Pulmonary embolism-
diagnosis and management

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SAHA conference November 2017
• Pulmonary thromboembolism is not a disease in itself.

• Rather it is a complication of underlying venous thrombosis.
Venous thromboembolism

• Annual incidence is 75-270 cases per 100,000 persons.

• Over 70 yrs of age-incidence 700 per 100,000.

• Incidence of public awareness much lower than heart attack, stroke, breast or prostate cancer and HIV.
Deep vein thrombosis (DVT)
Clinical presentation

- Abrupt onset of pleuritic chest pain (66%), dyspnoea (73%). Cough (37%), Haemoptysis (13%)

- Most patients have no obvious symptoms at presentation.

- Symptoms may vary from catastrophic haemodynamic collapse to gradually progressive dyspnoea.
Autopsy specimen showing saddle pulmonary embolism
Atypical symptoms:

- Syncope
- Fever
- Productive cough
- Wheezing
- Decreasing level of consciousness
- New onset atrial fibrillation
Physical signs of pulmonary embolism

- Tachypnea (respiratory rate >16/min): 96%
- Rales: 58%. Effusion, nil.
- Accentuated second heart sound: 53%
- Tachycardia (heart rate >100/min): 44%
- Fever (temperature >37.8°C [100.04°F]): 43%
- Diaphoresis: 36%
- $S_3$ or $S_4$ gallop: 34%
- Clinical signs and symptoms suggesting DVT: 32%
- Lower extremity edema: 24%
- Cardiac murmur: 23%
- Cyanosis: 19%. Shock with collapse.
• Challenging diagnosis.

• Often patients have nagging symptoms for weeks.

• Forty percent of patients were seen by a doctor in the weeks prior to their death.

• UNEXPLAINED SYMPTOMS AND SIGNS-THINK PULMONARY EMBOLISM
The following risk factors can be indications for the presence of pulmonary embolism:

- Venous stasis
- Hypercoagulable states
- Immobilization
- Surgery and trauma
- Pregnancy
- Oral contraceptives and estrogen replacement
- Malignancy
- Hereditary factors resulting in a hypercoagulable state
• Drug abuse (intravenous [IV] drugs)
• Hemolytic anemias
• Heparin-associated thrombocytopenia
• Homocystinuria
• Hyperlipidemias
• Thrombocytosis
• Varicose veins
• Venous pacemakers
• Warfarin (first few days of therapy)
• Inflammatory bowel disease
The PIOPED II study listed the following indicators for pulmonary embolism:

- Travel of 4 hours or more in the past month
- Surgery within the last 3 months
- Malignancy, especially lung cancer
- Current or past history of thrombophlebitis
- Trauma to the lower extremities and pelvis during the past 3 months
- Smoking
- Central venous instrumentation within the past 3 months
- Stroke, paresis, or paralysis
- Prior pulmonary embolism
- Heart failure
- Chronic obstructive pulmonary disease
• In the absence of hemodynamic instability at presentation, the diagnostic work-up of a patient with suspected acute PE begins with the assessment of the clinical or pre-test probability of PE.

• Whichever prediction rule (e.g., Wells or revised Geneva) is used, the proportion of patients with confirmed PE is expected to be approximately 10% in the low-probability category, 30% in the intermediate-probability category, and 65% in the high-clinical probability category.
<table>
<thead>
<tr>
<th>Clinical Characteristic</th>
<th>Score</th>
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<tbody>
<tr>
<td>Previous pulmonary embolism or deep vein thrombosis</td>
<td>+1.5</td>
</tr>
<tr>
<td>Heart rate &gt;100 beats per minute</td>
<td>+1.5</td>
</tr>
<tr>
<td>Recent surgery or immobilization (within the last 30 d)</td>
<td>+1.5</td>
</tr>
<tr>
<td>Clinical signs of deep vein thrombosis</td>
<td>+3</td>
</tr>
<tr>
<td>Alternative diagnosis less likely than pulmonary embolism</td>
<td>+3</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>+1</td>
</tr>
<tr>
<td>Cancer (treated within the last 6 mo)</td>
<td>+1</td>
</tr>
<tr>
<td>Clinical Probability of Pulmonary Embolism</td>
<td>Score</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Low</td>
<td>0-1</td>
</tr>
<tr>
<td>Intermediate</td>
<td>2-6</td>
</tr>
<tr>
<td>High</td>
<td>≥6</td>
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</table>

