 chamber**
- **Flattened intraventricular septum- pressure overload**
- **McConnell's sign**
- **Dilated IVC**



Imaging Evidence of RV Strain

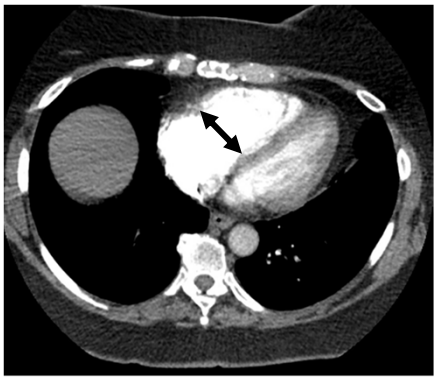


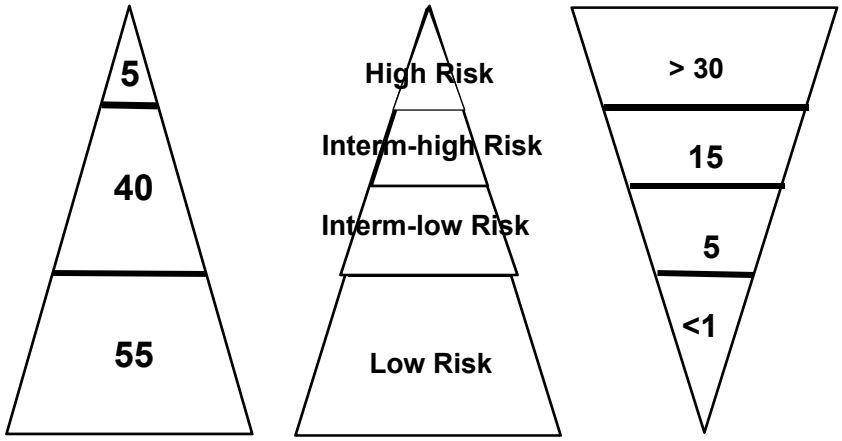
Imaging Evidence of RV Strain

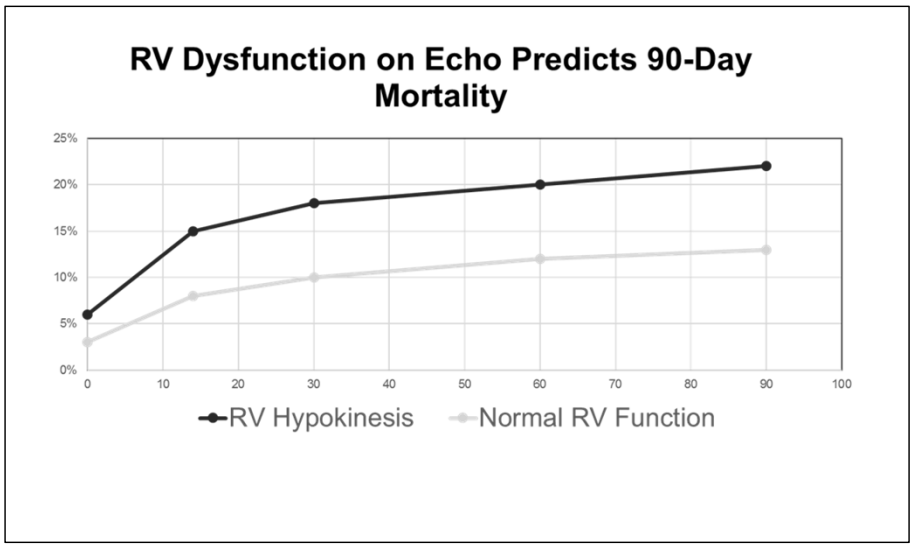


Imaging Evidence of RV Strain

CTPE
RV/LV ratio >1







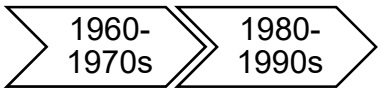
Goldhaber SZ, et al. Lancet. 1999;353:1386

Systemic Thrombolytics for Pulmonary Embolism

1960-1970s

- **1962 Streptokinase first used to lyse pulmonary emboli in dogs and humans**
- **1967 NHLI organized clinical trial that showed 12 hrs of urokinase vs heparin increased the resolution rate of PE (especially massive) documented with angiogram, hemodynamics and lung scans**

Systemic Thrombolytics for Pulmonary Embolism



- **Late 1980s recombinant tissue-type plasminogen activator (rt-PA) introduced in the treatment of PE.**
- **Randomized trial indicated its faster action and safety compared to urokinase.**
- **Multiple small trials in the 1990s shows clinically significant improvement in acute PE with rt-PA (alteplase)**

OSU Guidelines for Systemic Thrombolytics in PE

ALTEPLASE FOR CARDIAC ARREST SECONDARY TO PULMONARY EMBOLISM (PE)	ALTEPLASE FOR PULMONARY EMBOLISM (PE) NOT ASSOCIATED WITH CARDIAC ARREST
Dose is 50 mg or 0.6 mg/kg (max 50 mg)	Bolus of 10 mg followed by 90 mg infused over 2 hours

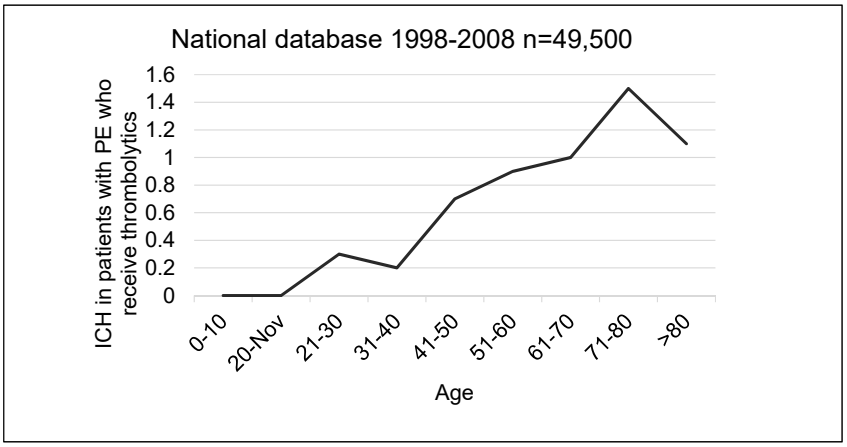
Pulmonary Embolism(PE)- Evaluation and Management OSU guidelines updated 2018

