Disorders of the Pulmonary Circulation

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Outline

- Pulmonary edema
  - High pressure
  - Low pressure
- Pulmonary embolism
- Pulmonary hypertension

  • Robbins, Chapter 15, pg 680-682, 706-707
  • Pathophysiology of Disease, available through Access Medicine, Chapt 9.

Objectives

- Be able to differentiate high pressure pulmonary edema from low pressure pulmonary edema.
- List the treatments for high pressure pulmonary edema
- List the treatments for low pressure pulmonary edema
- List the risk factors for pulmonary thromboembolic disease
- List the treatments for pulmonary thromboembolic disease
- Be able to differentiate between primary and secondary pulmonary hypertension.
Pulmonary Edema

High Pressure Pulmonary Edema

• A.K.A. Cardiogenic pulmonary edema.
• Elevated LVEDP causes elevated hydrostatic pressures which result in increased edema formation.
High Pressure Pulmonary Edema

- Associated with other signs of elevated LVEDP and cardiac dysfunction.
  - PE, JVD, S3, Hepatomegaly, edema, cool extremities, thready pulse.
  - CXR: vascular engorgement, perihilar infiltrates, cephalization, Kerley B lines, pleural effusions are common.
- Causes- LV systolic or diastolic dysfunction, mitral valve disease, hypervolemia with normal cardiac function (acute renal failure).
Micro of high pressure pulmonary edema: engorged alveolar capillaries, intraalveolar pink grany precipitate, hemosiderin-laden macrophages

High Pressure Pulmonary Edema - Treatment

- Oxygen, noninvasive mask ventilation
- Decrease preload (PCWP)
  - nitrates, diuretics, venodilators
- Decrease afterload
  - ACE inhibitors, hydralazine
- Increase contractility
  - Dobutamine, miirinone
Low Pressure Pulmonary Edema

- A.K.A. Acute Respiratory Distress Syndrome (ARDS) or Acute Lung Injury (ALI).
- Increased permeability (leaky capillaries) causes increased edema.
- Follows any of a number of insults.  
  - Most commonly sepsis, trauma, pancreatitis.
- Edema has protein concentration approaching serum.

ARDs - Definition

Table 3. The Berlin Definition of Acute Respiratory Distress Syndrome

<table>
<thead>
<tr>
<th>Timing</th>
<th>1 week of a known clinical insult or new or unmasking respiratory symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging</td>
<td>Bilateral opacities—not fully explained by effusions, collapse, or nodules</td>
</tr>
<tr>
<td>Origin</td>
<td>Acute respiratory failure not fully explained by cardiac failure or fluid overload</td>
</tr>
<tr>
<td></td>
<td>Need objective assessment [eg, echocardiography] to exclude hydrostatic edema (no gas exchange defect present)</td>
</tr>
<tr>
<td>Oxygenation</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>PP&lt;100 mm Hg, PAO&lt; 60 mm Hg, PEEP&lt; 5 cm H2O</td>
</tr>
<tr>
<td>Moderate</td>
<td>PP&lt;100 mm Hg, PAO&lt; 60 mm Hg, PEEP&lt; 5 cm H2O</td>
</tr>
<tr>
<td>Severe</td>
<td>PP&lt;100 mm Hg, PAO&lt; 60 mm Hg, PEEP&gt; 5 cm H2O</td>
</tr>
</tbody>
</table>

Alternative, CPP: continuing invasive arterial pressure, P<0.2 fraction of inspired oxygen, P>0.2 partial pressure of arterial oxygen, P>0.2 cardiac and pulmonary physiology, P>0.2 right mean arterial pressure.  

Edema Flow = [(Pmv-Pis) - (Pmv-Pis)] \( \downarrow \sigma \) \( \uparrow \) Kf

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Low Pressure Pulmonary Edema

- Physical Exam is typically notable for:
  - Lack of signs of elevated filling pressures.
  - If sepsis is the underlying cause, there are typically warm extremities, bounding pulses and a wide pulse pressure.
- Refractory hypoxemia is usually the early problem, later in the course of the disease hypercapnia becomes more problematic.

Pathology of ARDS

- Diffuse Alveolar Damage

<table>
<thead>
<tr>
<th>Table 16</th>
<th>Defining Features of acute lung injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Alveolar epithelial and capillary endothelial injury</td>
<td></td>
</tr>
<tr>
<td>- Alveolar edema</td>
<td></td>
</tr>
<tr>
<td>- Fibrosis</td>
<td></td>
</tr>
</tbody>
</table>

CXR shows diffuse four quadrant fluffy infiltrates.

