Pulmonary Embolism in Intensive Care Unit

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Agenda

- Frequency of pulmonary embolism in ICUs
- Health care costs of VTE
- Pathophysiology of Pulmonary Embolism
- Risk factors for VTE in ICU
- Diagnostic considerations to suspected Acute Pulmonary Embolism in the ICU
- Treatment of Acute Pulmonary Embolism in the ICU
- Prognosis
- Prevention

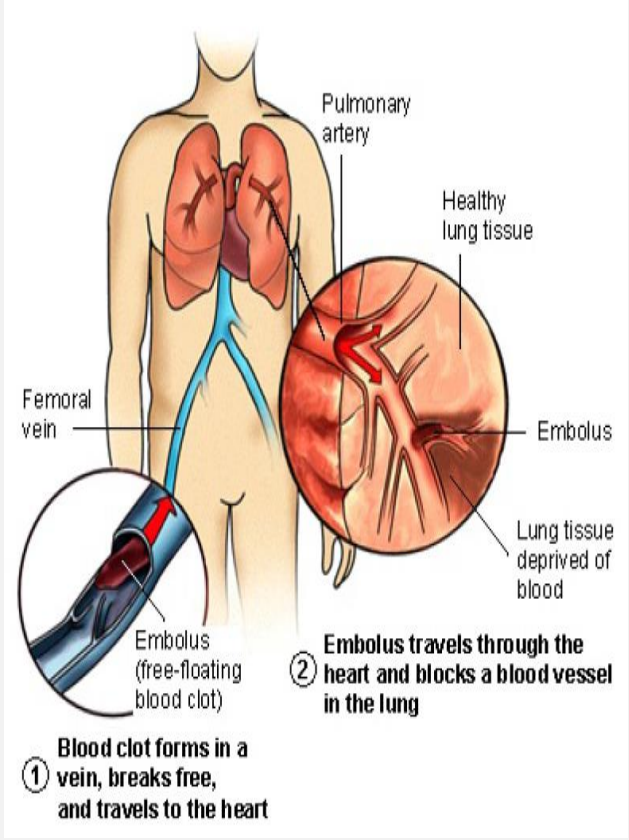
Introduction

- **Embolus:**

Is an intravascular mass (solid, liquid or gaseous) removed from its origin & carried in the blood stream to be lodged in the pulmonary arteries and arterioles.

- **Pulmonary Embolus (PE):**
  - ***Thrombotic (detached thrombus fragment)***
    - **-Septic embolism**
  - ***Non-thrombotic***
    - **Air embolism**
    - **Fat embolism**
    - **Amniotic fluid embolism**
    - **Tumor embolism**

- **VTE = venous thromboembolism is (PE plus DVT)**



Frequency of pulmonary embolism in ICUs

- **ICU patients: higher risk for both DVT & PE.**
- **PE occurs** in **up to 50%** of patients with **proximal DVT.**
- About **79%** of patients with **PE** have evidence of **LL DVT.**
- **DVT in critically ill:** vary from **22% to almost 80%,** depending on patient characteristics
- The **incidence of PE was poorly described**, and systematic screening was not performed.
- The **rate of symptomatic PE ranged from 0.7% to 6%.**
- PM studies on ICU patients → **7 to 27%** of autopsies have incidental **PE** in which **1 to 3%** of these PE **are cause of death.**

Health care costs of VTE

- **Inpatient DVT → + $8000 /** entire hospital bill
- **Inpatient PE → + $14,000 / entire hospital bill**
- **DVT+PE→ +~ $28,000 per case**
- **Hidden costs:** readmission, bleeding complications or recurrent VTE.
- **VTE in ICU → increases 1 to 4 more days length of ICU stay**
- Hence **VTE in critical care patients can result in significant hospital costs.**