Contraindications to Systemic Thrombolytics

Absolute contraindications to thrombolysis become relative in patient with cardiac arrest or immediately life-threatening high-risk PE.			
4			Known intracranial neoplasm, arteriovenous malformation or aneurysm
5			History of hemorrhagic stroke or stroke of unknown origin at any time
7			Active internal bleeding
8			Recent major trauma / major surgery / any neurosurgery / head injury /major bleeding within **3 weeks**
Warning/Precaution Considerations **Check all that apply:**			
Use careful consideration and risk vs. benefit analysis. Patient may receive thrombolytic therapy despite ≥ 1 of the below.			
9			SBP > 180 mmHg or DBP > 110 mmHg
10			Known bleeding diathesis or acquired coagulopathies
11			Platelet count < 100,000/mm^3
12			Therapeutic anticoagulation
13			Current or recent use of: Ticagrelor (Brilinta®) within last 5 days or Prasugrel (Effient®) within last 7 days
14			Arterial puncture at non-compressible site, organ biopsy or lumbar puncture within last 7 days
15			Any history of ischemic stroke
16			Any neurosurgical procedure within **3 months**, consider contacting surgeon to balance risk and benefit
17			Pregnancy, or within one week postpartum
18			Low body weight (< 60 kg), consider reduced dose (0.6 mg/kg)
19			Suspected or known infective endocarditis
20			Suspected or known pericardial effusion
21			Age < 18 years old

Pulmonary Embolism(PE)- Evaluation and Management OSU guidelines updated 2018

ICH with Thrombolysis for Acute PE



Stein PD. Am J Med 2012; 125: 50-56

Recommendations For Systemic Thrombolytics	Class	Level
• Fibrinolysis is reasonable for patients with massive acute PE and acceptable risk of bleeding complications (AHA 2011)	IIa	B
	II	B
• In patients with acute PE associated with hypotension (eg, systolic BP <90 mm Hg) who do not have a high bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy (CHEST 2016)	I	C
• Systemic thrombolytic therapy is recommended for high-risk (massive) PE (ESC 2019)		

Systemic Thrombolytics for Pulmonary Embolism

1960-1970s → 1980-1990s → **2000-present**

- **Multiple studies evaluating systemic thrombolytics in the Intermediate risk (submassive) population**
- **PEITHO (2014) –largest trial ~1000 pts randomized to heparin/ placebo vs heparin/tenectaplase.**
- **Primary outcome composite all cause mortality or hemodynamic decompensation/ collapse- better in tenectaplase group.**
- **2% hemorrhagic stroke in lytic group**

Recommendations For Systemic Thrombolytics	Class	Level
• Fibrinolysis is not recommended for patients with low-risk PE or submassive acute PE with minor RV dysfunction, minor myocardial necrosis, and no clinical worsening (AHA 2011)	III	B
• Routine use of primary systemic thrombolytics is not recommended in intermediate or low risk PE (ESC 2019)	III	B

Anticoagulation

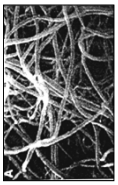
- UFH recommended in Massive PE
- 80 U/kg bolus followed by 18 U/kg/hr (if less than 125kg) or 12 U/kg/hr (if greater to or equal than 125 kg)
- If lytics given then UFH is held during alteplase infusion and reinitiated at the end of this infusion.
- LMWH preferred in Submassive if no procedures planned

Percutaneous Therapies for Pulmonary Embolism

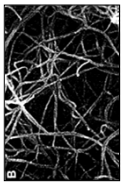
- Next step was to evaluate catheter directed therapies
- ??? Less bleeding and improved outcomes
- Mechanical fragmentation- pigtail catheter
- Rheolytic thrombectomy- Angiojet
- Catheter directed lysis- EKOS system, Unifuse
- Suction embolectomy- Flow Triever, Angiovac, Penumbrum

Ultrasound Accelerated Catheter Directed Fibrinolysis (EKOS)

Fibrin Separation
Ultrasound separates fibrin without fragmentation of emboli



Without Ultrasound

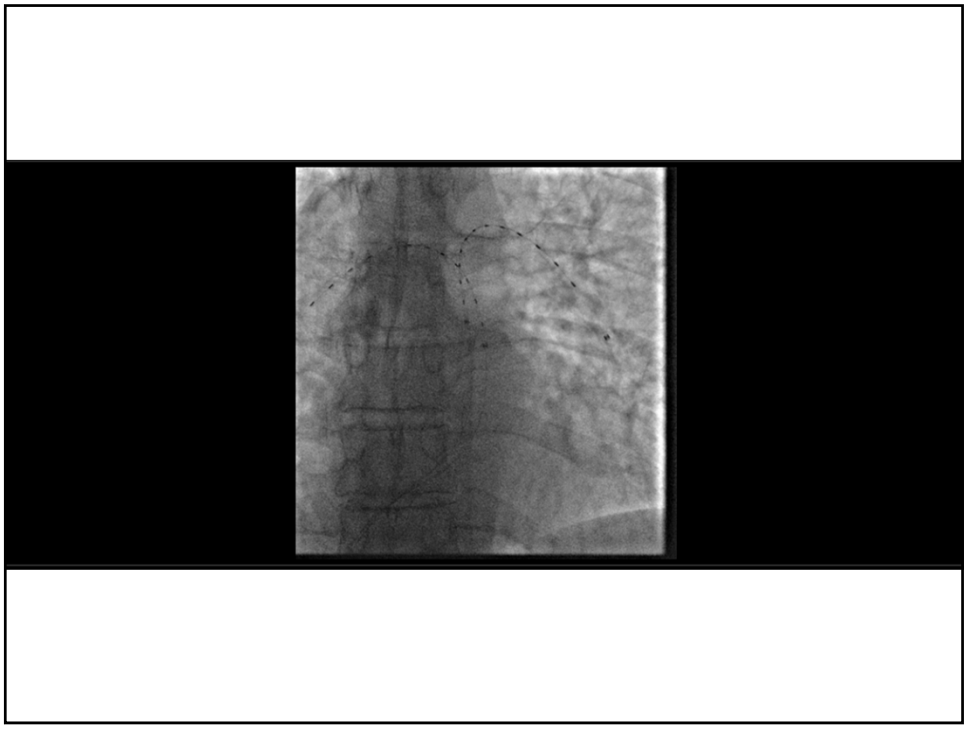


With Ultrasound

Delivers thrombolytics directly into pulmonary artery thrombus.

