DEEP VEIN THROMBOSIS (DVT) PULMONARY EMBOLISM (PE)

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Risk Factors for Venous Thromboembolism (ACQUIRED)

- Virchow's Triad(stasis, venous injury, hypercoagulable state)
- Prior history of thromboembolic disease
- Prior surgical history or trauma
- Immobilization/paralysis
- Cancer
- Estrogen Therapy
- Pregnancy/Postpartum
- Antiphospholipid antibody syndrome

Established or Potential Hypercoagulable States

- •Activated protein C resistance
- •Alpha-macroglobulin deficiency
- •Anticardiolipin antibiodies
- •Antithrombin deficiency
- •Dysfibrinogenemia
- •Factor V Leiden
- •Factor V deficiency/excess
- •Factor VII excess
- •Factor VIII excess
- •Factor XI excess
- •Heparin cofactor II deficiency
- •Hyperhomocysteinemia
- •Hyperfibrinogenemia
- •Lupus anticoagulants
- •PAI-1 excess
- •Plasminogen deficiency
- •Protein C deficiency
- •Protein S deficiency
- •Prothrombin G20210A
- •tPA deficiency
- •TFPI deficiency
- •Thrombomodulin deficiency

When to suspect a hypercoagulable state?

- Clots in low risk patient
- Clots in odd locations
- Recurrent clots
- Family history of clots
- Spontaneous abortion

Hypercoagulable states associated with BOTH Arterial and Venous Thrombosis

- Cancer
- Myeloproliferative syndromes
- Antiphospholipid antibodies (APA)
- Hyperhomocysteinemia
- Heparin-induced thrombocytopenia
- Nephrotic syndrome

DVT IN MALIGNANCY

- **A Presenting sign in:**
- Pancreatic cancer
- Prostate cancer

- **Late sign in:**
- Breast cancer
- Lung cancer
- Uterine cancer
- Brain cancer

Διαφορική Διάγνωση DVT

- Bakers Cyst
- Cellulitis
- Gout – if really bad it can sometimes look like a cellulitis
- If bilateral think about CHF, Nephrotic syndrome, liver failure, venous insufficiency, pregnancy or pelvic mass, vasodilators esp nifedipine

PATHOPHYSIOLOGY IN PE

- Key consequences are hemodynamic
- Emboli abruptly increase pulmonary vascular resistance to a level of afterload which cannot be matched by the RV.
- Sudden death may occur usually in the form of electromechanical dissociation
- These effects depend:
- On the extent of the obstruction
- On the duration over which obstruction accumulates
- On the preexisting cardiopulmonary state of patient

Symptoms of P.E.

- Dyspnea
- Pleuritic pain
- Cough
- Hemoptysis (blood tinged/streaked/ pure blood)

Signs of P.E.

- **Tachypnea**
- Rales
- **Tachycardia**
- **Hypoxia**
- S4
- Accentuated pulmonic component of S2
- Fever: < 38.5 C

Signs in Massive P.E.

- “Massive PE”: hemodynamic instability with SBP <90 or a drop in baseline SBP by >/=40mmHg
- Signs as before **PLUS**:
  - Acute right heart failure
    - Elevated J.V.P.
    - Right-sided S3
    - Parasternal lift

Diagnostic algorithm-Clinical pretest probability

Wells' Criteria for Assessment of Pretest Probability

The Wells Criteria for assessing pretest probability is important for diagnosing DVT and PE. Below describes the criteria and scoring system:

Criteria	Points
Suspected DVT	3.0
An alternative diagnosis is less likely than PE	3.0
Heart rate > 100 beats per minute	1.5
Immobilization or surgery in the previous four weeks	1.5
Previous DVT or PE	1.5
Hemoptysis	1.0
Malignancy (on treatment, treated in the past six months or palliative)	1.0

Score range	Mean probability of PE	% with this score	Interpretation of risk
<2 points	3.6%	40	Low
2 to 6 points	20.5%	53	Moderate
>6 points	66.7%	7	High

Pulmonary Embolism Severity Index

Estimates the risk of 30-day mortality from PE

Table 1 Points assigned to prognostic variables in the prognostic model

Prognostic variables	Points assigned
Demographics	
Age (years)	Age
Male sex	+10
Comorbid conditions	
Cancer	+30
Heart failure	+10
Chronic lung disease	+10
Clinical findings	
Pulse ≥110 per minute	+20
Systolic blood pressure <100 mmHg	+30
Respiratory rate ≥30 per minute	+20
Temperature < 36°C	+20
Altered mental status[a]	+60
Arterial oxygen saturation <90%[b]	+20

Class (Risk)	Score/Points	30-Day Mortality
I (Very Low)	<66	0%
II (Low)	66-85	1%
III (Intermed)	86-105	3.1%
IV (High)	106-125	10.4%
V (Very High)	>125	24.4%

Total point score obtained by summing patients age in years and the points for each applicable characteristic

Aujesky D et al, Eur Heart J 2006; 27:476-481.