Pathophysiology of Pulmonary Embolism

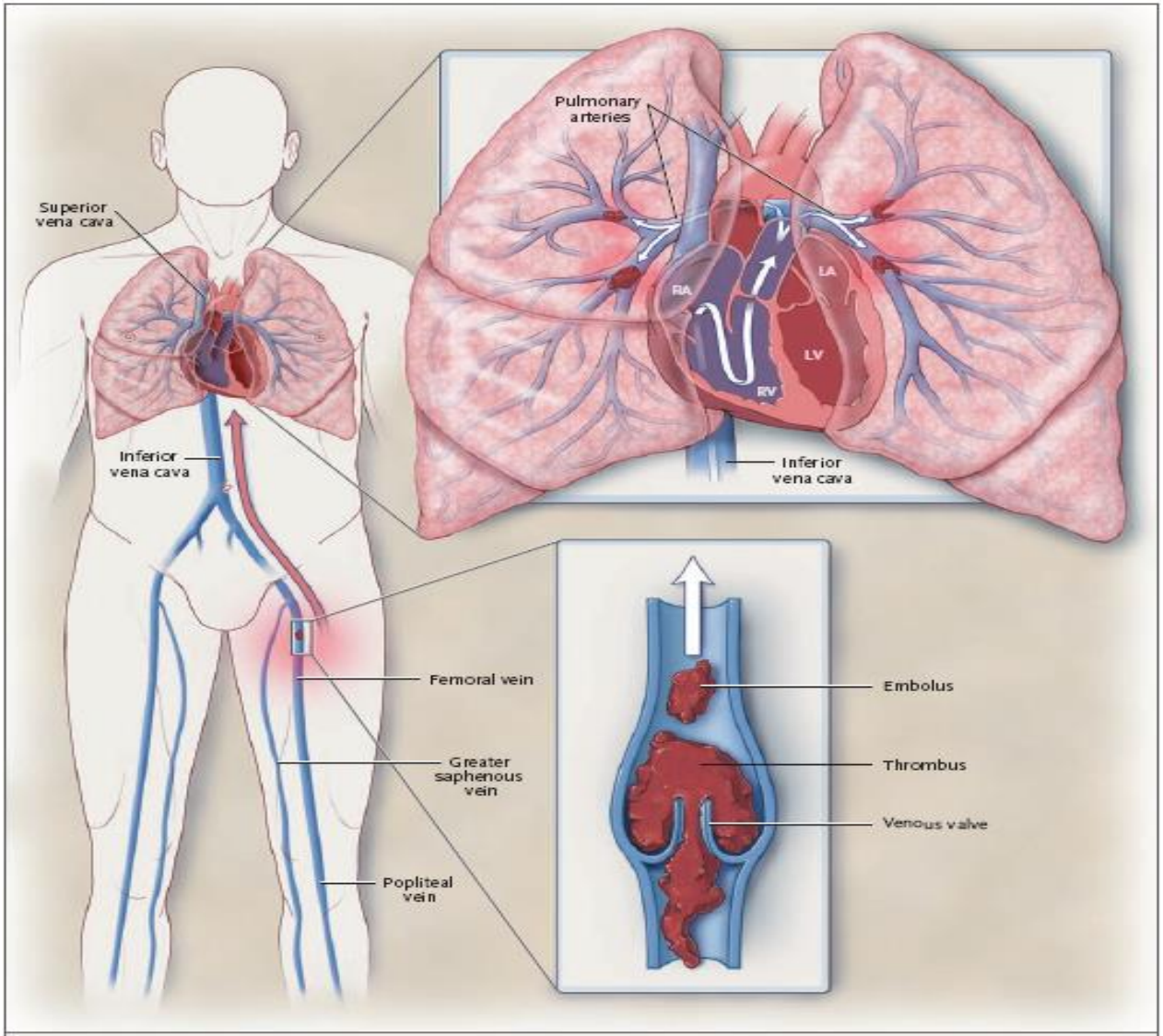


Figure 1. Pathophysiology of Pulmonary Embolism.

Risk factors for VTE in ICU

Virchow's Triad and Risk of Venous Thromboembolism in the Intensive Care Unit

	Hypercoagulability	Stasis	Vessel Injury
Major surgery	x	x	x
Trauma	x	x	x
Acute myocardial infarction		x	
Congestive heart failure		x	
Stroke		x	
Burns		x	
Sepsis	x	x	
Catheter	x	x	x

Risk factors for VTE in ICU

Intensive Care Unit Acquired Risk Factors	
General Medical Risk Factors	**ICU Acquired Risk Factors**
Advanced age	Immobilization
Malignancy	Stroke
Recent surgery	Trauma
Prior venous thromboemboli	Mechanical ventilation
Pregnancy	Invasive procedures/tests
Obesity	Central venous catheters
Oral contraceptives	Sepsis
Nephrotic syndrome	Heart failure
Inherited or acquired hemophilia	Vasopressor use
Inflammatory bowel disease	Cardiopulmonary failure

PE in ICU: A Difficult Diagnosis

- **Unable to complain** of the usual symptoms of PE & **physical examination findings are limited**.
- **Readily available alternate explanations** for hypoxemia, pulmonary infiltrates, respiratory failure, and hemodynamic instability.
- **Too hemodynamically unstable for transport** to the diagnostic imaging suite.
- **Impaired renal function** due to critical illness **precludes CTPA**.
- **D-dimer** levels had false positive results.
- DVT may **not be suspected** in ICU patient until the patient manifest sign symptoms of PE.

Clinical presentation

- **None of symptoms and signs of PE are specific.**
- **Dx:**
  Clinical findings +laboratory tests + imaging studies
- ***Suspicion should increase in the presence of:***
  - **Supporting symptoms and signs**
  - **Presence of risk factors**

Symptoms	
Dyspnoea	80%
Chest pain (pleuritic)	52%
Chest pain (substernal)	12%
Cough	20%
Haemoptysis	11%
Syncope	19%
Signs	
Tachypnoea (≥20/min)	70%
Tachycardia (>100/min)	26%
Signs of DVT	15%
Fever (>38.5°C)	7%
Cyanosis	11%

Clinical presentation

- **ICU signs of PE:**
  Unexplained:
  - **Hypoxemia and/or shock.**
  - **Hypotension or tachycardia**
  - **Increased physiologic dead space (end-tidal CO2)**
  - **Increased pulmonary artery pressure (in the absence of other causes).**

Assessment of clinical probability

- Estimation of the clinical probability of PE according to scoring systems→ **a validated prediction rule**

Wells Prediction Rule for Diagnosing PE: Clinical Evaluation Table for Predicting Probability of PE	
Clinical characteristic	Score
DVT suspected	3
Alternative diagnose less likely than PE	3
Recent surgery or immobilization (within last 30 days)	1.5
Heart rate> 100 beats per minute	1.5
Previous PE or DVT	1.5
Hemoptysis	1
Cancer (treated within previous 6 months)	1
Clinical probability (2 levels)	
PE unlikely	0–4
PE likely	>4

Assessment of clinical probability

Definition of Massive PE:

- **Acute PE *with sustained hypotension***

  (SBP <90 mm Hg for at least **15 minutes** or **requiring inotropic support**, not due to a cause **other than PE, such as arrhythmia, hypovolemia, sepsis, or left ventricular [LV] dysfunction),**

  - **Acute PE *with Pulselessness, or persistent profound bradycardia***

    (heart rate <40 bpm with signs or symptoms of shock).