- Pleural effusions and cardiomegaly are rare.
Swan-Ganz Catheter

- 3 ports
- Balloon tip
- Proximal port
- Distal port (Pressure transducer and a Thermister and/or oximeter)

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Differentiating High and Low Pressure Edema Clinically

<table>
<thead>
<tr>
<th>High Pressure Pulmonary Edema</th>
<th>Low Pressure Pulmonary Edema</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated Neck Veins</td>
<td>Flat</td>
</tr>
<tr>
<td>+ S3</td>
<td>Extra Heart sounds</td>
</tr>
<tr>
<td>Crackles</td>
<td>None</td>
</tr>
<tr>
<td>Presence</td>
<td>Peripheral Edema</td>
</tr>
<tr>
<td>Cool</td>
<td>Extremities</td>
</tr>
<tr>
<td>Narrow</td>
<td>Pulse Pressure</td>
</tr>
<tr>
<td>&gt;20</td>
<td>Wedge Pressure</td>
</tr>
<tr>
<td>Low</td>
<td>Edema Protein Conc.</td>
</tr>
<tr>
<td>Elevated</td>
<td>Flat</td>
</tr>
<tr>
<td>Extra Heart sounds</td>
<td>None</td>
</tr>
<tr>
<td>Crackles or Clear</td>
<td>None</td>
</tr>
<tr>
<td>Present</td>
<td>Warm and well perfused</td>
</tr>
<tr>
<td>Cool</td>
<td>None</td>
</tr>
<tr>
<td>Narrow</td>
<td>Wide</td>
</tr>
<tr>
<td>&gt;20</td>
<td>&lt;18</td>
</tr>
<tr>
<td>Low</td>
<td>High</td>
</tr>
</tbody>
</table>

Low Pressure Pulmonary Edema- Treatment

- Fix the underlying problem
- Lower the hydrostatic pressures
- Oxygen (but recognize that this is shunt)
- Mechanical Ventilation
  - High PEEP
  - Low tidal volumes
- Salvage therapy- ECMO
Edema Flow = [(P_{mv} - P_s) - (\pi_{mv} - \pi_s)] \uparrow K_f
Pulmonary Embolism

Pulmonary Embolism—pathophysiology
- Hypercoagulability, venous stasis, and/or intimal injury lead to thrombus formation.
- Clot may propagate proximally.
- DVT may dislodge and embolize.
- Pulmonary arterial obstruction leads to:
  - increased PVR
  - redistribution of blood flow → V/Q mismatch
  - hyperventilation
  - RV pressure overload, ischemia

Pulmonary Embolism—epidemiology
- Approximately 600,000 DVTs per year.
- Approximately 10-30% of DVTs lead to pulmonary embolus if not treated.
- PE mortality is 30% untreated.
- With therapy, mortality decreases to ~5%.
- Autopsy studies as late as 1988 suggest that only 30% of PEs are diagnosed antemortem.
## PE- Risk Factors

<table>
<thead>
<tr>
<th>Baseline Feature</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active smoker*</td>
<td>3</td>
</tr>
<tr>
<td>Previous VTE with the exclusion of superficial vein thrombosis</td>
<td>3</td>
</tr>
<tr>
<td>Reduced mobility1</td>
<td>3</td>
</tr>
<tr>
<td>Known thrombophilic condition</td>
<td>3</td>
</tr>
<tr>
<td>sepsis (at least 3 days)</td>
<td>2</td>
</tr>
<tr>
<td>Elderly age (≥70 years)</td>
<td>1</td>
</tr>
<tr>
<td>Heart and/or respiratory failure</td>
<td>1</td>
</tr>
<tr>
<td>Acute myocardial infarction or ischemic stroke</td>
<td>1</td>
</tr>
<tr>
<td>Acute infection and/or rheumatologic disorder</td>
<td>1</td>
</tr>
<tr>
<td>Obesity (BMI ≥30)</td>
<td>1</td>
</tr>
<tr>
<td>Ongoing hormonal treatment</td>
<td>1</td>
</tr>
</tbody>
</table>

### Padua Prediction Score


## PE- Clinical Presentation

<table>
<thead>
<tr>
<th>Symptoms (n=327)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td>88</td>
</tr>
<tr>
<td>Pleuritic</td>
<td>74</td>
</tr>
<tr>
<td>Non-pleuritic</td>
<td>14</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>84</td>
</tr>
<tr>
<td>Apprehension</td>
<td>59</td>
</tr>
<tr>
<td>Cough</td>
<td>53</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>30</td>
</tr>
<tr>
<td>Syncope</td>
<td>13</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Signs (n=327)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiration &gt;16/min</td>
<td>92</td>
</tr>
<tr>
<td>Rales</td>
<td>58</td>
</tr>
<tr>
<td><em>S</em>P</td>
<td>53</td>
</tr>
<tr>
<td>Pulse &gt;100/min</td>
<td>44</td>
</tr>
<tr>
<td>T &gt;37.8ºC</td>
<td>43</td>
</tr>
<tr>
<td>Phlebitis</td>
<td>32</td>
</tr>
<tr>
<td>Gallop</td>
<td>34</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>36</td>
</tr>
<tr>
<td>Edema</td>
<td>24</td>
</tr>
<tr>
<td>Murmur</td>
<td>23</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>19</td>
</tr>
</tbody>
</table>

### Urokinase-Streptokinase in PE


## Pathology of PE

Fig. 15-26: Robbins and Cotran

Fig. Robbins and Cotran
PE - Chest X-rays

- Cardiomegaly (27%)
- Normal (24%)
- Pleural effusions (23%)
- Elevated hemidiaphragm (20%)
- PA enlargement (19%)
- Atelectasis (18%)

No finding was sensitive or specific or correlated with echo findings.


