Acute Pulmonary Embolism: 2014 Update

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Objectives

- Summarize the current status of MDCTA in suspected acute venous thromboembolism (VTE)
- Review current guidelines for the diagnosis of patients suspected of VTE including special patient groups
- Recognize the current controversy regarding the diagnosis and treatment of subsegmental pulmonary emboli
- List emerging imaging technologies in suspected VTE

Outline

- Background
- CTPA interpretation
  - Imaging features
  - Imaging pitfalls
- Clinical utility of CTPA
- Diagnostic approach to the patient with suspected PE
- Risk assessment
- Concerns about the use of CTPA
- Emerging technologies

Background

- Third leading cause of cardiovascular mortality
  - 2% in normotensive patients without evidence of right ventricular dysfunction
  - 30% with shock
  - 65% in patients with cardiac arrest at presentation
- 5-10% of all deaths in US hospitals
- Difficult to diagnose clinically
- Incidence increases with age
  - 65-69 yrs: 1.3 per 1000
  - 85-89 yrs: 2.8 per 1000
- Most associated with other co-morbidities, e.g. hospitalization, cardiac disease, severe pneumonia

CT Angiography for PE

- First publication in 1992
- Rapid advances in technology over 20 years

Financial Disclosures

- None
Tests in Patients with PE (%)

- V/Q
- US leg veins
- Pulmonary angiography
- CT angiography

Year


Stein P, Pulmonary Embolism, Blackwell Futura 2007 Chapter 58, p.261

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Acute PE – Diagnosis

- Filling defect on at least two consecutive images
- Confidence level – segmental vs subsegmental
- CTPA findings
  - Complete occlusion
  - Central filling defect – “target sign” or “polo mint sign”
  - Eccentric filling defect
    - Acute angle with vessel wall
    - Arterial dilatation
    - Right atrial/ventricular clot in transit
    - Patent foramen ovale ➔ systemic emboli

Signs of Acute PE

RA Embolus across PFO, Systemic Emboli

Diagnostic Pitfalls

- Anatomical
  - Veins
  - Adjacent hilar lymph nodes
  - Mucus-filled bronchi
- Technical
  - Vessel orientation
  - Motion or respiratory artifacts
  - Flow-related artifacts
- Physiological
  - Insufficient enhancement
Transient Interruption of Contrast – IVC Inflow
• Contrast interruption by unopacified blood entering right atrium from IVC
• Seen with normal right heart and pulmonary arterial pressures
• Occurs after deep inspiration or release of Valsalva maneuver
• Brief and variable change in density

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Diagnostic Performance of CTPA
• Based on poor quality studies mostly done with 4 detector CT or less and compared with suboptimal gold standard
• Reported sensitivities between 83-100% and specificities between 89-97%
• Outcome studies good

Outcome Studies of MDCTA for PE
• Meta-analysis of 15 studies
  – 3500 patients with negative CTPA
  – 3 month incidence of PE = 1-2.8%
  – Negative predictive value ≈ 99%
• Similar to conventional invasive pulmonary angiography
• Similar to V/Q scan

Advantages of CTA in Suspected PE
• Test of choice
  – Available
  – Fast
  – Alternative diagnosis in 11-85%
  – Ancillary information
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Diagnostic Approach to the Patient with Suspected PE

• Clinical prediction rule
• D-dimer
• Imaging

Clinical Prediction Rule

• Wells score
• Revised Geneva score
• Pisa score

D-dimer

• First choice test in patients with low to moderate pretest probability of VTE
  – High NPV and low PPV
  – >0.5 mg/L – sensitivity = 95%, specificity = 55% for VTE
  – Higher level correlates with worse outcome
• Highly sensitive assay (ELISA), can exclude PE in low or moderate pretest probability without further testing
  – 3-month thromboembolic risk <1%

D-dimer

• Not helpful for patients with high-probability clinical assessment as may be false negative
• Normal levels uncommon
  – Prior DVT or PE
  – Older patients (> 80 years)
  – Pregnant patients (especially > 20 weeks)
  – Cancer and hospitalized patients

Diagnostic Algorithm for Evaluation of Patients with Suspected PE
Lower Extremity Imaging