Definition of Submassive PE

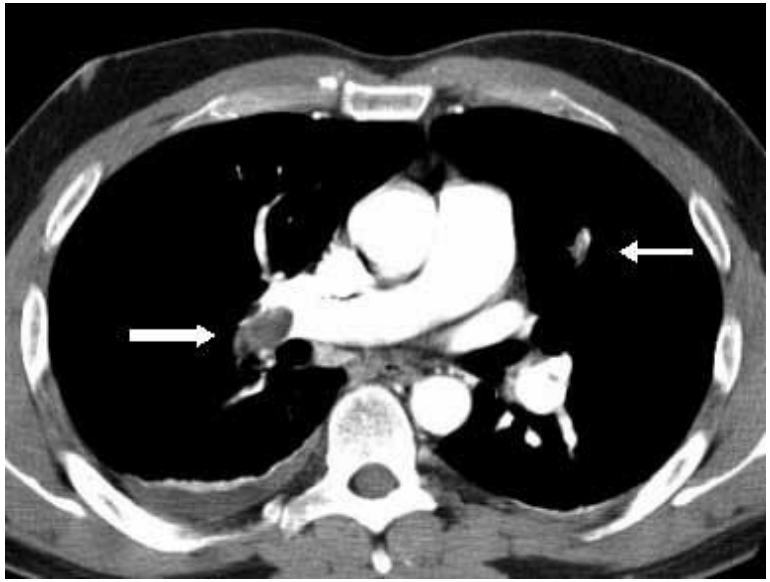
- **Acute PE without systemic hypotension** (systolic blood pressure >90 mm Hg)
- **but *with either RV dysfunction or myocardial necrosis.***

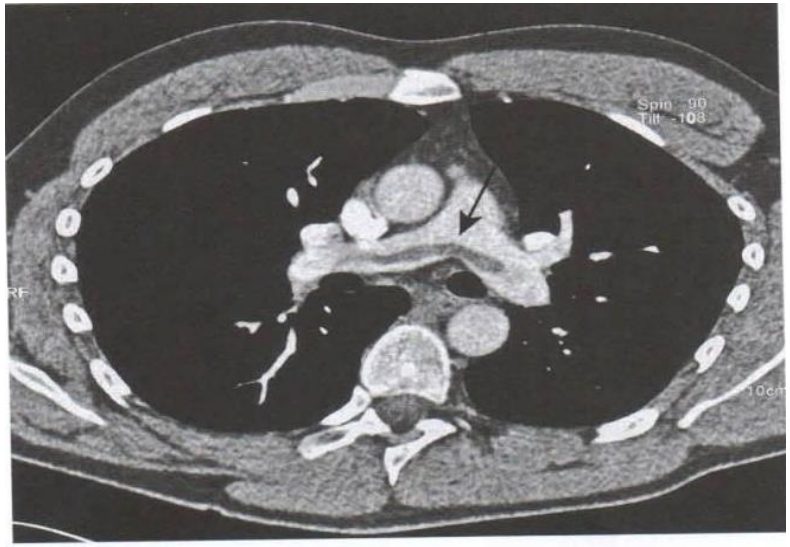
Diagnostic Tests

- **Imaging Studies**
  - CXR
  - V/Q Scans (major renal dysfunction or anaphylaxis to intravenous contrast)
  - **CTPA (CT- Pulmonary Angiography)**
  - Pulmonary Angiography
  - **Echocardiography**
  - **U/S on LL & pelvic vines**
- **Laboratory Analysis**
  - **D-Dimer**
  - **ABG's**
  - ECG
  - Cardiac troponin

CT Pulmonary Angiography

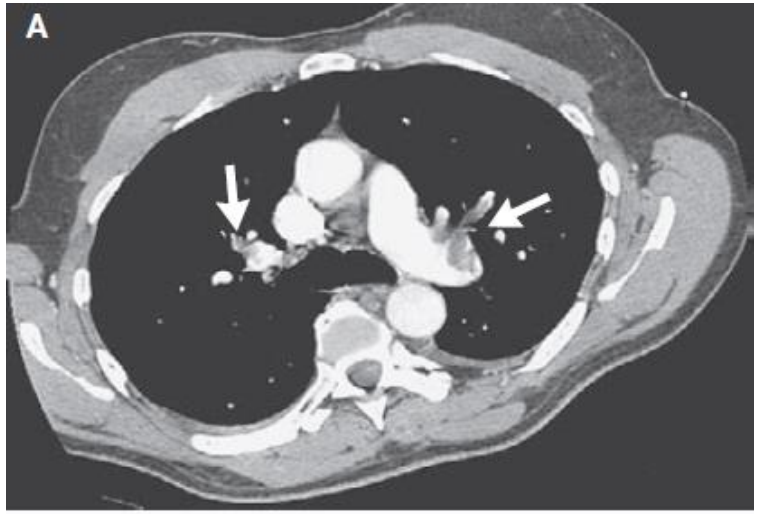
- **1st line diagnostic test**
- **Look for filling defects in pulmonary arteries.**
- **SDCT or MDCT** showing a thrombus up to the segmental level can be taken as adequate evidence of PE
- **Attractive to clinicians because**
  - It yields a ***Yes/No answer***
  - Can demonstrate ***an alternate diagnosis***
  - Is ***not affected by pulmonary disease***
- **SDCT** sensitivity and specificity rates **~70% & ~ 90%**
- **MDCT** sensitivity and specificity rates of **83% & 96%.**

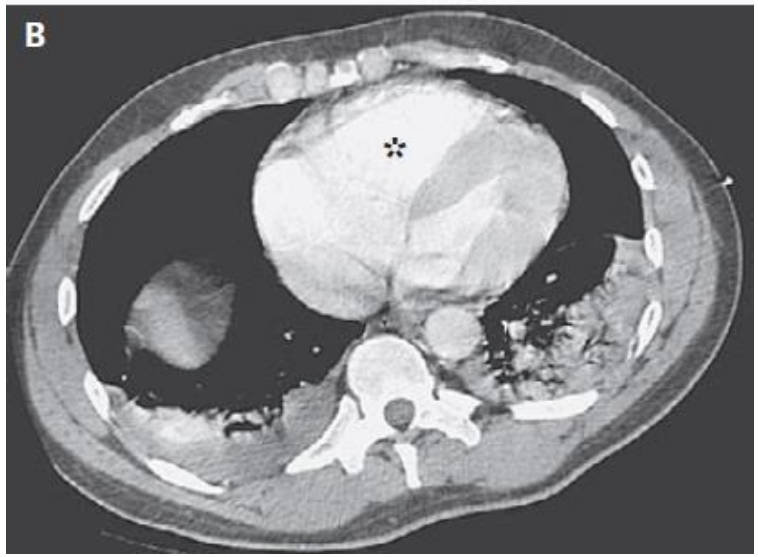




CT Pulmonary Angiography

- ***High clinical probability PE:***
  - ***Positive SDCT or MDCT → confirms PE***
  - ***Negative SDCT → further testing***
  - ***Negative MDCT → No further testing***
- ***Non-high clinical probability PE:***
  - ***Negative MDCT → excludes PE***
  - ***Negative SDCT + negative proximal US LL → excludes PE***



