Approach to Internal Medicine

A Resource Book for Clinical Practice

David Hui · Alexander A. Leung · Christopher Ma *Editors*

Fifth Edition

Springer

Editors
David Hui
The University of Texas MD
Anderson Cancer Center
Houston, TX
USA

Christopher Ma
University of Calgary
Calgary, AB
Canada

Alexander A. Leung
University of Calgary
Calgary, AB
Canada

ISBN 978-3-030-72979-0 ISBN 978-3-030-72980-6 (eBook)
https://doi.org/10.1007/978-3-030-72980-6

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Pulmonary Embolism

Kearon. *Chest* 2012;141(2 Suppl)
Kearon. *Chest* 2016;149(2)

PATHOPHYSIOLOGY

VIRCHOW TRIAD—risk factors for venous thromboembolism

- **ENDOTHELIAL OR VESSEL WALL INJURY**—fracture of pelvis, femur, or tibia
- **HYPERCOAGULABILITY**—obesity, pregnancy, estrogen, smoking, **cancer** (high suspicion of occult malignancy in patients who develop pulmonary embolism while on anticoagulation), **autoimmune disorders** (antiphospholipid antibody syndrome, lupus anticoagulant, IBD), **genetics** (history of DVT/PE, factor V Leiden, antithrombin III deficiency, protein C/S deficiency, prothrombin G20210A mutation, hyperhomocysteinemia)
- **STASIS**—surgery requiring >30 min of anesthesia, prolonged immobilization, CVA, HF

CLINICAL FEATURES

HISTORY—dyspnea (sudden onset), pleuritic chest pain, cough, hemoptysis, pre/syncope, unilateral leg swelling/pain, past medical history (previous DVT/PE, active cancer, immobilization or surgery in last 4 weeks, miscarriages), medications (birth control pill, anticoagulation)

PHYSICAL—vitals (tachycardia, tachypnea, hypotension, fever, hypoxemia), respiratory examination (pulmonary hypertension if chronic PE), cardiac examination (right heart strain), leg swelling

RATIONAL CLINICAL EXAMINATION SERIES: DOES THIS PATIENT HAVE PULMONARY EMBOLISM?

PREDICTION RULES—Wells criteria, PISA-PED, Geneva rule

APPROACH—combining the pretest probability with results of D-dimer testing reduces the need for further investigations in patients with low (<15%) to moderate (15–35%) clinical pretest probability. A patient with low to moderate clinical probability of PE with a normal D-dimer has a LR of 0 (95% CI 0–0.06) for PE. When there is a discrepancy between clinical gestalt and clinical prediction rule, consider placing the patient into the higher pretest probability group

Chunilal et al. *JAMA* 2003;290(21)
Simel et al. *The Rational Clinical Examination*. McGraw-Hill, 2009

INVESTIGATIONS

BASIC

- **LABS**—CBC, lytes, urea, Cr, PTT, INR, troponin/CK × 3, D-dimer (if low probability for PE or outpatient), βhCG in women of reproductive age
- **IMAGING**—CXR, duplex US of legs, V/Q scan, CT chest (PE protocol)
- **ECG**—may see normal sinus rhythm (most common), sinus tachycardia (most common abnormality), atrial fibrillation, right ventricular strain (T wave inversion in anterior precordial leads), non-specific ST-T wave changes, right axis deviation, right bundle branch block and/or $S_1Q_3T_3$ (tall S wave in lead I, Q wave and inverted T wave in lead III)
- **ABG**—if respiratory distress

SPECIAL

- **ECHOCARDIOGRAM**—to check for right heart strain (dilated RV and elevated RVSP). Particularly important if hemodynamic changes
- **PULMONARY ANGIOGRAM**—gold standard (usually not needed)
- **THROMBOPHILIA WORKUP**—factor V Leiden, prothrombin G20210A, anticardiolipin antibody, lupus anticoagulant, protein C, protein S, antithrombin III, fibrinogen; consider homocysteine level and workup for paroxysmal nocturnal hemoglobinuria and

INVESTIGATIONS (CONT'D)

antiphospholipid syndrome in cases of combined arterial–venous thrombosis. Routine testing for hypercoagulable disorders is ***not*** warranted

DIAGNOSTIC ISSUES

CXR FINDINGS IN PULMONARY EMBOLISM—normal, atelectasis, unilateral small pleural effusion, enlarged central pulmonary artery, elevated hemidiaphragm, Westermark sign (abrupt truncation of pulmonary vessel), Hampton hump (wedge infarct)

D-DIMER (sens 85–96%, spec 45–68%, LR+ 1.7–2.7, LR– 0.09–0.22)—a normal D-dimer can rule out PE if low clinical suspicion

V/Q SCAN (sens high, spec high)—result often not definitive (intermediate probability) because of other intraparenchymal abnormalities

CT PE PROTOCOL (sens 57–100%, spec 78–100%)—can be very helpful as it provides clues to other potential diagnoses/pathologies as well

LEG VEIN DOPPLER (sens 50%, spec moderate)—serial dopplers may be used for diagnosis of DVT if CT or V/Q scan failed to demonstrate PE but clinical suspicion still high