Simplification of the Pulmonary Embolism Severity Index for Prognostication in Patients With Acute Symptomatic Pulmonary Embolism

David Jiménez, MD, PhD; Drahomir Aujesky, MD; Lisa Moores, MD; Vicente Gómez, MD; José Luis Lobo, MD, PhD; Fernando Uresandi, MD, PhD; Remedios Otero, MD, PhD; Manuel Monreal, MD, PhD; Alfonso Muriel, MSc; Roger D. Yusen, MD; for the RIETE Investigators

Simplified Version
(Score > 1 = high risk)
- age > 80 y
- history of cancer
- COPD
- pulse ≥110 bpm
- BP < 100 mmHg
- art O2 sat < 90%

Patients in Simplified PESI:
Low risk 30-day mortality of 1%
High risk 30-day mortality of 10.9%

Estimates the risk of 30-day mortality from PE

Arch Intern Med 2010; 170: 1383

Lab & Radiologic Findings in P.E.

- ABG
- BNP
- Cardiac Enzymes: Troponin
- D-dimer
- EKG
- CXR
- Ultrasound
- V/Q Scan
- Angiography

ABG

- Hypoxemia
- Hypocapnia (low CO2)
- Respiratory Alkalosis
- *Massive PE: hypercapnia, mix resp and metabolic acidosis (inc lactic acid)*
- Patients with RA **pulse ox readings <95%** are at increased risk of in-hospital complications, resp failure, cardiogenic shock, death

BNP(beta natruretic peptide)

- Insensitive test
- Patient's with PE have higher levels than pts without, but not ALL patients with PE have high BNP
- **Good prognostic value measure**: if **BNP >90** associated with adverse clinical outcomes (death, CPR, mechanical vent, pressure support, thrombolysis, embolectomy)

Troponin

- High in 30-50% of pts with mod to large PE
- Prognostic value if combined pro-NT BNP
  - Trop I >0.07 + NT-proBNP >600 = high 40 day mortality

D-dimers

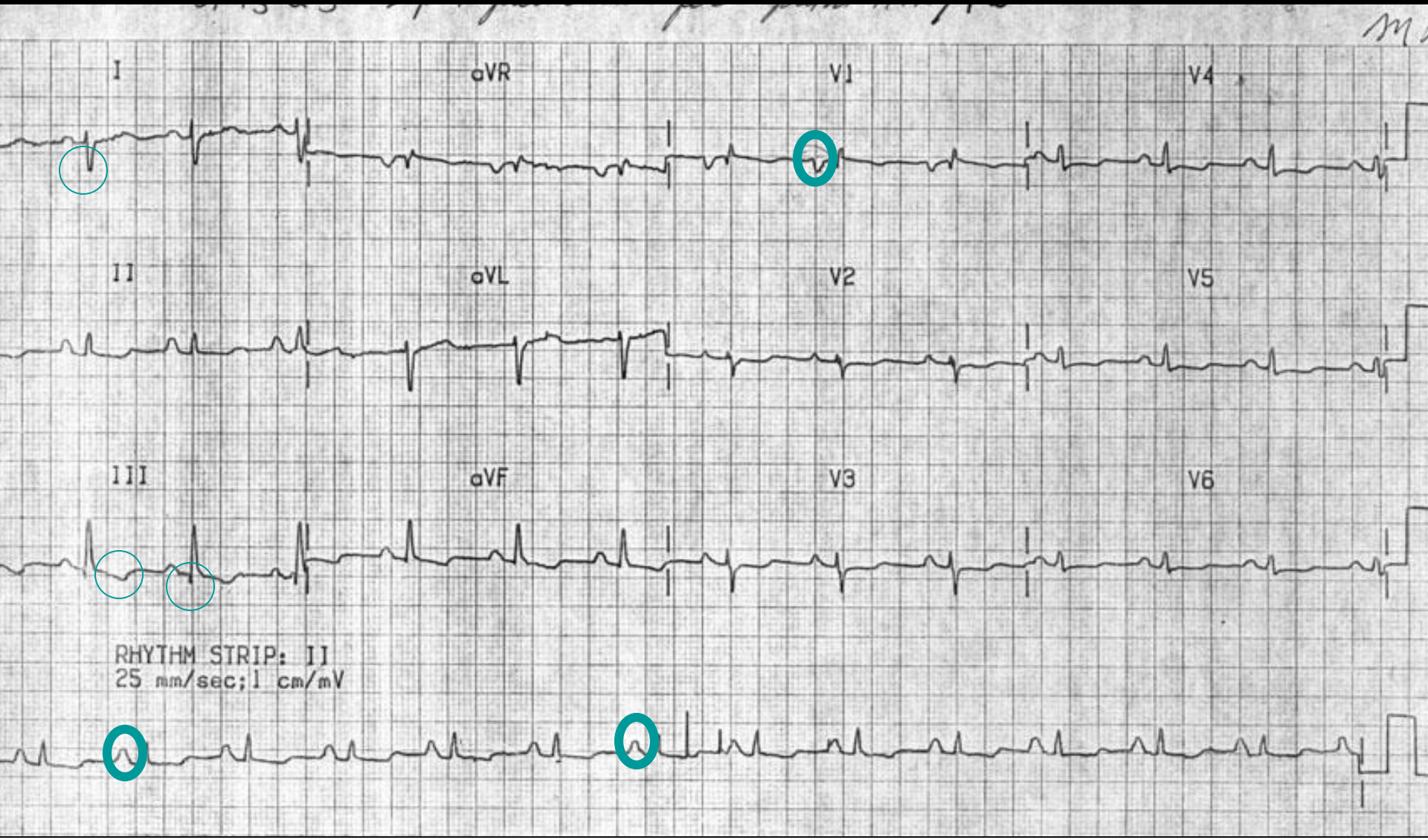
- Degradation product of fibrin
- >500 is abnormal
- Sensitivity: High, 95% of PE pts will be positive
- Specificity: Low
- Negative Predictive Value: Excellent