Accuracy of clinical diagnosis

<table>
<thead>
<tr>
<th>Clinical probability</th>
<th>PIOPED (n = 951)</th>
<th>PISA-PED (n = 783)</th>
<th>Hull (n = 305)</th>
<th>Wells (n = 1239)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very likely</td>
<td>99 (68%)</td>
<td>235 (91%)</td>
<td>76 (82%)</td>
<td>102 (78%)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>569 (30%)</td>
<td>179 (47%)</td>
<td>81 (48%)</td>
<td>403 (28%)</td>
</tr>
<tr>
<td>Unlikely</td>
<td>228 (9%)</td>
<td>349 (4%)</td>
<td>26 (31%)</td>
<td>734 (3%)</td>
</tr>
</tbody>
</table>

PE - Diagnostic Testing

- D- Dimer
  - sensitive, but not specific (good at ruling disease out)
- Lower extremity ultrasonography
  - specific, but not sensitive (good at ruling disease in)
- V/Q scan
- Pulmonary angiography
- CT Angiography
Pulmonary Angiogram

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VF Tapson. NEJM 2008;358:1037-1052.
PE- Therapy

- Prevention
- Anticoagulation
  - This is appropriate initial therapy in almost everyone, unless there is a contraindication
  - Heparin
  - Coumadin (vitamin K antagonist) for at least 3 months
  - New oral anticoagulants (NOACs) which are either direct thrombin inhibitors (dabigatran) or factor Xa inhibitors (rivaroxaban or apixaban)

PE- Therapy

- IVC filter
  - Reduce the rate of recurrent PE without improving survival
  - Indicated if an absolute contraindication to anticoagulation
- Thrombolytics
  - Only proven to improve survival in shock
- Surgical/Catheter Thrombectomy
Pulmonary Hypertension

Pulmonary Hypertension (PH)

- The RV is a low pressure, high volume system. Normal PA pressures run ~20/10.
- Acutely the RV cannot generate pressures over 40mmHg.
- Chronically, pulmonary pressures approaching systemic can be generated, but not without consequences.
- PH is mean PA pressure > 25 mmHg
Classification of PH

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Pulmonary Arterial Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2</td>
<td>Pulmonary Hypertension due to left heart disease</td>
</tr>
<tr>
<td>Group 3</td>
<td>Pulmonary Hypertension due to lung disease/hypoxia</td>
</tr>
<tr>
<td>Group 4</td>
<td>Chronic Thromboembolic Pulmonary Hypertension</td>
</tr>
<tr>
<td>Group 5</td>
<td>Pulmonary Hypertension with unclear mechanisms</td>
</tr>
</tbody>
</table>

Formally known as Primary pulmonary hypertension (PPH)

- Aminorex
- Fenfluramine
- Rapeseed oil
- Amphetamines
- Cocaine
- Scleroderma
- Lupus

- Pulmonary arterial hypertension (PAH)
  - Heritable
  - BMPR2
  - alpha-thalassemia
  - Drug- and toxin-induced
  - Associated with connective tissue disease
  - HIV infection
  - Portal hypertension
  - Congenital heart disease
  - Schistosomiasis
  - Chronic hemolytic anemia
  - Persistent pulmonary hypertension of the newborn

- Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
- Pulmonary hypertension owing to left heart disease
  - Systemic sclerosis
  - Diastolic dysfunction
  - Vascular disease
  - Pulmonary hypertension owing to lung diseases and/or hypoxia
  - Chronic obstructive pulmonary disease
  - Interstitial lung diseases
  - Other pulmonary diseases with mixed restrictive and obstructive pattern
  - Sleep-disordered breathing
  - Acute hypoxic pulmonary disorders
  - Chronic exposure to high altitude
  - Developmental abnormalities
- Chronic thromboembolic pulmonary hypertension (CTEPH)
- Pulmonary hypertension with venous multifactorial mechanisms
  - Hemodynamic disorders: mitral/atrial valve diseases, pulmonary hypertension
  - Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis, lymphangioleiomyomatosis
  - Metabolic disorders: glycogen storage disease, Gaucher disease, myelofibrosis
  - Others: tumor obstruction, bleeding neangiomas, chronic renal failure on dialysis
Pathology of Pulmonary Hypertension

Fig. 15-29: Robbins and Cotran

Pulmonary Hypertension - Treatment

• Pulmonary rehabilitation.
• Oxygen if needed.
• ~10% of patients can have a response to calcium channel blockers
• All other vasodilators cause systemic hypotension before pulmonary vasodilation.

NEJM 2004:351:1425

Ambrisentan
Bosentan
Macitentan
Sildenafil
Tadalafil
Epoprostenol
Iloprost
Treprostinil
Soluble Guanylate Cyclase Stimulation - Riociguat
Pulmonary Hypertension - Treatment

- Consider anticoagulation
- Diuretics (with caution)
- Digoxin?
- Lung Transplant can be a treatment option if the patient is otherwise stable.

Questions?