Alteplase 1mg/hr x 12 hrs per catheter

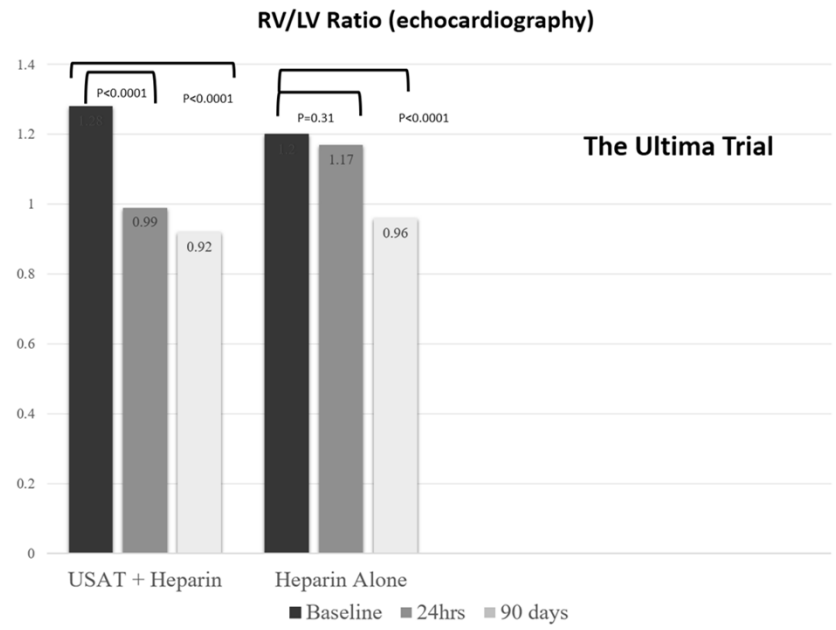
Heparin gtt peripheral IV



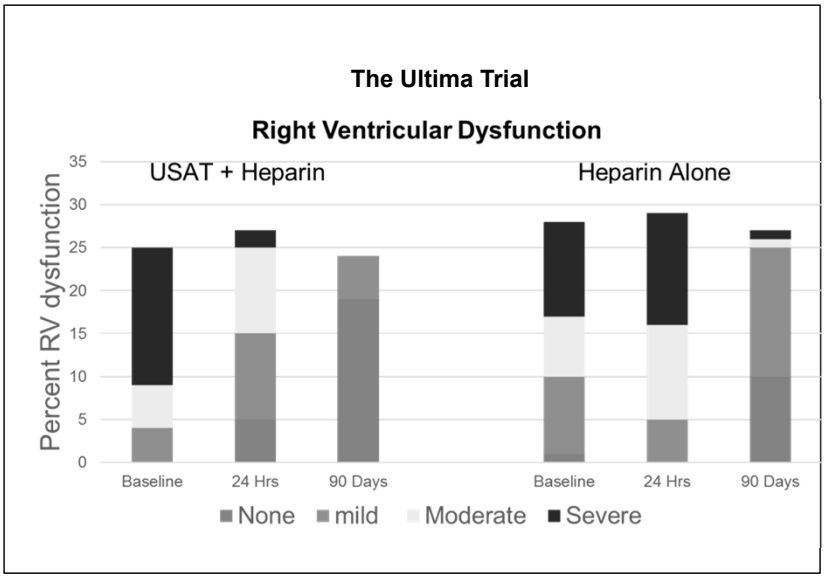
Percutaneous Therapies for Pulmonary Embolism

- **Catheter directed lysis (CDL) in patients with acute PE**
- **ULTIMA Trial 2013- randomized to EKOS thrombolysis + heparin vs heparin alone N=59**
- **SEATTLE II Trial 2015 -single arm with EKOS (ultrasound accelerated thrombolysis) using total 24mg alteplase N=150 Massive 20%**
- **At 48hrs RV/LV ratio, PA pressures and modified Miller score all statistically significantly reduced in EKOS group. No intracranial hemorrhages.**

Piazza GA et al. JACC Cardiovasc Interv 2015



Kucher,N et al. Circulation 2014 129(4)479-486.



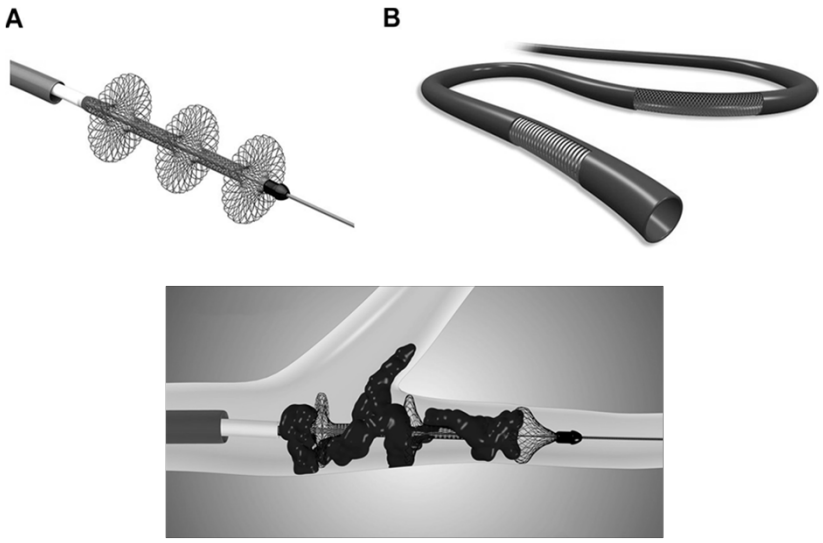
Kutchner, N. et al. Circulation 2014 129(4) 479-486.