Revised Geneva score
<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age older than 65 y</td>
<td>1</td>
</tr>
<tr>
<td>Previous DVT or pulmonary embolism</td>
<td>3</td>
</tr>
<tr>
<td>Surgery (under <em>general anesthesia</em>) or fracture (of the lower limbs) within 1 mo</td>
<td>2</td>
</tr>
<tr>
<td>Active malignant condition (solid or hematologic, currently active or considered cured &lt; 1 y)</td>
<td>2</td>
</tr>
</tbody>
</table>

**Symptoms**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral lower limb pain</td>
<td>3</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>2</td>
</tr>
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</table>

**Clinical Signs**

<table>
<thead>
<tr>
<th>Clinical Sign</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate 75-94 beats/min</td>
<td>3</td>
</tr>
<tr>
<td>Heart rate ≥95 beats/min</td>
<td>5</td>
</tr>
<tr>
<td>Pain on lower limb deep venous palpation and unilateral edema</td>
<td>4</td>
</tr>
</tbody>
</table>

**Clinical Probability**

<table>
<thead>
<tr>
<th>Probability</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>0-3 total</td>
</tr>
<tr>
<td>Intermediate</td>
<td>4-10 total</td>
</tr>
<tr>
<td>High</td>
<td>≥11 total</td>
</tr>
</tbody>
</table>
Gestalt

• Emerging evidence illustrates that a physician Gestalt may perform better than sole reliance on a clinical scoring system.

• This new body of research illustrates the German concept of Gestalt theory, a philosophical and psychiatric principle in which the process is taken into consideration versus the content—in other words, the whole is not the sum of its parts, but greater than the sum of its parts.

• A physician’s clinical judgment should not be replaced by clinical scoring systems, but should instead be used in conjunction with evidence-based validated systems when deciding the most likely diagnosis for a patient.

• Clinical Gestalt between a new intern and a seasoned clinician with a decade of experience is not expected to be the same when compared with a validated scoring system.
PERC Rule-Pulmonary Embolism Rule out Criteria
(Use when clinical Gestalt is low.)

• Age greater than or equal to 50 years.
• HR greater than or equal to 100/minute.
• SATS on room air < 95%.
• Venous thromboembolism.
• Recent (<28days) trauma or surgery.
• Unilateral leg swelling.
• Haemoptysis.
• Oral hormone use.

PERC EVALUATION POSITIVE IF ANY ONE OF THE 8 CRITERIA ARE MET
ACCP 2015 guidelines

• Patients with elevated D-dimer should have imaging.

• Patients with negative D-dimer but high risk should have CTPA.

• Only use V/Q scan if CTPA is unavailable. (and decreased renal function)

• Clinicians should use validated clinical prediction scores.
ACCP 2015 guidelines

• D-dimer tests more appropriate for low or intermediate risk patients.
• Use either the Wells or Geneva rules to choose tests based on risk.
• If low risk use the PERC and if patient does not meet any of the eight criteria no testing is needed.
• If intermediate risk or low risk and any of the PERC criteria met do D-dimer.
• In patients older than 50 years use age adjusted D–dimer(age X 10ug/ml).
• Patients with D-dimer below age adjusted levels no further testing required.
Potentially useful laboratory tests in patients with suspected pulmonary embolism

• D-dimer testing—high sensitivity, low specificity

• White blood cell count

• Arterial blood gases

• Serum troponin levels

• Brain natriuretic peptide
D-dimer test

• Low specificity, high sensitivity.

• Study of 3346 patients with normal age adjusted D-dimer did not undergo CTPA-increased the number of patients over 75 yrs or older in whom PE could be excluded from 6,4% to 30%.
Imaging studies that aid in the diagnosis of pulmonary embolism

• Computed tomography angiography (CTPA): Multidetector CTA (MDCTA) is the criterion standard for diagnosing pulmonary embolism.