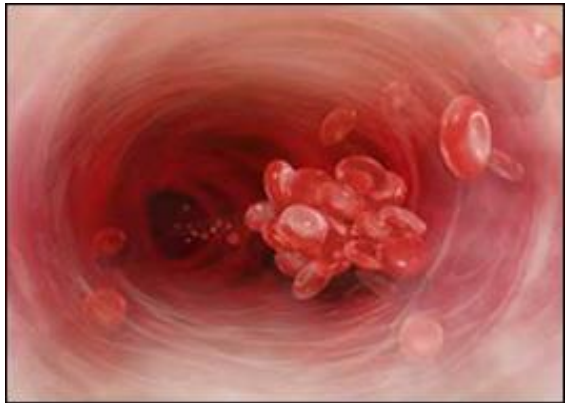


D-dimer

- A **degradation** product of crosslinked **fibrin.**
- D-dimer levels are **elevated in plasma** in the presence of an **acute clot (VTE & PE).**
- **Nonspecific**, since it may be **positive** in patients with ***infection, cancer, trauma, pregnancy, liver diseases and other inflammatory states*** and thus cannot inform decisions about treatment
- **Normal D- dimer level have a high negative predictive value (NPV) in excluding P.E→ Good negative test**

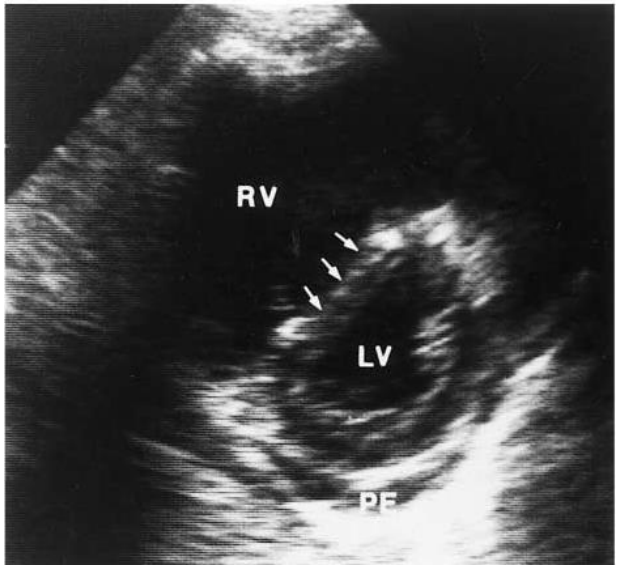
D-dimer

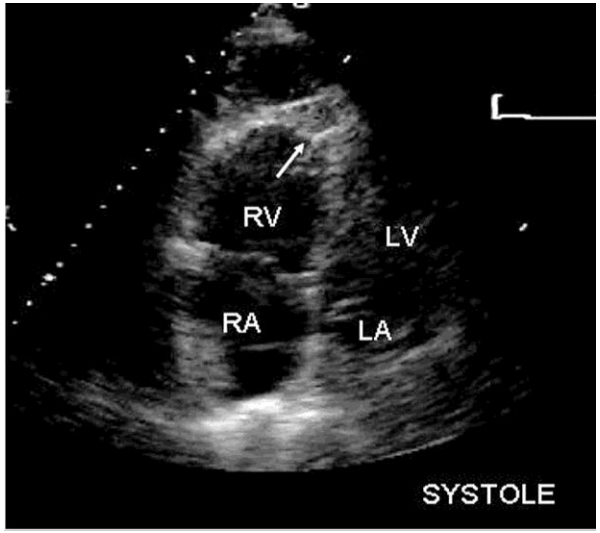
- d-dimer testing is best considered together with clinical probability:
  - **Negative ELISA-based d-dimer + low or moderate clinical pretest probability→ PE or DVT unlikely → no need for CTPA.**
  - **High clinical pretest probability → CTPA instead of d-dimer testing.**