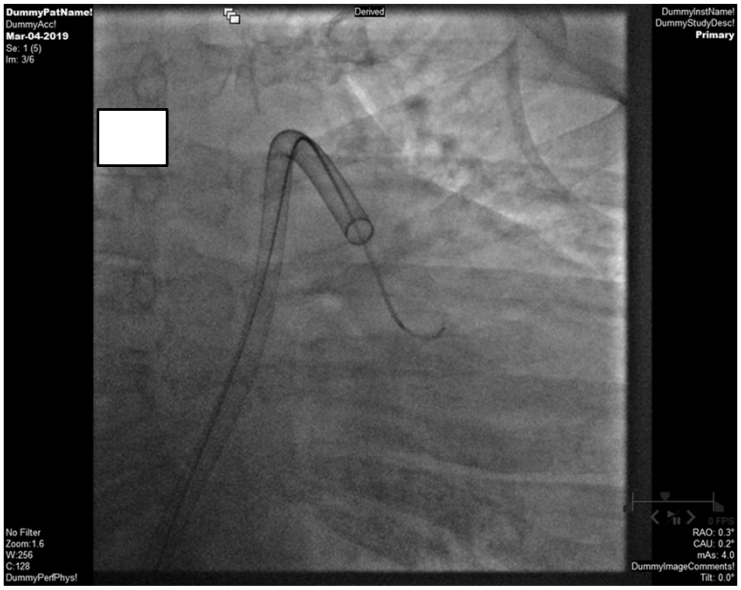
Percutaneous Therapies for Pulmonary Embolism

- **Mechanical embolectomy devices introduced.**
- **FLARE trial 2019 – single arm multicenter trial of catheter directed mechanical thrombectomy (Flow Triever) in submassive PE**
- **At 48hrs RV/LV ratio reduction statistically significant**

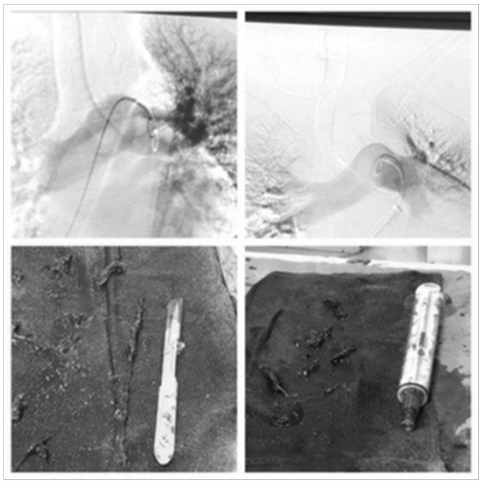
Tu t et al. JACC Cardiovasc Interv 2019

Mechanical Embolectomy





Mechanical Embolectomy



Recommendations for Catheter Directed Therapies

- **Can be considered in patients with hemodynamic or respiratory deterioration on anticoagulation therapy**
- **Patients with massive PE who have contraindication for systemic thrombolytics**
- **Patients that receive systemic thrombolytics and remain unstable**

AHA 2011
CHEST 2016
ESC 2019

IIa

Surgical Therapies for Pulmonary Embolism

- The Society of Thoracic Surgeons (STS) Database from 2011-2015
- 1075 cases Isolated Acute Surgical Pulmonary Embolectomy without prior cardiac surgery
- Overall mortality 16% (NCS= 8%, CS= 23%, and CS/CA=44%)

Kon ZN et al. The Annuals of Thoracic Surgery 2019 197(5)1401-1408.

Indications for Surgical Embolectomy

Massive or Submassive PE with any of the following:

- Contraindication to thrombolytic therapy
- Failed thrombolytic therapy
- Patent foramen ovale
- Pregnancy
- Right heart failure or cardiogenic shock
- Thrombus-in-transit within the right heart chambers

Licha CRM et al. Ann Thorc Cardiovasc Surg 2019

Surgical Therapies for Pulmonary Embolism

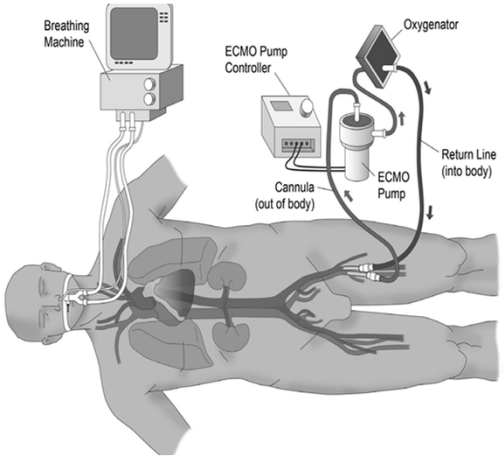
Adjunctive Therapies

- Mechanical support for cardiogenic shock
- IVC filters

Extracorporeal membrane oxygenation (ECMO)

- Allows for acute hemodynamic stabilization in the patient with massive PE
- Small studies at experienced centers have shown improved survival in patients with ECMO vs no ECMO prior to therapies for massive PE

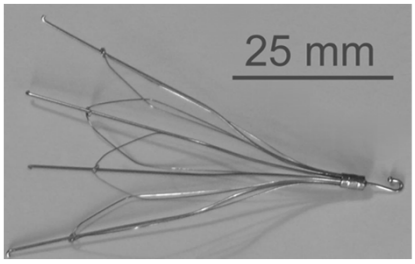
Ain DL, et al. Vasc Med 2018 Feb 60-64.



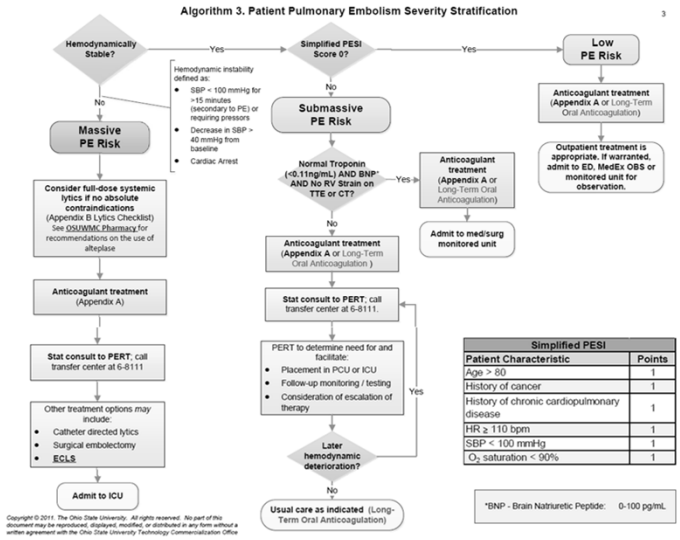
OSU one source patient education

Adjunctive Therapies in Massive and Sub-Massive PE

- Routine use of IVC filter is not recommended
- IVC filter is suggested in patients with PE and absolute contraindication to anticoagulation or recurrent PE despite anticoagulation.
- Placement of retrievable IVC filter in patients with hemodynamic compromise and residual proximal DVT is made on case by case basis



Author: BozMo (CC BY-SA 3.0)



Pulmonary Embolism Response Team (PERT)

- **Respond quickly to treat patients with massive and submassive PE**
- **Multidisciplinary approach to coordinating care**
- **Provide best option(s) for treating patients**
- **Develop protocols for full range of therapies available to standardize care**

Case Presentation

45 year old male presents to the ER with complaints of chest pain, shortness of breath and lightheadedness. He reports symptoms had begun 2 days prior. He reports the chest pain was worse with respirations. He had no prior cardiac history.