EKG

- Most Common finding on EKG:
  - Nonspecific ST-segment and T-wave changes
  - Sinus Tachycardia
- Historical abnormality suggestive of PE
  - S1Q3T3
  - Right ventricular strain
  - New incomplete RBBB

RAD

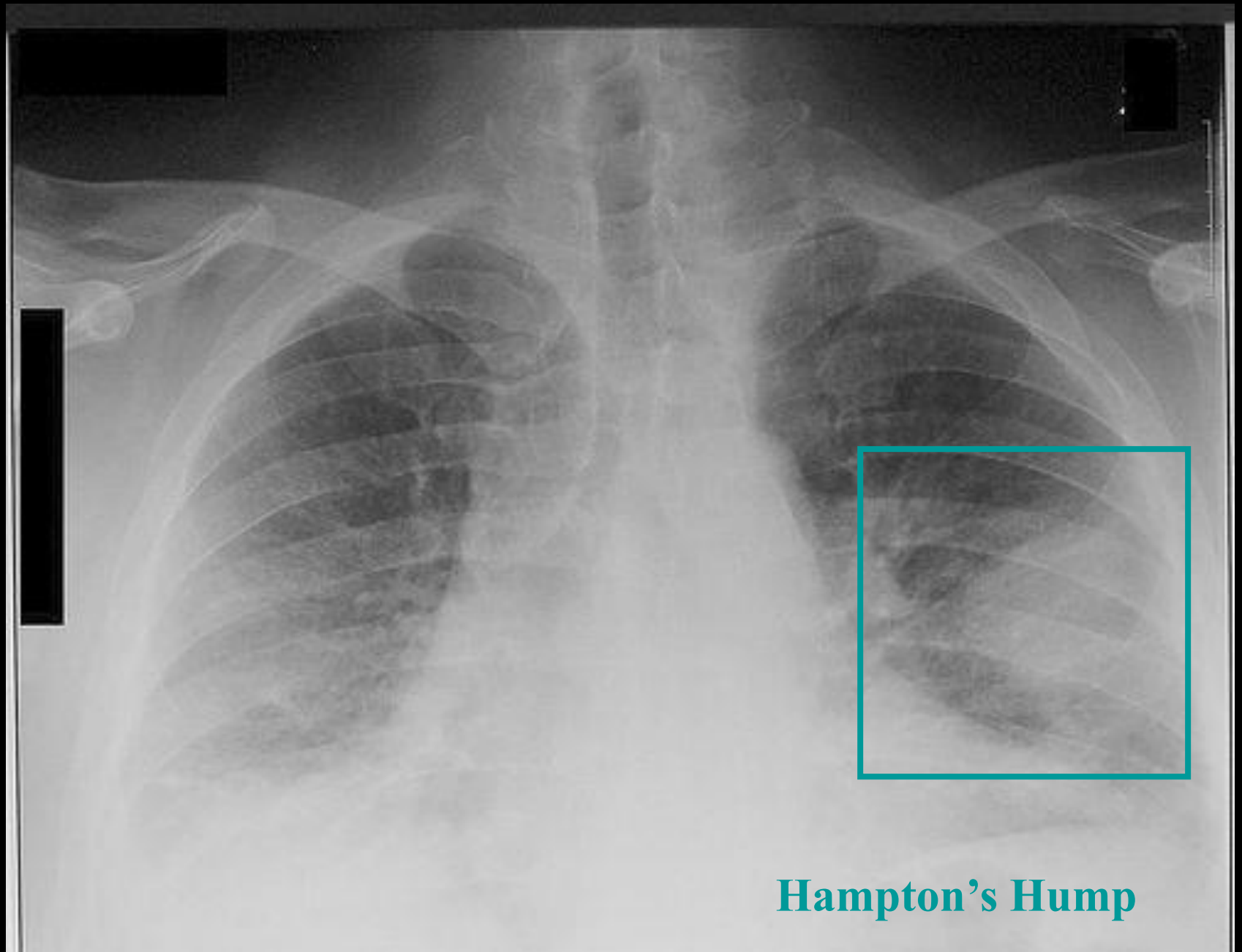
Right Atrial Enlargement



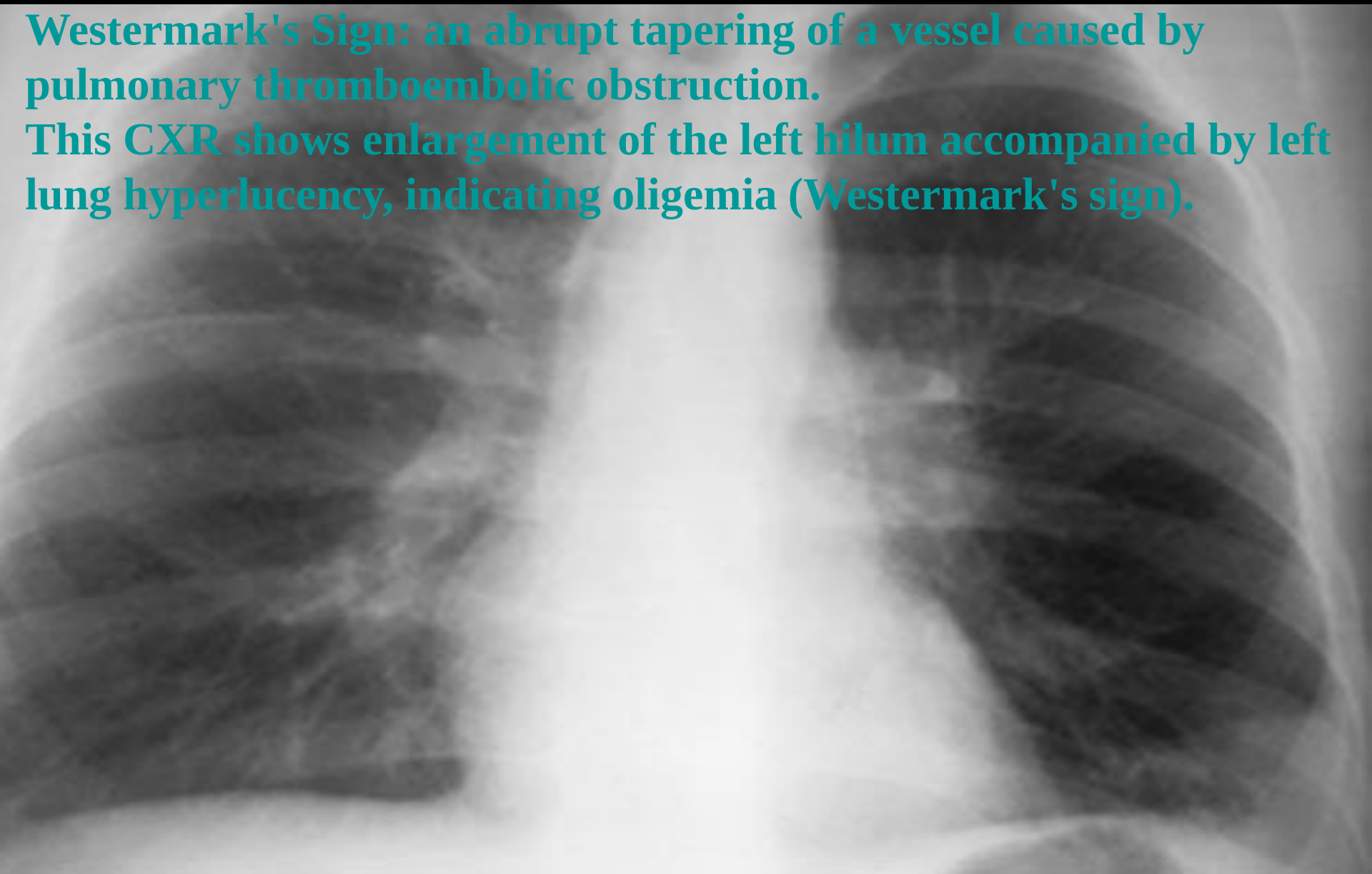
Radiology Findings in P.E.

- **CXR**:
  - Normal