• Pulmonary angiography: Criterion standard for diagnosing pulmonary embolism when MDCTA is not available.

• Chest radiography: Normal in most cases of pulmonary embolism, but nonspecific abnormalities can be seen.

• V/Q scanning: When CT scanning is not available or is contraindicated.

• ECG: Most common abnormalities are tachycardia and nonspecific ST-T wave abnormalities, particularly in RV leads.
CTPA and V/Q scans

• There is a fair incidence of over diagnosis of PE and the clinical significance of subsegmental PE is uncertain.

• Pitfalls and errors in misdiagnosis of PE may be frequent in clinical practice.

• V/Q scans have a high proportion of nonconclusive results.
Pulmonary angiogram showing pulmonary embolism
High-probability ventilation-perfusion scan (A)
• MRI: Using standard or gated spin-echo techniques, pulmonary emboli demonstrate increased signal intensity within the pulmonary artery

• Echocardiography: Transthoracic and Transesophageal echocardiography – RV dilatation, PAP elevated, paradoxical septal motion, thrombus

• Venography: Criterion standard for diagnosing DVT

• Duplex ultrasonography: Non-invasive diagnosis of pulmonary embolism by demonstrating the presence of a DVT at any site
Risk stratification following diagnosis of PE

• More than 95% patients with PE are haemodynamically stable at presentation.

• PESI-pulmonary embolism severity index
<table>
<thead>
<tr>
<th>Predictors</th>
<th>Points assigned</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic characteristics</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>Age</td>
</tr>
<tr>
<td>Male sex</td>
<td>+10</td>
</tr>
<tr>
<td>Co-morbid illnesses</td>
<td></td>
</tr>
<tr>
<td>Cancer (previous or active)</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>Clinical findings</td>
<td></td>
</tr>
<tr>
<td>Pulse $\geq 110$ min$^{-1}$</td>
<td>+20</td>
</tr>
<tr>
<td>Systolic blood pressure $&lt; 100$ mmHg</td>
<td>+30</td>
</tr>
<tr>
<td>Respiratory rate $\geq 30$ min$^{-1}$</td>
<td>+20</td>
</tr>
<tr>
<td>Temperature $&lt; 36^\circ$C</td>
<td>+20</td>
</tr>
<tr>
<td>Altered mental status (disorientation, lethargy, stupor or coma)</td>
<td>+60</td>
</tr>
<tr>
<td>Arterial oxygen saturation $&lt; 90%$ (with or without the administration of supplemental oxygen)</td>
<td>+20</td>
</tr>
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<table>
<thead>
<tr>
<th>Risk classes</th>
<th>Points</th>
<th>Risk stratification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>$\leq 65$</td>
<td>Very low risk</td>
</tr>
<tr>
<td>Class II</td>
<td>66–85</td>
<td>Low risk</td>
</tr>
<tr>
<td>Class III</td>
<td>86–105</td>
<td>Intermediate risk</td>
</tr>
<tr>
<td>Class IV</td>
<td>106–125</td>
<td>High risk</td>
</tr>
<tr>
<td>Class V</td>
<td>$&gt; 125$</td>
<td>Very high risk</td>
</tr>
<tr>
<td>Condition</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>------------------------------------------------</td>
<td>----</td>
<td>-----</td>
</tr>
<tr>
<td>Age &gt; 80 years</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>History of cancer</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>History of chronic cardiopulmonary disease</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Heart rate ≥ 110</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Systolic BP &lt; 100 mm Hg</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>O2 saturation &lt; 90%</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Simplified PESI (Pulmonary Embolism Severity Index)

Hospital mortality according to PESI risk classification.