PMH:
Hypertension
Osteoarthritis
Morbid obesity

Medications:
Altace 10 mg daily
Celebrex 200mg daily
Multivitamin

Social History:
+ tobacco and EtOH.
Denies illicit drugs.

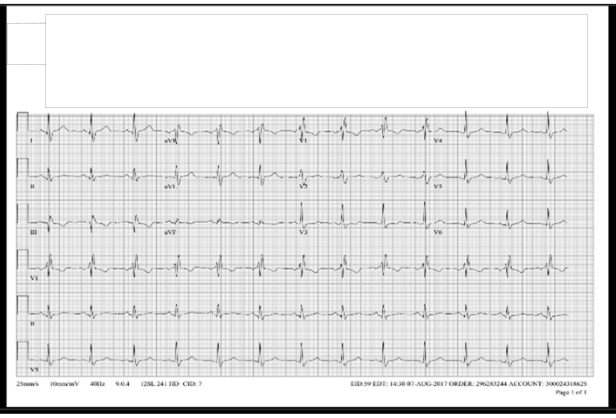
Family History:
No premature CAD
No history of hypercoaguable states.

Case Presentation

Physical Exam:
Blood pressure 100/60
Heart rate 105
RR 20
O2 sat RA 89%

General: anxious appearing
HEENT: Normal
CV: regular, tachycardia. No M/R/G
Lungs: tachypneic, clear
Abdomen: + BS , soft, obese
Extremities: Mild right pretibial and pedal swelling.
Pulses: intact and equal upper and lower extremities.

Labs:
Troponin 0.85
BNP 200
BMP and CBC WNL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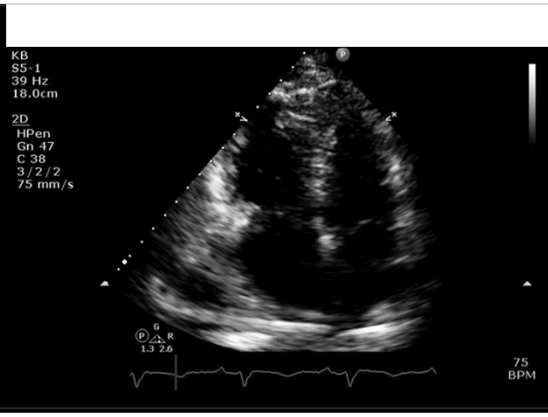
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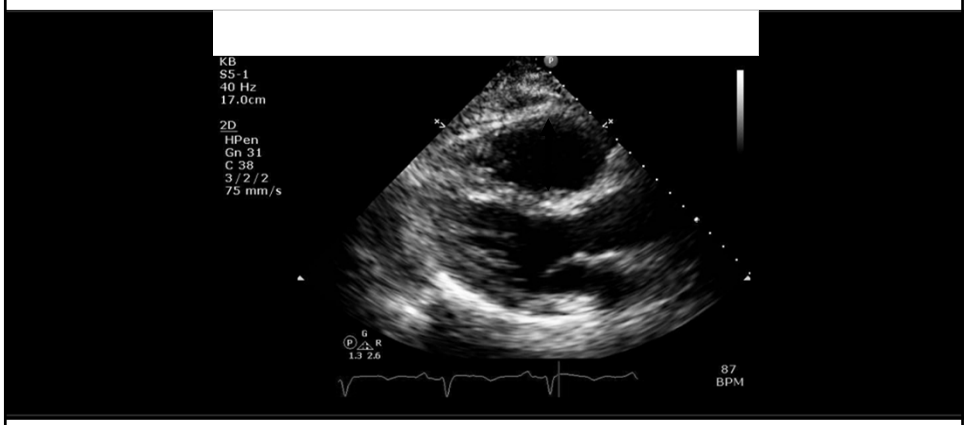
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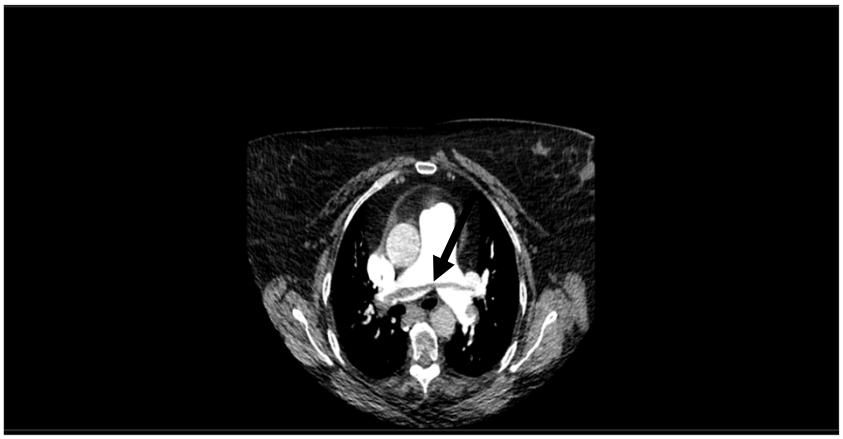
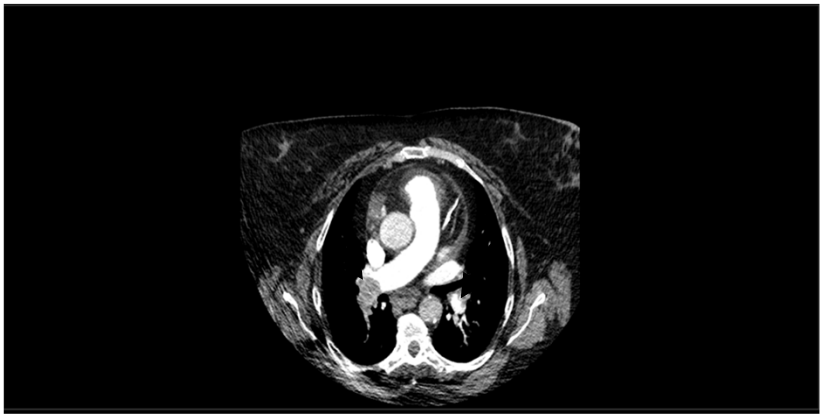
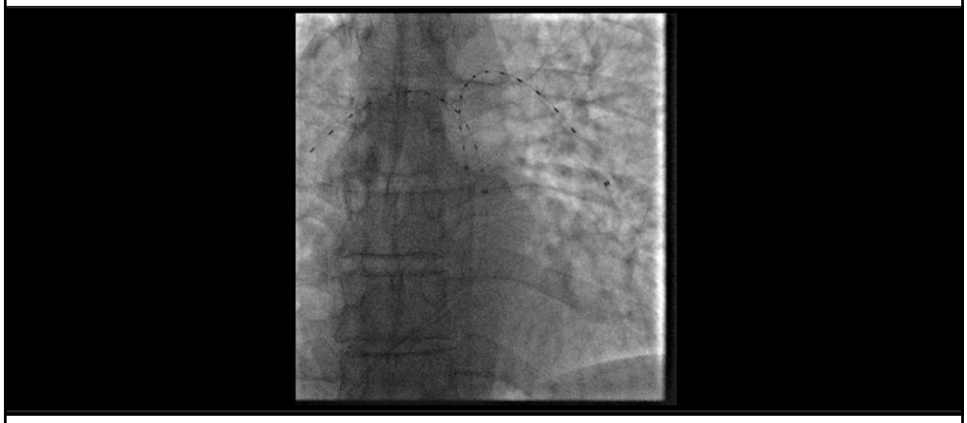