  - Atelectasis and/or pulmonary parenchymal abnormality
  - Pleural Effusion
  - Cardiomegaly

What's This???



How About This???



Westermark's Sign: an abrupt tapering of a vessel caused by pulmonary thromboembolic obstruction.
This CXR shows enlargement of the left hilum accompanied by left lung hyperlucency, indicating oligemia (Westermark's sign).

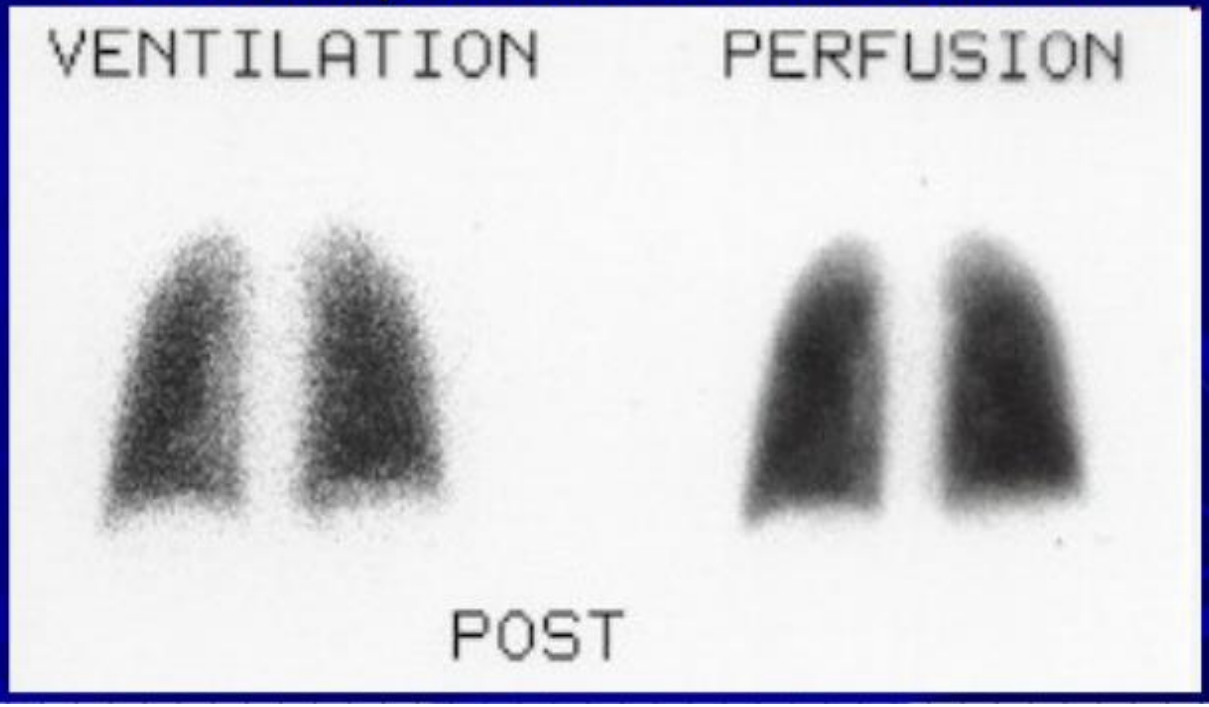
V/Q Scan:

- Results: High, Intermediate, Low Probability
- Best if combined with Clinical Probability
  - **High** Clinical Prob + **High** Prob VQ= **95% likelihood of having a P.E.**
  - **Low** Clinical Prob + **Low** Prob VQ= **4% likelihood of having a P.E.**

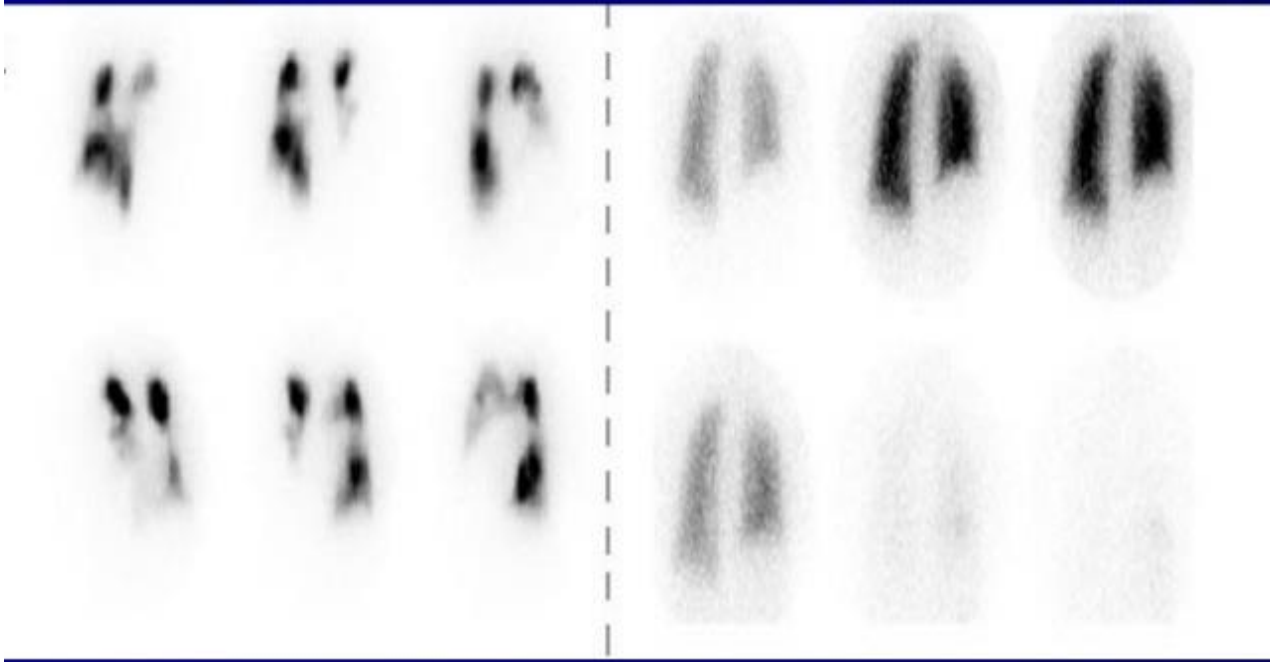
(2) Ventilation-perfusion scintigraphy

- It has to be correlated with chest x-ray.
- There are 3 V/Q lung scan patterns:

1. A normal perfusion scan rule out PE:



2. High probability scan:

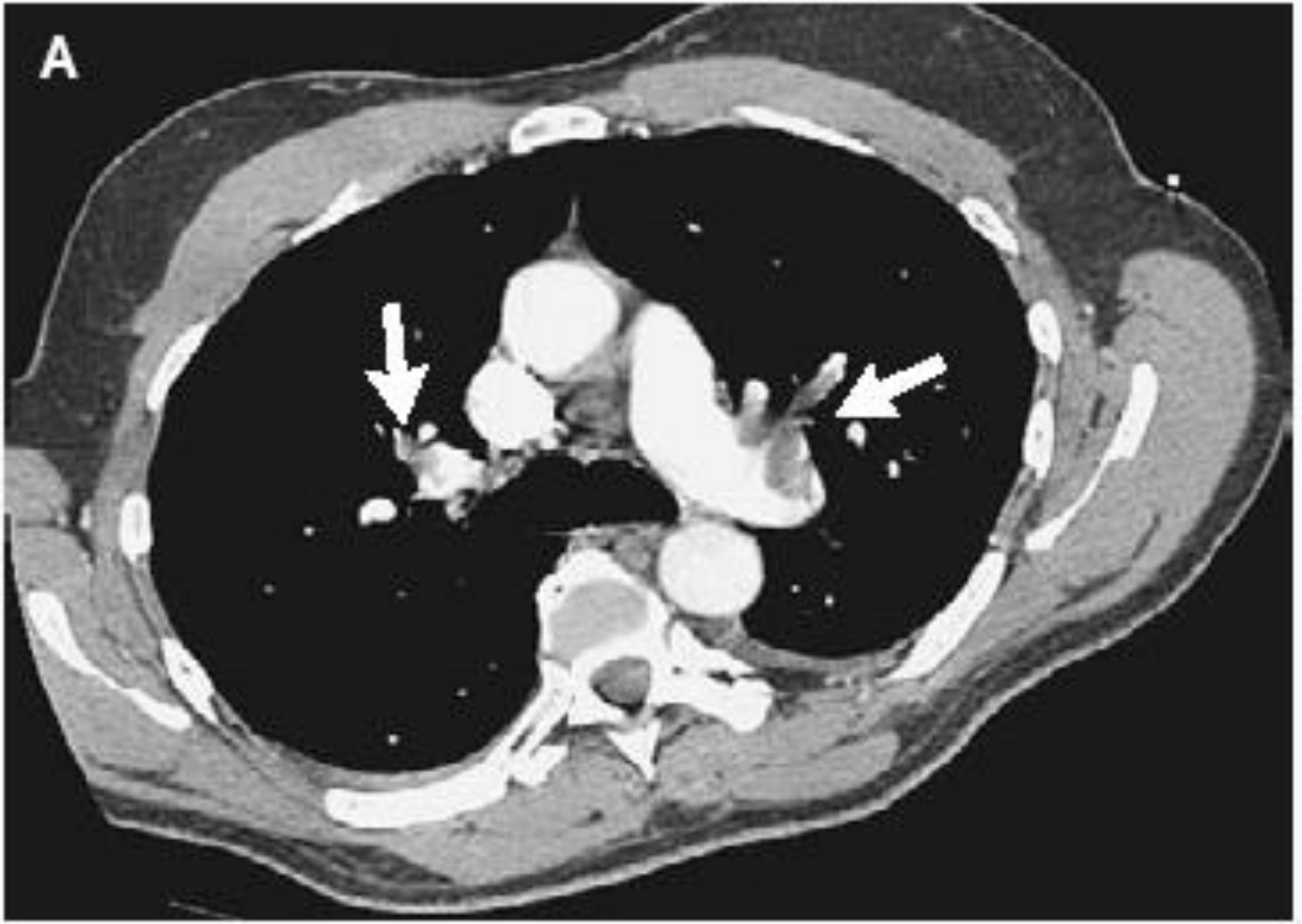


Lower Extremity Ultrasounds

- If DVT found then treatment is same if patient has a P.E.
- Disadvantage:
  - If negative, patients with PE may be missed
  - If false positive (3%), unnecessary intervention

CT PULMONARY ANGIOGRAPHY

- Widely used
- Institution dependent
- Sensitivity (83%)
- Specificity (96%): if negative, very low likelihood that patient has P.E.


A

Echocardiogram

- Increased Right Ventricle Size
- Decreased Right Ventricular Function
- Tricuspid Regurgitation

Rarely:

- RV thrombus
- Regional wall motion abnormalities that spare the right ventricle apex (McConnell's Sign)

Hypercoagulability Work Up

- No consensus on who to test
- Increased likelihood if:
  - Age <50y/o without immediate identifiable risk factors (idiopathic or provoked)
  - Family history
  - Recurrent clots
  - If clot is in an unusual site (portal, hepatic, mesenteric, cerebral)
  - Unprovoked upper extremity clot (no catheter, no surgeries)
  - Patient's with warfarin induced skin necrosis (they may have protein C deficiency

Hypercoagulability Work Up

- Protein C/S deficiency
- Factor V leiden deficiency
- AntiThrombin III deficiency
- Prothrombin 20210 mutation
- Antiphospholipid antibody
- High Homocysteine