WELLS CRITERIA FOR PULMONARY EMBOLISM

- **SCORING**—signs/symptoms of DVT (+3), alternative diagnosis less likely (+3), HR >100 (+1.5), immobilization or surgery in last 4 weeks (+1.5), previous DVT/PE (+1.5), hemoptysis (+1), active cancer (+1)
- **LOW SUSPICION** (sum 0–1, <10% chance)—D-dimer → if positive, CT or V/Q scan
- **INTERMEDIATE SUSPICION** (sum 2–6, 30% chance)—D-dimer → CT or V/Q scan → if negative but suspicious, leg doppler → if negative but still suspicious, pulmonary angiogram
- **HIGH SUSPICION** (sum >6, >70% chance)—CT or V/Q scan → if negative but suspicious, leg Doppler → if negative but still suspicious, pulmonary angiogram
- **MODIFIED WELLS SCORE**—PE likely (score >4); PE unlikely ≤4)

Related Topics
Anticoagulation Therapies (p. 179)
DVT (p. 177)
Hypercoagulable States (p. 174)
Pulmonary Embolism in Pregnancy (p. 464)

MANAGEMENT

ACUTE—ABC, $\mathbf{O_2}$ to keep sat >94%, IV

THROMBOLYTICS—controversial as increased risk of intracranial bleed and multiple contraindications (see below). Consider only if hemodynamically unstable, right ventricular strain or life-threatening massive pulmonary embolism. Must be done in ICU. *TPA* 100 mg IV over 2 h, or *streptokinase* 250,000 IU over 30 min, the 100,000 IU/h over 12–24 h or 1.5 million IU over 2 h. Unfractionated heparin may be used concurrently

ANTICOAGULATION—if moderate to high risk of developing PE, consider initiating anticoagulation while waiting for investigations. **Heparin** (*unfractionated heparin* 5,000 U IV bolus, then 1,000 U/h and adjust to 1.5–2.5 × normal PTT; use UFH if considering thrombolysis), **LMWH** (*enoxaparin* 1 mg/kg SC BID or 1.5 mg/kg SC daily, *tinzaparin* 175 U/kg SC daily), or ***fondaparinux*** 5 mg SC daily (<50 kg), 7.5 mg SC daily (50–100 kg), or 10 mg SC daily (>100 kg). If using vitamin K antagonist, start ***warfarin*** 5 mg PO daily within 48 h and continue heparin/LMWH/fondaparinux for at least 5 days and until INR is between 2 and 3 for at least 48 h. **Factor Xa inhibitors** (e.g. rivaroxaban, apixaban) are the only direct oral anticoagulants that have been studied and approved as monotherapy (not requiring pre-treatment with heparin). **Direct thrombin inhibitors** (e.g. dabigatran) require a short course of LMWH for 5 days prior to transitioning to oral therapy (see Approach to Anticoagulation Therapies p. 179)

SURGICAL—embolectomy. Consider if thrombolysis failed or contraindicated or if hemodynamically unstable

IVC FILTER—if anticoagulation contraindicated

TREATMENT ISSUES

CONTRAINDICATIONS TO THROMBOLYTIC THERAPY

- **ABSOLUTE CONTRAINDICATIONS**—history of hemorrhagic stroke or stroke of unknown origin, ischemic stroke in previous 3 months, malignant intracranial neoplasm, suspected aortic dissection, active bleeding, major trauma in previous 2 months, intracranial surgery or head injury within 3 weeks
- **RELATIVE CONTRAINDICATIONS**—TIA within 6 months, oral anticoagulation, pregnancy or within 1 week postpartum, non-compressible puncture sites, traumatic/prolonged (>10 min) CPR, uncontrolled hypertension (SBP >185 mmHg, DBP >110 mmHg), recent bleeding

TREATMENT ISSUES (CONT'D)

(<2–4 weeks), current use of anticoagulants, advanced liver disease, infective endocarditis, active peptic ulcer, thrombocytopenia

ANTICOAGULATION DURATION

- **FIRST PULMONARY EMBOLISM WITH REVERSIBLE OR TIME-LIMITED RISK FACTOR**—anticoagulation for at least 3 months
- **UNPROVOKED PE**—at least 3 months of treatment. If no obvious risk factors for bleeding, consider indefinite anticoagulation
- **PE AND MALIGNANCY**—direct oral anticoagulants (DOACs) and SC LMWH are generally preferred over warfarin. Treatment should be continued until eradication of cancer as long as there are no significant contraindications to anticoagulation
- **PE AND RENAL DISEASE** (CrCl <30 mL/min)—treatment with warfarin
- **PE AND LIVER DISEASE**—SC LMWH; warfarin difficult to control and INR may not reflect antithrombotic effect
- **PE AND PREGNANCY OR PREGNANCY RISK**—SC LMWH is preferred for outpatient treatment. Total duration of therapy should be 3–6 months until 6 weeks post-partum unless patient has risk factors for hypercoagulable state

SPECIFIC ENTITIES

FAT EMBOLISM

- **PATHOPHYSIOLOGY**—embolism of fat globules to lungs, brain, and other organs → metabolized to fatty acids leading to inflammatory response. Commonly caused by closed fractures of long bones, but may also occur with pelvic fractures, orthopedic procedures, bone marrow harvest, bone tumor lysis, osteomyelitis, liposuction, fatty liver, pancreatitis and sickle cell disease
- **CLINICAL FEATURES**—triad of dyspnea, neurological abnormalities (confusion), and petechial rash (head and neck, chest, axilla). May also have fever, thrombocytopenia and DIC
- **DIAGNOSIS**—clinical diagnosis (rash is pathognomonic). Investigations may include CXR, V/Q scan, CT chest and MRI head
- **TREATMENTS**—supportive care as most patients will fully recover. Mortality is 10%. Primary prophylaxis includes early mobilization. Consider trial of systemic steroids