Hospital Course

- **Placed on IV heparin gtt and admitted to the cardiac unit.**
- **Overnight O2 requirement increased with no improvement in blood pressure**
- **Decision was made to perform catheter directed lysis in the cardiac catheterization laboratory**



Follow-up

- **Patient discharged on day 3 with Xarelto**
- **Followed up in Cardiology office in 3 months with repeat imaging. Echo showed near normalization of RV size and function.**
- **Etiology likely obesity with decreased mobility. Hypercoaguable workup after off OAC.**
- **Plan to continue OAC for 6 months.**

Case Presentation

60 year old male presents to the ED by squad with syncope and lethargy. He had been convalescing at home after recent admission for community acquired pneumonia. The patient's family reports he had been sedentary since discharge from the hospital two weeks ago. Today they noticed he was short of breath and then passed out while walking from his bedroom to the restroom. His fall was witnessed. No head trauma.

PMH:
Hypertension
COPD
CAD

Family History:
CAD
no hypercoagulable states

Medications:
Aspirin 81 mg daily
HCTZ 25 mg daily
Metoprolol 25 mg BID
Albuterol inhaler prn

Social History:
Former smoker.

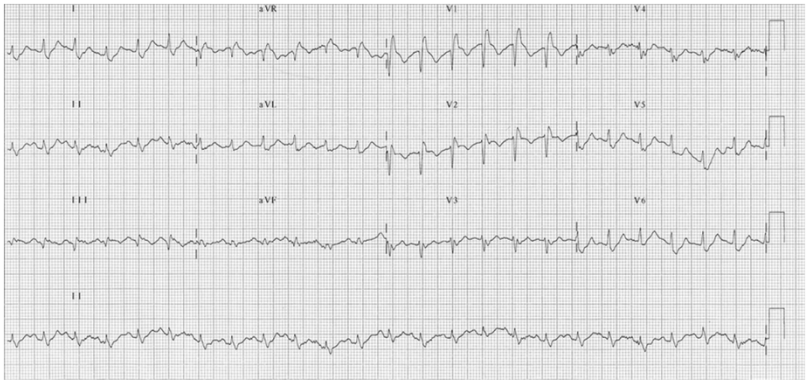
Case Presentation

Physical Exam:
Blood pressure 80/40
Heart rate 140
RR 20
O2 sat on non-rebreather 90%

General: lethargic but answers questions
HEENT: Normal
CV: regular, tachycardia. No M/R/G
Lungs: tachypneic, diminished throughout
Abdomen: + BS , soft, NTND
Extremities: cool, trace bilateral ankle edema
Pulses: intact and equal upper and lower extremities.

Labs:
Troponin 1.2
BNP 158

CXR: mild LLL patchy infiltrate (improved from recent admission)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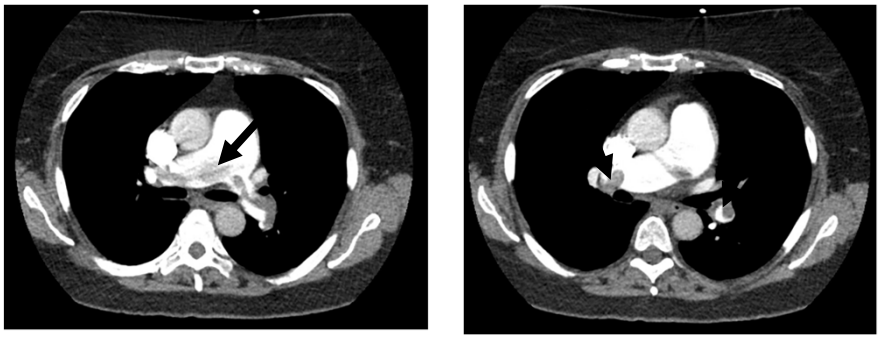
V2
V5
III
aVF
V3
V6
II



Follow-up

- **Patient admitted to ICU**
- **BP normalized over the next several hours**
- **Echo showed dilated and hypokinetic RV**
- **Patient discharged home on day 4 with Xarelto**
- **Seen in Cardiology outpatient follow-up at 8 weeks. Doing well with no apparent sequelae.**

Case Presentation

61 year old female that presented several day history of chest pain and shortness of breath. She had been admitted to the hospital several weeks prior for cholecystitis and sepsis. She had noticed swelling in her right lower extremity the week prior to presentation

PMH:
Breast ca s/p resection chemo and radiation 2014

Family History:
No hypercoagulable states

Medications:
Aspirin 81 mg daily
Augmentin BID
Anastrazole 1 mg daily

Social History:
Nonsmoker.

