DEEP VEIN THROMBOSIS (DVT) PULMONARY EMBOLISM (PE)
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 antibodies
- 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
• Hemothysis (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
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:

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected DVT</td>
<td>3.0</td>
</tr>
<tr>
<td>An alternative diagnosis is less likely than PE</td>
<td>3.0</td>
</tr>
<tr>
<td>Heart rate &gt; 100 beats per minute</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilization or surgery in the previous four weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Previous DVT or PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1.0</td>
</tr>
<tr>
<td>Malignancy (on treatment, treated in the past six months or palliative)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Score range</th>
<th>Mean probability of PE</th>
<th>% with this score</th>
<th>Interpretation of risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 points</td>
<td>3.6%</td>
<td>40</td>
<td>Low</td>
</tr>
<tr>
<td>2 to 6 points</td>
<td>20.5%</td>
<td>53</td>
<td>Moderate</td>
</tr>
<tr>
<td>&gt;6 points</td>
<td>66.7%</td>
<td>7</td>
<td>High</td>
</tr>
</tbody>
</table>
**Pulmonary Embolism Severity Index**

*Estimates the risk of 30-day mortality from PE*

### Table 1: Points assigned to prognostic variables in the prognostic model

<table>
<thead>
<tr>
<th>Prognostic variables</th>
<th>Points assigned</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>Age</td>
</tr>
<tr>
<td>Male sex</td>
<td>+10</td>
</tr>
<tr>
<td><strong>Comorbid conditions</strong></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>+30</td>
</tr>
<tr>
<td>Heart failure</td>
<td>+10</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>+10</td>
</tr>
<tr>
<td><strong>Clinical findings</strong></td>
<td></td>
</tr>
<tr>
<td>Pulse ≥110 per minute</td>
<td>+20</td>
</tr>
<tr>
<td>Systolic blood pressure &lt; 100 mmHg</td>
<td>+30</td>
</tr>
<tr>
<td>Respiratory rate ≥ 30 per minute</td>
<td>+20</td>
</tr>
<tr>
<td>Temperature &lt; 36°C</td>
<td>+20</td>
</tr>
<tr>
<td>Altered mental status$^a$</td>
<td>+60</td>
</tr>
<tr>
<td>Arterial oxygen saturation &lt; 90%$^b$</td>
<td>+20</td>
</tr>
</tbody>
</table>

### 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.

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

David Jiménez, MD, PhD; Draholmir 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???

Hampton’s Hump
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.
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 Hypercoagulability

- 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

Acute Pulmonary Embolism

Persistent hypotension or shock?

yes

High-risk (massive) PE

Thrombolysis
(if contraindicated: surgical or interventional embolectomy)
Unfractionated heparin

no

Non-massive PE

RV dysfunction
(echocardiography or MDCT)
and/or

Myocardial injury
(e.g. cardiac troponins)

Submassive PE

LMWH or fondaparinux
No routine thrombolysis
(can be given in selected cases)
Hemodynamic monitoring

Low-risk PE

LMWH or fondaparinux
No thrombolysis
(possible candidates for home treatment)
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 (e.g., 6, 12, or 24 months) (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 3 months over (i) treatment of a shorter period (Grade 1B) and (ii) treatment of a longer time-limited period (e.g., 6, 12, or 24 months) (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.
<table>
<thead>
<tr>
<th>Type of VTE</th>
<th>Recommended Duration of Treatment 2012</th>
<th>Recommended Duration of Treatment 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal DVT of the leg or PE provoked by surgery</td>
<td>3 months</td>
<td>3 months</td>
</tr>
<tr>
<td>DVT of the leg or PE provoked by a nonsurgical transient risk factor</td>
<td>3 months</td>
<td>3 months</td>
</tr>
<tr>
<td>Isolated distal DVT of the leg provoked by surgery or nonsurgical transient risk factor</td>
<td>3 months</td>
<td>3 months</td>
</tr>
<tr>
<td>Unprovoked PE or DVT of the leg</td>
<td>At least 3 months</td>
<td>At least 3 months</td>
</tr>
<tr>
<td>Pt’s first DVT that is an unprovoked proximal DVT of the leg or PE</td>
<td>At least 3 months</td>
<td>Extended therapy (no scheduled stop date)</td>
</tr>
<tr>
<td>In patients with a second unprovoked VTE with a low bleeding risk</td>
<td>Recommend extended therapy</td>
<td>Extended therapy (no scheduled stop date)</td>
</tr>
<tr>
<td>In patients with a second unprovoked VTE with a moderate bleeding risk</td>
<td>Suggest extended therapy</td>
<td>At least 3 months</td>
</tr>
<tr>
<td>In patients with a second unprovoked VTE with a high bleeding risk</td>
<td>Suggest 3 months</td>
<td>3 months</td>
</tr>
<tr>
<td>Patients with DVT of the leg and active cancer w/ or w/o high risk of bleeding</td>
<td>Extended therapy</td>
<td>Extended therapy (no scheduled stop date)</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Agents and regimens</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Streptokinase</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td><strong>Absolute</strong></td>
</tr>
<tr>
<td>250 000 U as a loading dose over 30 min, followed by 100 000 U/h over 12–24 h</td>
<td>History of haemorrhagic stroke or stroke of unknown origin</td>
</tr>
<tr>
<td>Accelerated regimen: 1.5 million IU over 2 h&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Ischaemic stroke in previous 6 months</td>
</tr>
<tr>
<td><strong>Urokinase</strong>&lt;sup&gt;a,c&lt;/sup&gt;</td>
<td>Central nervous system neoplasms</td>
</tr>
<tr>
<td>4400 U per kg of body weight as a loading dose over 10 min, followed by 4400 U/kg/h over 12–24 h</td>
<td>Major trauma, surgery, or head injury in previous 3 weeks</td>
</tr>
<tr>
<td>Accelerated regimen: 3 million U over 2 h&lt;sup&gt;b&lt;/sup&gt;</td>
<td><strong>Relative</strong></td>
</tr>
<tr>
<td><strong>Alteplase</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Transient ischaemic attack in previous 6 months</td>
</tr>
<tr>
<td>100 mg over 2 h&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Oral anticoagulation</td>
</tr>
<tr>
<td>Accelerated regimen: 0.6 mg/kg for 15 min</td>
<td>Pregnancy or first postpartum week</td>
</tr>
<tr>
<td><strong>Reteplase</strong>&lt;sup&gt;a,n&lt;/sup&gt;</td>
<td>Non-compressible puncture sites</td>
</tr>
<tr>
<td>Two bolus injections of 10 U 30 min apart</td>
<td>Traumatic resuscitation</td>
</tr>
<tr>
<td><strong>Tenecteplase</strong>&lt;sup&gt;f&lt;/sup&gt;</td>
<td>Refractory hypertension (systolic blood pressure &gt;180 mmHg)</td>
</tr>
<tr>
<td>30–50 mg bolus for 5–10 s adjusted for body weight</td>
<td>Advanced liver disease</td>
</tr>
<tr>
<td>&lt; 60 kg</td>
<td>Infective endocarditis</td>
</tr>
<tr>
<td>30 mg</td>
<td>Active peptic ulcer</td>
</tr>
<tr>
<td>≥60 to &lt; 70 kg</td>
<td>35 mg</td>
</tr>
<tr>
<td>≥70 to &lt; 80 kg</td>
<td>40 mg</td>
</tr>
<tr>
<td>≥80 to &lt; 90 kg</td>
<td>45 mg</td>
</tr>
<tr>
<td>≥90 kg</td>
<td>50 mg</td>
</tr>
</tbody>
</table>
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