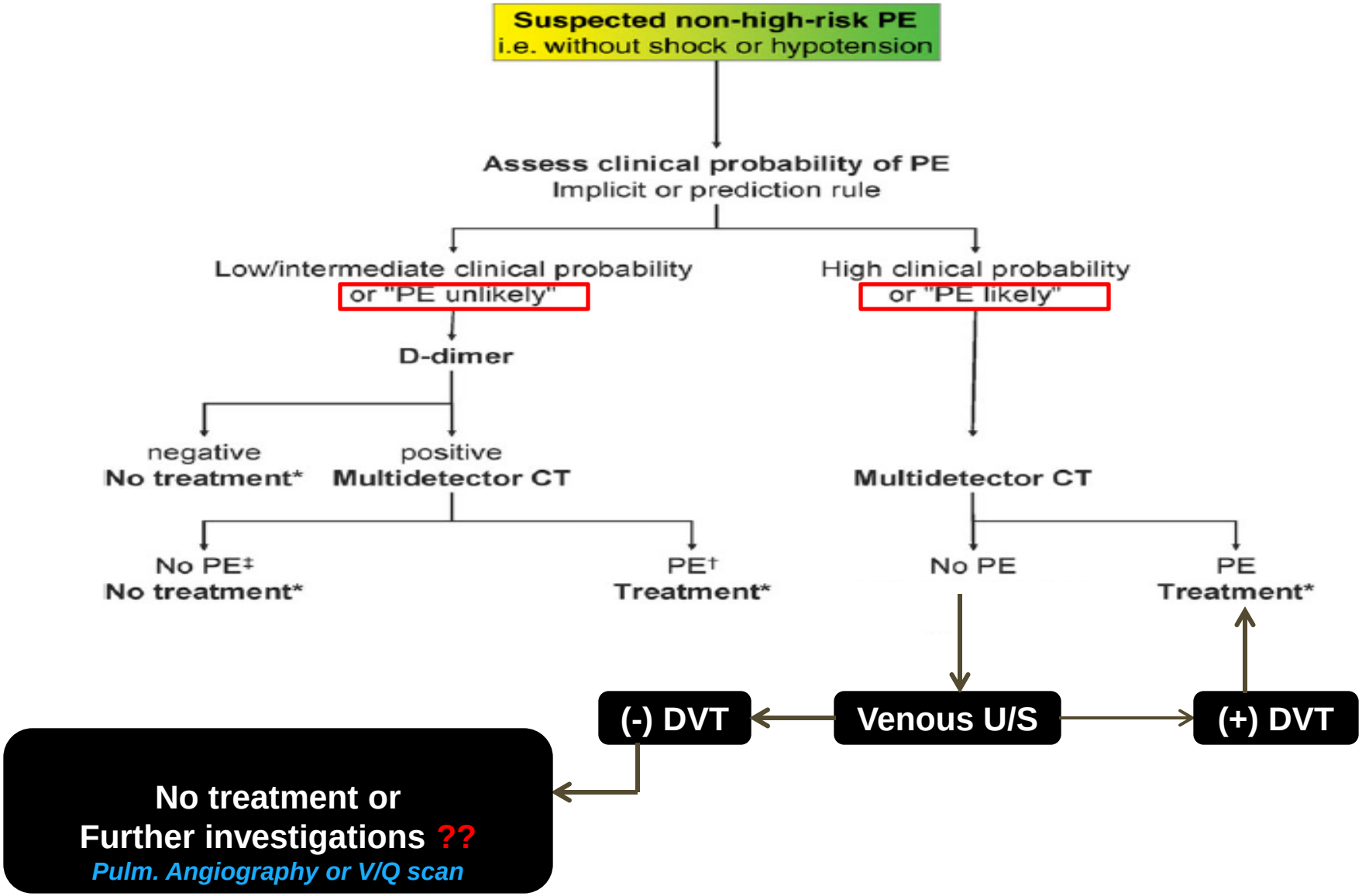
Echocardiography

- **Useful in ICU→ early therapy →until stabilization & further definitive testing patient**
- ***Findings:***
  - **RV enlargement or hypokinesis, especially free wall hypokinesis, with sparing of the apex (the McConnell sign)**
  - **Interventricular septal flattening and paradoxical motion toward the LV, resulting in a "D-shaped" LV in cross section**
  - **Tricuspid regurgitation & pulmonary HTN**
  - **Free-floating RV thrombus**

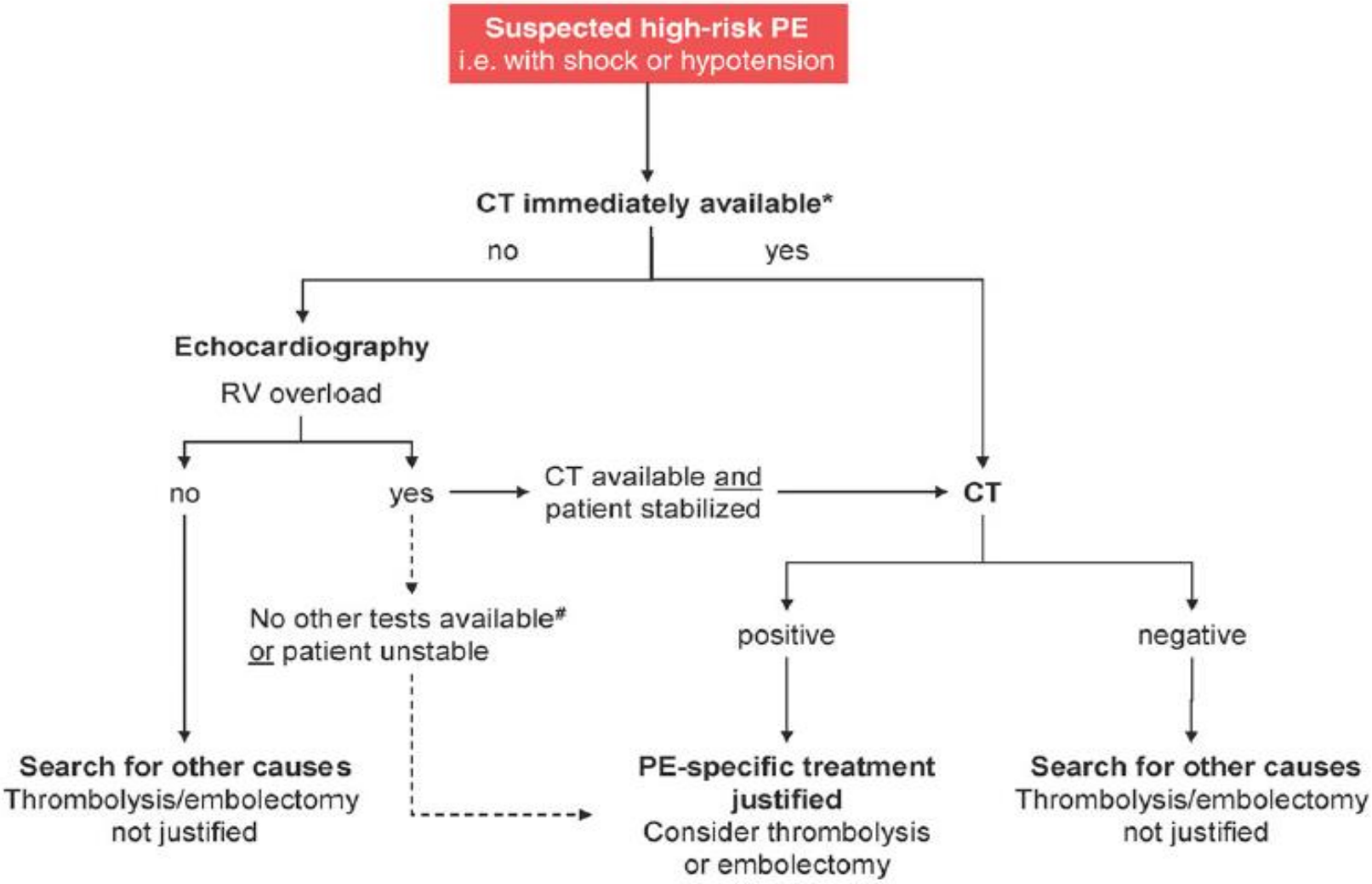




Suspected non-high-risk PE (without shock or hypotension)