Case Presentation

Physical Exam:
Blood pressure 117/77
Heart rate 129
RR 20
O2 sat 96%

General: anxious with pleuritic chest pain
HEENT: Normal
CV: regular, tachycardia. No M/R/G
Lungs: tachypneic, clear
Abdomen: + BS , soft, NTND
Extremities: right leg swollen and tender below the knee
Pulses: intact and equal upper and lower extremities.

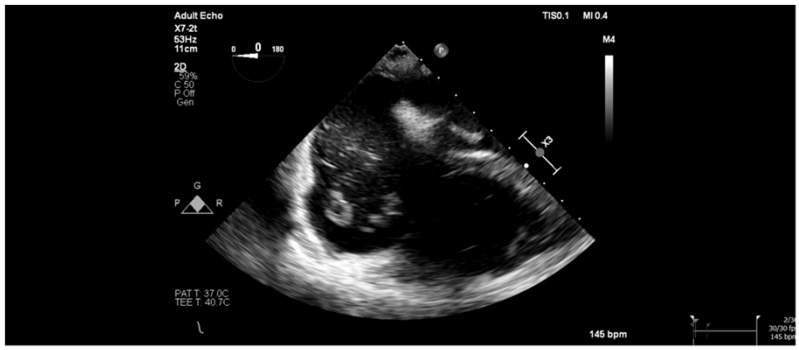
Labs:
Troponin 0.29
BNP 517

CXR: atelectasis at the right lung base

Case Presentation

- **CTPE study showed bilateral pulmonary emboli with evidence of right heart strain.**
- **ER bedside echo concerning for mobile mass in the right atrium**
- **PERT consult placed.**

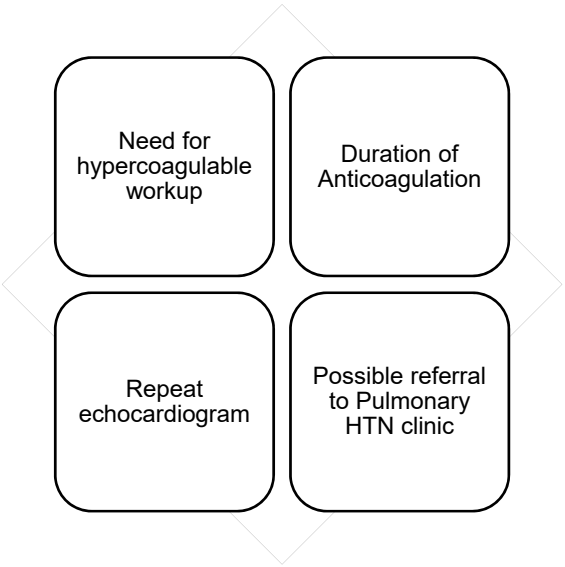
Case Presentation



Hospital Course

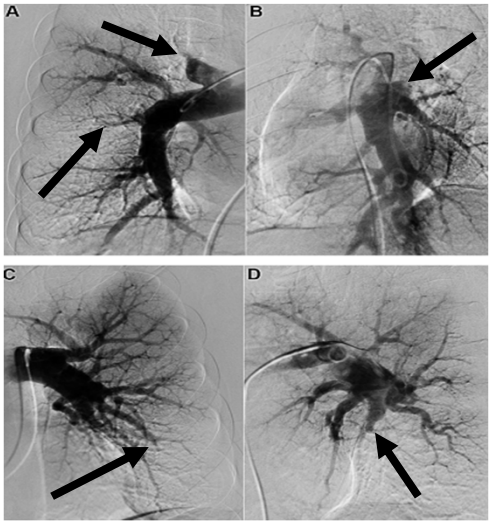
- To the OR for right atrial thrombectomy.
- Was placed on veno-arterial ECMO during surgery.
- Patient weaned from ECMO 5 days later
- Discharged to SNF after 2 weeks on Coumadin
- Follow up echo showed mild RV enlargement but no evidence of pulmonary HTN. Patient back to work at daycare center.

Follow up for Massive and Submassive PE

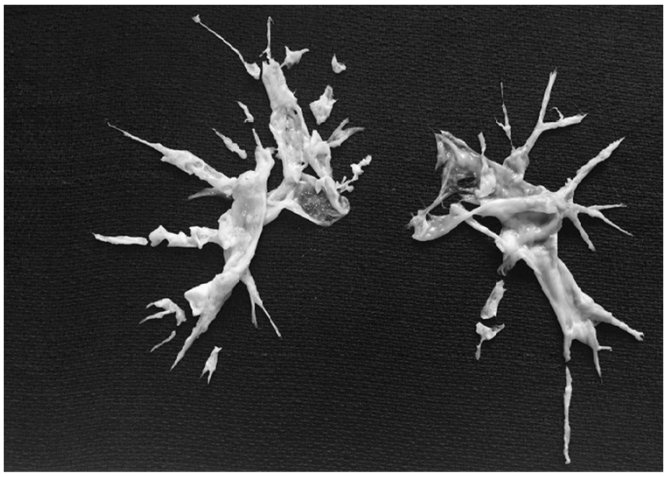


Chronic Thromboembolic Pulmonary HTN (CTEPH)

- **CTEPH is mean PAP ≥ 25mmHg after at least three months of effective anticoagulation and residual chronic thrombus.**
- **categorized by the WHO as Group 4 PH**
- **Between 500 and 2500 new cases of CTEPH diagnosed each year.**
- **In fact, as many as 1 out of every 25 previously treated PE patients (>3 months of anticoagulation) could develop CTEP**