- Ultrasound & CT venography have similar accuracy
- PIOPED II:
  - CTA sensitivity 83%, specificity 96%
  - CTA + CTV: sensitivity 90%, specificity 95%
- Adding CT venography for lower extremities increases sensitivity, but adds radiation and cost
- Convenient, but U/S probably preferred
  - Exceptions
    - Large, critically ill patients with extensive lower limb edema
    - Presence of lower extremity casts or bandages

Patients with Allergy to Iodinated Contrast

- Venous ultrasound
- Mild allergy
  - Premedicate with steroids → CTPA if ultrasound negative
- Severe allergy
  - V/Q if ultrasound negative

Patients with Impaired Renal Function

- Venous ultrasound
- V/Q if ultrasound negative

Patients in Extremis

- Bedside echocardiography and venous ultrasound
- CTPA when patient stabilizes

Suspected PE in Pregnancy

- VTE ultimately confirmed in <10% of pregnant women who present with concerning clinical features
- Pulmonary embolism (PE) accounts for 20% of maternal deaths in US
- Sensitivity and specificity of D-dimer 73% and 15%
  - Often falsely elevated later in pregnancy
  - Case reports of negative D-dimer and PE and DVT
- D-dimer should not be used to exclude PE

To CT or not to CT

- Risk of untreated PE vs risk of radiation
- Iodinated contrast – crosses placenta
  - Normal thyroxine levels in neonates of 344 pregnant women who had iodinated contrast for CT
Multi-society Guidelines

Developed with following assumptions
1. All studies equally available
2. Rapidity of diagnosis not critical
3. Equivalent local expertise for all tests

Other Recommendations for CTPA in Pregnancy
- 100 kVp
- 5-6 ml/sec injection rate
- Limit Z axis- stop at apex of right hemidiaphragm
- Lead shields for abdomen
- Increase iodine concentration
- +/- Breast shields
- +/- Ingested barium

Indices of PE Severity
- Clinical
- Biomarkers
- Imaging markers
- Risk stratification for optimal management
  - Monitoring
  - Therapeutic strategies

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Pulmonary Embolism Severity Index (PESI) Score

**Pulmonary Embolism Severity Index (PESI) Score**

- **Class I** - very low risk (≥ 65)
- **Class II** - low risk (66-85)
- **Class III** - intermediate risk (86-105)
- **Class IV** - high risk (106-125)
- **Class V** - very high risk (126)


**Cardiac Biomarkers**

- Mechanical obstruction and pulmonary artery vasoconstriction stimulated by neurohumoral substances and hypoxemia → increased pulmonary vascular resistance
- **Troponin**
  - Only briefly and mildly elevated
  - Due to abrupt increase in RV wall tension with compression of RCA and myocardial microinjury
- **Natriuretic peptide**
  - Related to ventricular myocyte stretch
  - Indicates RV dysfunction

**CTPA Predictors**

- **Right ventricular strain**
  - RV/LV ratio > 1.0
  - Sensitivity - 78-100%, specificity - 100%, PPV 100% compared to echo
  - 3.6 fold rate of admission to ICU
- **Clot burden**
  - Miller, Mastora, Qanadli
  - Score assigned
- **IVC and hepatic vein reflux**

CTA Predictors of Severe PE

- **RV/LV ratio**
  - Widest diameter from inner wall to inner wall
  - Measured at level of mitral and tricuspid valve


**Clot burden - no impact on short-term mortality**

Araoz PA et al. JTI 2003;18:207-16

**CT Predictors of Severe PE**

- **Strain Ratio**

S.R. = x/y

Risk of Death

Araoz PA et al. JTI 2003;18:207-16
European Society of Cardiology Model of PE Severity

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
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<tbody>
<tr>
<td>Massive (5%)</td>
<td>PE, RV dysfunction, systemic hypotension, elevated biomarkers. Mortality = 30%</td>
</tr>
<tr>
<td>Sub-massive (50%)</td>
<td>PE, RV dysfunction, no systemic hypotension, no elevated biomarkers. Mortality = 5-10%</td>
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<tr>
<td>Low-risk</td>
<td>PE, no RV dysfunction. Mortality &lt;4%</td>
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Concerns about the Use of CTPA

- Clinical impact and diagnosis of subsegmental PE
- Are we doing too many CTPA’s?
  - Radiation
  - Adverse effects of iodinated contrast
  - False positives – overtreatment and potential complications?
  - How can this be solved?