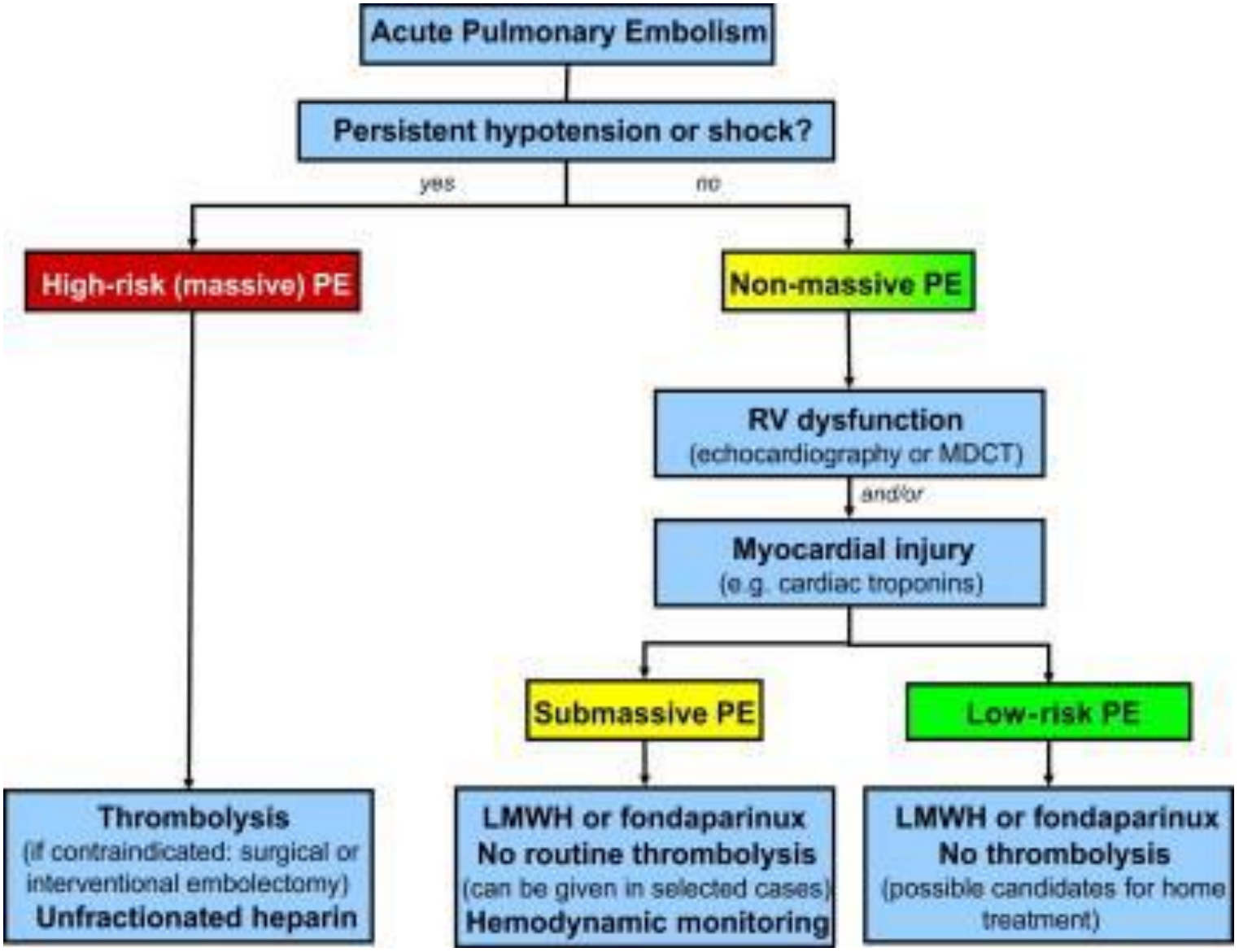
Most Common Cause of Congenital Hypercoagulablity

- Protein C resistance d/t Factor V leiden mutation

Initial Treatment of Pulmonary Embolism

- Anticoagulant treatment should be administered to all patients with high or intermediate clinical probability of acute PE, without awaiting definitive confirmation by imaging procedures

ΘΕΡΑΠΕΥΤΙΚΟΣ ΑΛΓΟΡΙΘΜΟΣ PE



- **Chest. 2016;149(2):315-352.**

Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report

Initial Treatment of PE

- Unfractionated heparin is the preferred mode of initial anticoagulation for patients with severe renal impairment (creatinine clearance <20–30 mL/min)
- for those at high risk of bleeding
- for high-risk hypotensive patients
- as a rule, for extremely overweight, underweight, or old patients

Initial Treatment of Pulmonary Embolism with the exception of these circumstances

- LMWH or fondaparinux is given subcutaneously at weight-adjusted doses

- Anticoagulation with unfractionated heparin or LMWH/fondaparinux should be continued for at least 5 days

Initial treatment of PE

- Oral anticoagulants (vitamin K antagonists) should be initiated as soon as possible in hemodynamically stable patients, preferably on the same day as heparin

- Parenteral anticoagulation can be stopped as soon as the international normalized ratio (INR) has been in the therapeutic range (between 2.0 and 3.0) on 2 consecutive days.

For VTE and no cancer, as long-term anticoagulant therapy

- dabigatran (Grade 2B) Pradaxa
- rivaroxaban (Grade 2B) Xarelto
- apixaban (Grade 2B), or Eliquis
- vitamin K antagonist (VKA) therapy

For VTE and Cancer as long-term anticoagulant therapy

- LMWH over VKA (Grade 2B),
- dabigatran (Grade 2C)
- rivaroxaban (Grade 2C)
- apixaban (Grade 2C), or

First VTE that is an unprovoked proximal DVT of the leg or PE and who have a low or moderate bleeding risk

- Extended anticoagulant therapy (no scheduled stop date) over 3 months of therapy (Grade 2B),
- For high bleeding risk , 3 months of anticoagulant therapy over extended therapy (no scheduled stop date)

Proximal DVT of the leg or PE provoked by surgery

- Treatment with anticoagulation for 3 months over (i) treatment of a shorter period (Grade 1B), (ii) treatment of a longer time-limited period (eg, 6, 12, or 24months) (Grade 1B), or (iii) extended therapy (no scheduled stop date) (Grade 1B).