Suspected high-risk PE (with shock or hypotension)



PE: Risk stratification

PE-related early MORTALITY RISK		RISK MARKERS			Potential treatment implications
		CLINICAL (shock or hypotension)	RV dysfunction	Myocardial injury	
HIGH >15%		+	(+)[a]	(+)[a]	Thrombolysis or embolectomy
NON HIGH	Intermediate 3–15%	–	+	+	Hospital admission
			+	–	
			–	+	
	Low <1%	–	–	–	Early discharge or home treatment

European Heart Journal (2008) 29, 2276–2315

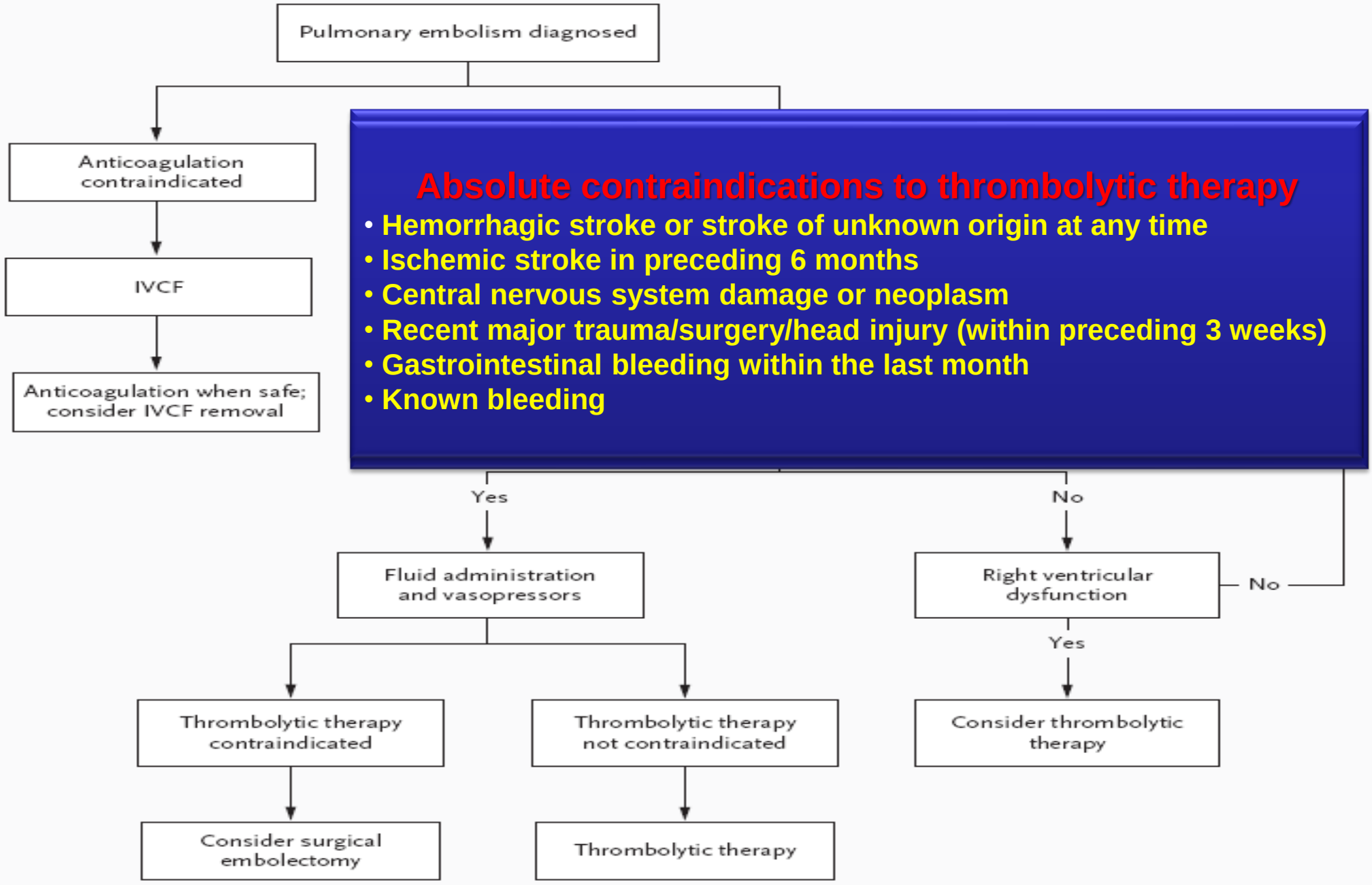
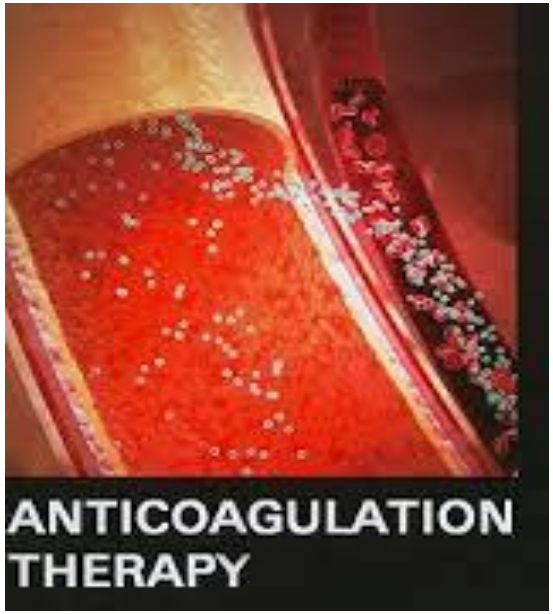


Figure 4. Treatment of Acute Pulmonary Embolism.