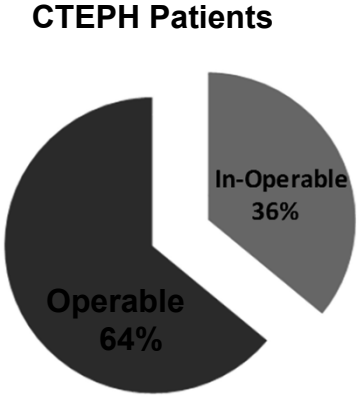


Author: ICA CTEPH CC BY-SA 4.0



Author: ICA CTEPH CC BY-SA 4.0

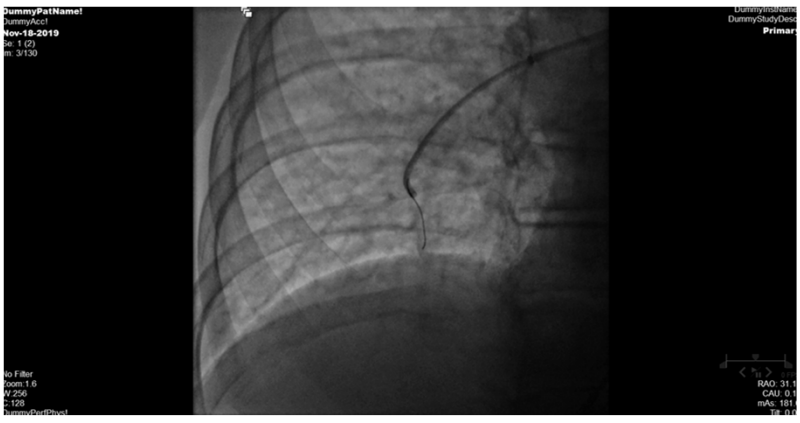
Chronic Thromboembolic Pulmonary HTN (CTEPH) Results from an International Prospective Registry



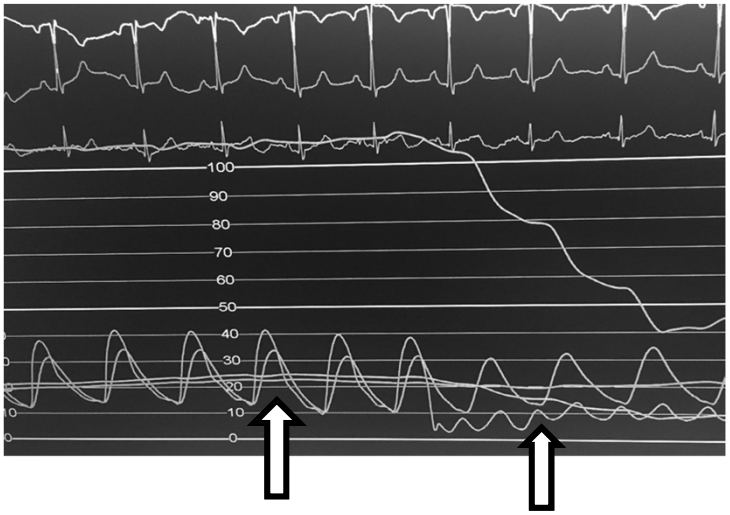
57% treated with Pulmonary Embolectomy

Circulation . 2011; 124:1973-1981

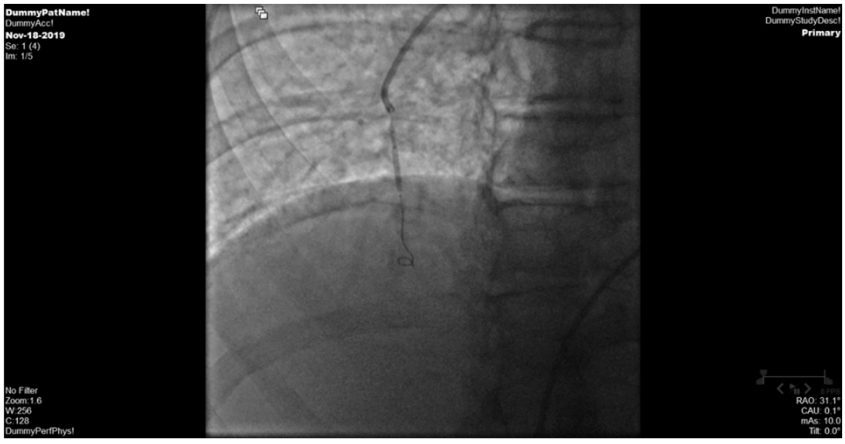
Balloon Pulmonary Angioplasty (BPA)- case



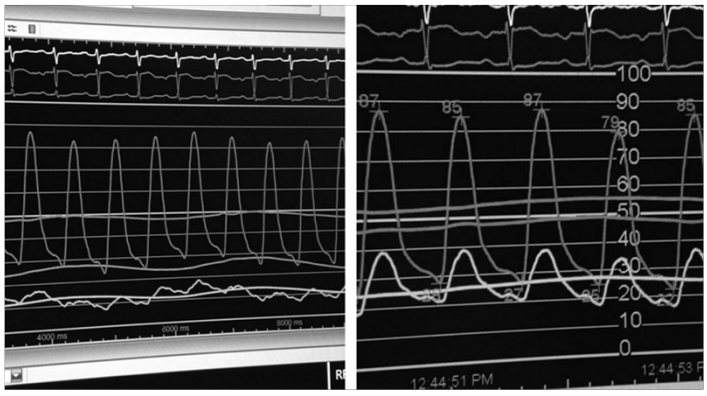
Pressure wire across the lesion



Balloon Pulmonary Angioplasty (BPA)- case

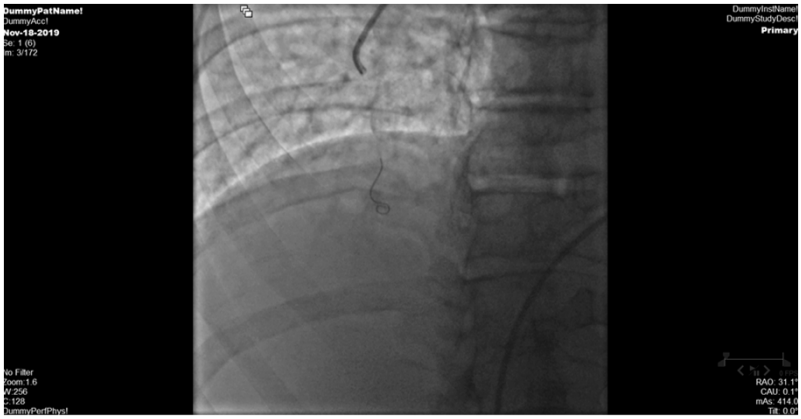


Pressure wire guided BPA



PRE BPA **POST BPA**

Balloon Pulmonary Angioplasty (BPA)- case



Conclusions

- **Patients with massive and submassive pulmonary embolus require emergent intervention to prevent hemodynamic decompensation and/or death.**
- **Options for treatment vary and many times require a multidisciplinary approach to determine the best intervention.**
- **Close follow up of these high risk patients is important to prevent and treat longterm sequelae.**