PESI, pulmonary embolism severity index; NS, not significant.
<table>
<thead>
<tr>
<th>Early Mortality Risk</th>
<th>Risk Parameters and Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Shock or Hypotension</td>
</tr>
<tr>
<td></td>
<td>PESI Class III–V or sPESI ≥1</td>
</tr>
<tr>
<td></td>
<td>Signs of RV Dysfunction on an Imaging Test</td>
</tr>
<tr>
<td></td>
<td>Cardiac Laboratory Biomarkers*</td>
</tr>
<tr>
<td>High</td>
<td>+</td>
</tr>
<tr>
<td>Intermediate-high</td>
<td>-</td>
</tr>
<tr>
<td>Intermediate-low</td>
<td>-</td>
</tr>
<tr>
<td>Low</td>
<td>-</td>
</tr>
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Stavros V. Konstantinides et al. JACC 2016;67:976-990
Management

Thrombolysis

• All patients with PE require risk stratification

  Generally all patients with acute PE with hypotension (BP<90mm Hg). Assess bleeding risk.

  In patients with RV dysfunction also benefit. Bleeding risk over 65yrs.

  Remains controversial in intermediate risk patients.
• Alteplase (Actylise) 100 mg infusion over 2hrs.

• Tenectaplaste (Metalyse) Rapid infusion
Management

Unfractionated heparin therapy

• Most patients should receive LMWH or fondaparinux instead of UFH.

• UFH –where procedures are likely. Short half life.

• Efficacy depends on critical therapeutic level-1.5-2 times aPTT.

• Initial bolus of 80U/kg or 5000 U followed by infusion of 1300u/h.
Management
Low-molecular weight heparin therapy

• Guidelines recommend LMWH over IV UFH.

• Choice between fondaparinux and LMWH-individual.

• LMWH-greater bioavailability, subcutaneous administration, longer duration of action. Fixed doses.

• Can safely be administered in an outpatient setting.
Enoxaparin-LMW (Clexane)

- 1mg/Kg sc 12hrly
Fondaparinux-factor Xa inhibitor (Arixtra)

- <50 kg: 5 mg SC once daily
- 50-100 kg: 7.5 mg SC once daily
- >100 kg: 10 mg SC once daily
Management

Factor Xa inhibitors

RIVAROXABAN (Xarelto)-factor Xa inhibitor
15mg bd X 3 weeks then 20 mg daily

• Approved by the FDA in 2012 for treatment of DVT and PE.
• Einstein-PE and Einstein-DVT. Non inferior to enoxaparin and warfarin
APIXABAN (factor Xa inhibitor)

• Approved for treatment of PE in 2014.
• Amplify and Amplify –EXT studies.

• EDOXABAN
• BETRIXABAN
DABIGATRAN – Pradaxa (direct thrombin inhibitor)
150 mg bd following 5 days clexane

• Approved by the FDA in 2014 for DVT and PE and reducing recurrence.
• Re-Cover and Re-Cover 2 studies.
• Difference was patients were 1st given enoxaparan then either warfarin or dabigatran.
Warfarin therapy

• Should be started same day as anticoagulation therapy.
• Parenteral anticoagulation therapy continued 5 days until INR is 2-3.
Duration of anticoagulation therapy

• In the setting of reversible risk factors-warfarin for at least 3 months.

• ACCP guidelines recommend patients with unprovoked PE receive 3 months treatment (grade 1B). With low risk of bleeding extend to 6 months (grade 2B).

• In second unprovoked venous thromboembolism extended therapy is recommended (grade 1B)

• With any coagulation deficiency such as antithrombin 3, protein C and S, Factor V leidin—long-term anticoagulation.
Cancer patients

• ACCP guidelines recommend long-term management because of increased risk of recurrence.

• For treatment of PE in cancer patients LMWH is preferential to Warfarin (grade 2B).

• If patient against injections then warfarin preferred over NOACS.
Pulmonary embolism in pregnancy

- Risk of thromboembolism increased in pregnancy and 6-12 weeks post partum.
- Investigate as usual including venous dopplers and CT scan.
- LMWH treatment of choice.
Embolectomy

• Either catheter embolectomy or surgical embolectomy in massive PE who have contraindications to thrombolysis.

Vena Cava Filters

• If there is an absolute contraindication to anticoagulation.
• Patients who have recurrent events despite adequate anticoagulation.
Supportive care

- Compression stockings following a proximal DVT for 2 years.
- Early ambulation recommended (grade 2C)
- Pharmaecological support of the CV system-inotropes, ventilation.
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