Proximal DVT of the leg or PE provoked by a nonsurgical transient risk factor

- Treatment with anticoagulation for 3months over (i) treatment of a shorter period (Grade1B) and (ii) treatment of a longer time-limited period (eg, 6, 12, or 24months) (Grade 1B).

Duration of Anticoagulation

- Patients who have pulmonary embolism and preexisting irreversible risk factors, such as deficiency of antithrombin III, protein S and C, factor V Leiden mutation, or the presence of antiphospholipid antibodies, should be placed on long-term anticoagulation.

Duration of AC Treatment Based on Type of VTE

Type of VTE	Recommended Duration of Treatment 2012	Recommended Duration of Treatment 2016
Proximal DVT of the leg or PE provoked by surgery	3 months	3 months
DVT of the leg or PE provoked by a nonsurgical transient risk factor	3 months	3 months
Isolated distal DVT of the leg provoked by surgery or nonsurgical transient risk factor	3 months	3 months
Unprovoked PE or DVT of the leg	At least 3 months	At least 3 months
Pt's first DVT that is an unprovoked proximal DVT of the leg or PE	At least 3 months	Extended therapy (no scheduled stop date)
In patients with a second unprovoked VTE with a low bleeding risk	Recommend extended therapy	Extended therapy (no scheduled stop date)
In patients with a second unprovoked VTE with a moderate bleeding risk	Suggest extended therapy	At least 3 months
In patients with a second unprovoked VTE with a high bleeding risk	Suggest 3 months	3 months
Patients with DVT of the leg and active cancer w/ or w/o high risk of bleeding	Extended therapy	Extended therapy (no scheduled stop date)

Thrombolytic Therapy

- Thrombolytic therapy is clearly indicated for hemodynamically unstable patient who lack contraindication
- In only one randomized thrombolysis trial with clinical endpoints, early thrombolytic treatment given to normotensive patients with evidence of RV dysfunction significantly reduced the need for emergency escalation of therapy during the hospital stay

Thrombolytic Therapy

- Overall, >90% of patients with PE appear to respond favorably to thrombolysis as indicated by clinical and echocardiographic improvement within the first 36 h.
- The greatest benefit is observed when treatment is initiated within 48 h of symptoms onset, but thrombolysis can still be useful in patients who have had symptoms for 6–14 days.

Θρομβολυτικά θεραπευτικά πρωτόκολλα

Agents and regimens	
Streptokinase[a]	
250 000 U as a loading dose over 30 min, followed by 100 000 U/h over 12–24 h	
Accelerated regimen: 1.5 million IU over 2 h[b]	
Urokinase[a,c]	
4400 U per kg of body weight as a loading dose over 10 min, followed by 4400 U/kg/h over 12–24 h	
Accelerated regimen: 3 million U over 2 h[b]	
Alteplase[a]	
100 mg over 2 h[d]	
Accelerated regimen: 0.6 mg/kg for 15 min	
Reteplase[a,e]	
Two bolus injections of 10 U 30 min apart	
Tenecteplase[f]	
30–50 mg bolus for 5–10 s adjusted for body weight	
<60 kg	30 mg
≥60 to <70 kg	35 mg
≥70 to <80 kg	40 mg
≥80 to <90 kg	45 mg
≥90 kg	50 mg

Contraindications
Absolute
History of haemorrhagic stroke or stroke of unknown origin
Ischaemic stroke in previous 6 months
Central nervous system neoplasms
Major trauma, surgery, or head injury in previous 3 weeks
Relative
Transient ischaemic attack in previous 6 months
Oral anticoagulation
Pregnancy or first postpartum week
Non-compressible puncture sites
Traumatic resuscitation
Refractory hypertension (systolic blood pressure >180 mmHg)
Advanced liver disease
Infective endocarditis
Active peptic ulcer

Indications for Vena Cava Interruption

- 1. Contraindication to anticoagulation
- 2. Recurrent emboli on adequate Tx
- 3. Serious bleeding on anticoagulation
- 4. Massive pulmonary embolism
- 5. Psychosocial reasons

Surgical Treatment

- Pulmonary embolectomy is a recommended therapeutic option in patients with high-risk PE in whom there are absolute contraindications to thrombolysis, or if thrombolysis has failed.

- Recent technical advances in transportable extracorporeal assist systems, and particularly the timely early involvement of the cardiac surgeon as part of an interdisciplinary approach to high-risk PE before hemodynamic collapse, have contributed to improved postoperative outcomes and case fatality rates as low as 23%.

Interventional Treatment
In case of absolute contraindications to thrombolysis:

- Thrombus fragmentation
- Rheolytic thrombectomy
- Suction thrombectomy
- Rotational thrombectomy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HELLENIC COAST GUARD