Anticoagulation Therapy

When? **as early as possible parenteral anticoagulants in**

- **High clinical suspicion for acute PE**
- **Intermediate clinical suspicion for acute PE if results >4 h.**
- **Low clinical suspicion for acute PE if results >24 h.**



Which parenteral form?

- **SC LMWH: Preferred in haemodynamically stable pts. with acute PE.**
  - ***Advantages over UFH***: greater bioavailability, more predictable dosing, SC delivery & a lower risk of heparin-induced thrombocytopenia (HIT)

Anticoagulation Therapy

- **IV UFH:**
  - **Preferred in hemodynamically unstable or renal failure (easy to monitor aPTT)**
  - **Increased risk of bleeding, morbidly obese (?SC absorption), significant edema or thrombolysis required.**
  - **aPTT checked Q6h until it is =1.5 to 2.5 X control**
- **Direct thrombin inhibitor (e.g., argatroban or lepirudin) for HIT**

Dose?

- **IV UFH: 80 units/kg bolus & start a drip at 18 units/kg/hr.**
- **Enoxaparin: 1 mg/kg/12h sc**
- **Fondaparinux: 7.5 mg/24h sc**
  (5mg→<50 kg & 10mg →>100kg)
- **Tinzaparin: 175 IU/kg/24h sc**
- **Dalteparin: 100 IU/kg/12h sc**

Anticoagulation Therapy

When to start oral anticoagulation?

- **Warfarin (Merivan,Coumadin)**
- **Initiated on day 1 or 2**
- **Bridging with heparin for least 5 days or until INR therapeutic(2-3)for 24 hrs.**
- **Initiated at 5mg/d ~3mg/d Target INR 2-3.**

Duration of treatment:

- **1st episode/reversible risk factor: least 3 months.**
- **Recurrent PE: 2 or more: Indefinite treatment.**

New oral anticoagulation

Rivaroxaban: Specific, direct factor Xa inhibitor

Out patient treatment of APE

Thrombolytic therapy

When? Documented PE with

- **Persistent hypotension(SBP<90mmHg)** **ONLY widely accepted indication.**
- **??High risk considered on case by case basis:**
  - Severe hypoxemia, Right ventricular dysfunction
  - Extensive embolic burden on CTPA
  - Free-floating right atrial or ventricular thrombus
  - Cardiopulmonary resuscitation

Which form & dose?

Streptokinase	250 000 IU as a loading dose over 30 min, followed by 100 000 IU/h over 12–24 h
	Accelerated regimen: 1.5 million IU over 2 h
Urokinase	4400 IU/kg as a loading dose over 10 min, followed by 4400 IU/kg/h over 12–24 h
	Accelerated regimen: 3 million IU over 2 h
rtPA	100 mg over 2 h
	or 0.6 mg/kg over 15 min (maximum dose 50 mg)

Thrombolytic therapy

- **Catheter-directed intrapulmonary arterial thrombolytic. X**
- **Stopping UFH during t-PA infusion &**
- **restarting it when aPTT is ≤80 sec after t-PA is complete.**
- **Significantly higher risk of bleeding compared to other therapies.**

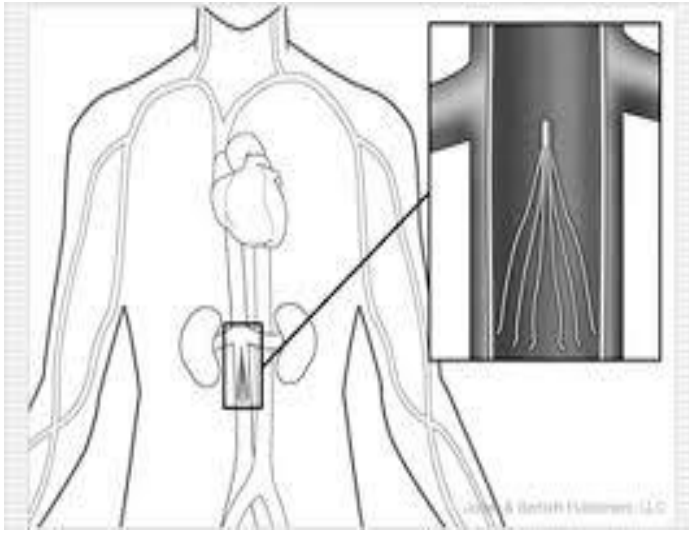
Inferior Vena Cava Filters

Indications:

- Absolute contraindication to anticoagulation.
- Complications developing during anticoagulation(e.g. severe internal bleeding).
- ?Recurrent embolism under adequate therapy

Outcome:

- Filters are effective in reducing the incidence of PE.
- They increase the subsequent incidence of DVT
- Do not increase overall survival