Management of Subsegmental PE

Donato AA et al. 2010
- 93 patients with isolated subsegmental PE without DVT
- 3-month clinical outcomes (anticoagulation use, recurrence, death, hemorrhage)
- 76% treated – 5.3% major hemorrhage, no deaths
- 24% observed – no recurrent PE, no deaths

Donato AA et al. Thrombosis Research 2010:126 e266–e270

Impact of CTPA on Case Fatality Rate and Mortality Rates

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What Does this Mean?

- Systematic review of literature – proportion isolated subsegmental PE (SSPE) reported has increased (5\(\rightarrow\)10%)
- Additional cases of PE might be associated with a lower severity of illness
- Randomized controlled trial comparing utility of CTPA and V/Q
  - Greater # of PE diagnosed with CTPA than V/Q
  - Rate of VTE at 3 months identical in untreated patients
  - Additional PE cases on CTPA clinically unimportant

Carrier M et al. JTH 2010;8:1716-1722
Anderson DR et al. JAMA 2007;298:2743-2753
Donato AA et al. Thrombosis Research 2010;126 e266–e270

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Isolated SSPE Treatment vs. No Treatment

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<th>Reference</th>
<th>Method</th>
<th>Recurrence</th>
<th>PE Wt.</th>
<th>Anticoagulation</th>
<th>PE Wt. No</th>
<th>Anticoagulation</th>
<th>DVT</th>
<th>Clinical Follow-up (mo)</th>
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Importance of SSPE Diagnosis

- Management of single or multiple SSPE without DVT is controversial.
- Risk of anticoagulation may outweigh risk of PE.

Patients with Isolated SSPE

- Adequate cardiopulmonary reserve
- No evidence of DVT
- Major risk factor for PE no longer present, i.e., surgery, trauma, and no continuing risk factor
- No history of central venous catheterization
- No history of atrial fibrillation
- Compliant and trustworthy patient who would return for serial noninvasive leg tests

How do we stem the tide of (inappropriate) CTPA requests?

- CTPA positive in: 9.84% patients overall, 6.36% of ED patients, 13.46% inpatients
- In the absence of risk factors, PE is extremely unlikely (0.95% chance)

Pulmonary Embolism at CT Angiography: Implications for Appropriateness, Cost, and Radiation Exposure in 2003 Patients

- CTPA positive in:
  - 9.84% patients overall
  - 6.36% of ED patients
  - 13.46% inpatients
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Computerized Clinical Decision Support

- Quarterly CTPA use \( \uparrow \) 82.1% before implementation, from 14.5 to 26.4 examinations per 1000 patients between 2003 and 2007
- After implementation, quarterly use \( \downarrow \) 20.1%, from 26.4 to 21.1 examinations per 1000 patients in subsequent two years
- Positivity rate for CTPE \( \uparrow \) from 5.8% to 9.4%

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Emerging Technologies

- Magnetic resonance imaging including angiography and venography
- CTPA
  - Dual energy CT
    - Perfusion maps
    - Monochromatic energy
  - Radiation dose reduction techniques
    - Iterative reconstruction
    - 80 kVp
    - High-pitch helical CT
    - Z-axis limitation
  - Computer-aided diagnosis

MR Angiography

Dual Energy Perfusion Imaging

- Dual energy MDCT enables detection of perfusion defects secondary to obstructive clots
  - 60 patients with PE
    - Perfusion defect volume significantly higher in patients with adverse outcomes \( p=0.002 \)

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High-pitch Dual Source CT for PE

  - Reduced dose
  - Potential benefit in patients who cannot breath-hold
  - Reduced cardiac motion artifacts

Take Home Messages

- MDCTA in suspected acute venous thromboembolism (VTE) still in evolution
- Management of PE is changing
- Radiologists should be at the forefront of educating clinicians concerning appropriate use of CTPA
- Radiologists should initiate development of tools to guide clinicians towards appropriate requests