Embolectomy

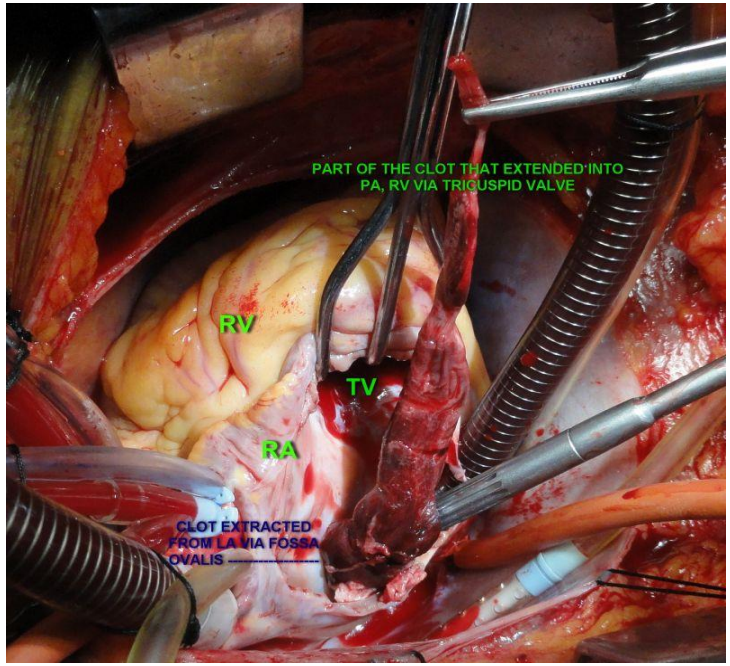
Surgical pulmonary embolectomy or

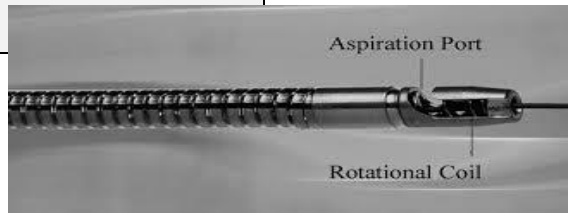
Percutaneous catheter embolectomy

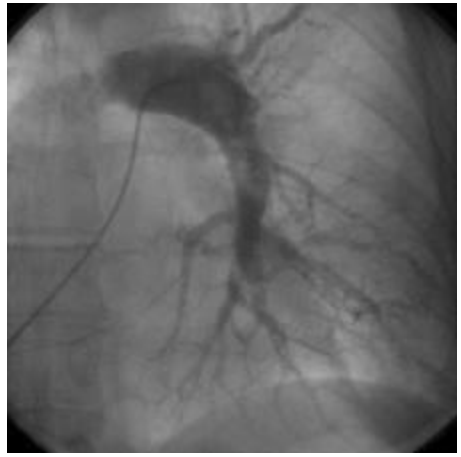
Indications:

- Documented PE with hemodynamically instability when thrombolytic therapy is contraindicated or failed.

- Which modality chosen depends on institutional expertise.







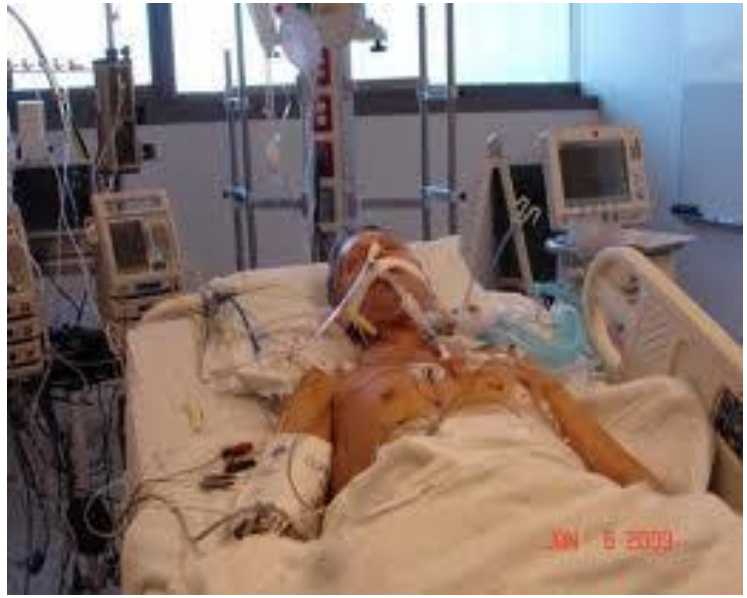
Hemodynamic and respiratory support

Indications:

- In suspected or confirmed PE presenting with shock or hypotension.

Respiratory support:

- Supplemental oxygen up to intubation and ventilation.



Hemodynamic support:

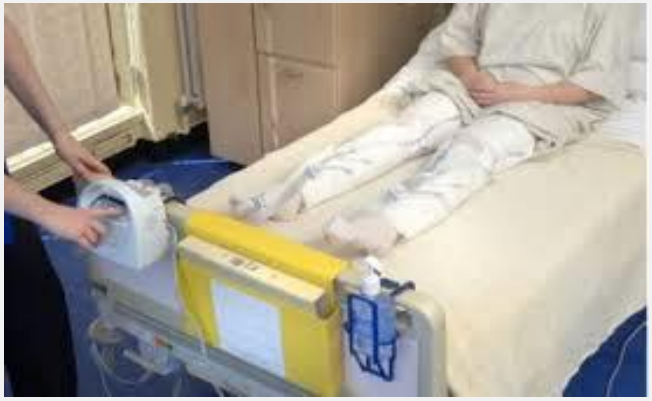
- In acute PE and hypotension(SBP<90mmHg)
- ***IV fluids:***

  Caution with placing increased strain on RV, worsening RHF.
- ***Vasopressor support:*** No improvement on IV fluids.

Prevention of VTE in ICU

- No routine ultrasound screening for DVT
- Pharmacological thromboprophylaxis:
  - LMWH 4000 – 6000 Anti-Xa once daily
  - *or* Low Dose Heparin (LDUH) 5000 U SC Twice a Day

    (bleeding or high risk of major bleeding,
  - Graduated Compression Stockings (GCS)
  - or Intermittent pneumatic compression (IPS)
- Early ambulation
- Optimise fluids



Conclusions

- VTE Common disorder, All ICU patients are at risk of VTE.
- VTE is a major cause of morbidity and mortality in patients admitted to the ICU
- Suspected Acute PE demands prompt diagnostic testing, assessment of risk factors, clinical probability & a validated clinical prediction score.
- Management of PE in the critically ill patient can be exceedingly complex.
- Anticoagulation is appropriate for most patients with VTE.
- Placement of an inferior vena cava filter when there is contraindication or complications developing from anticoagulation.

Conclusions

- **Thrombolytic therapy, catheter or surgical embolectomy, and pharmacologic support with vasoactive agents may be indicated in massive PE.**
- **Preventive efforts are crucial.**

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Thank you