CT of Pulmonary Embolism: Evidence for Overdiagnosis

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Disclosure

- I do not now have and have not within the past 12 months had a financial interest or other relationship with a commercial organization that may have an interest in the content of this educational activity.
Outline

- Advantages of CT
- Disadvantages of CT
- Evidence for Overdiagnosis
  - Clinical trials
  - Cohort studies
  - Clinical series
  - Descriptions
  - Metaanalysis
Advantages of CT

- Quick
  - Seconds
  - Scanner in ED
- Anatomic images easier for clinicians to understand vs VQ
- Binary interpretation vs. traditional probability interpretation of VQ
  - Negatives safe to discharge- similar to VQ
Advantages of CT vs VQ

- Alternative diagnoses that explain symptoms in many negatives
  - Atelectasis (acutely V/Q mismatch)
  - Pneumonia
  - Pulmonary edema
  - Cancer
  - Rib lesions
Advantages of CT

- **Chronic PE** develop in ~ 3-4% after 2 years

- **Etiologies:** failure of PE lysis, anticardiolipin antibody 10%, in situ thrombosis in PA hypertension

- **CT findings:** dilated central PAs, organized mural thrombi, intimal irregularity, calcium 10%, strictures, abrupt cutoff, webs, bronchial collaterals
Advantages of CT

- Pulmonary artery tumors
- Rare
- Primary vs secondary
- Angiosarcoma most common primary
Advantages of CT

- Complications of PE
  - Pulmonary infarction
  - Pleuritic chest pain
  - Hemoptysis
- Right heart dysfunction
  - Predictor of increased morbidity and mortality
Disadvantages of CT

- Radiation exposure
  Dose reduction strategies and techniques evolving (breast shields, dose modulation, low kVp, ASIR)
  Best dose reduction strategy - refrain from unnecessary imaging
- Iodinated contrast
  Renal failure
  Allergic reactions
- Indication creep: reflected by decreased PE positivity rates, initially ~20%, now as low as 5-6% in some centers
Disadvantages of CT

- Growing evidence for **overdiagnosis** of PE on CT
- **Definition:** diagnosis of clinically unimportant disease
- Overdiagnosis **does not mean** that the diagnosis is wrong
- Paradox of detailed, excellent CT images
- CT of every body part depicts “pathology” of uncertain significance
  - Lung nodules, atherosclerosis, pulmonary emboli, pancreatic, liver and adrenal lesions
Evidence for Overdiagnosis: Clinical Trials

PIOPED II: CT for suspected PE vs composite reference standard including Wells score & additional imaging

### Table 5. Positive and Negative Predictive Values of CTA, as Compared with Previous Clinical Assessment.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>High Clinical Probability</th>
<th>Intermediate Clinical Probability</th>
<th>Low Clinical Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No./Total No.</td>
<td>Value (95% CI)</td>
<td>No./Total No.</td>
</tr>
<tr>
<td>Positive predictive value of CTA</td>
<td>22/23</td>
<td>96 (78–99)</td>
<td>93/101</td>
</tr>
<tr>
<td>Positive predictive value of CTA or CTV</td>
<td>27/28</td>
<td>96 (81–99)</td>
<td>100/111</td>
</tr>
<tr>
<td>Negative predictive value of CTA</td>
<td>9/15</td>
<td>60 (32–83)</td>
<td>121/136</td>
</tr>
<tr>
<td>Negative predictive value of both CTA and CTV</td>
<td>9/11</td>
<td>82 (48–97)</td>
<td>114/124</td>
</tr>
</tbody>
</table>

* The clinical probability of pulmonary embolism was based on the Wells score: less than 2.0, low probability; 2.0 to 6.0, moderate probability; and more than 6.0, high probability. CI denotes confidence interval.

† To avoid bias for the calculation of the negative predictive value in patients deemed to have a low probability of pulmonary embolism on previous clinical assessment, only patients with a reference test diagnosis by ventilation–perfusion scanning or conventional pulmonary DSA were included.
PPV 58% low clinical probability, 56% VQ in PIOPED I
Anticoagulation subjects patients to serious risk of bleeding: morbidity 7-10% in the elderly, mortality 1%

“…. results of outcome studies in which many such patients were probably not treated on the basis of false negative…… suggest that most that most such thrombi do not need to be treated & therefore do not need to be detected.”
Evidence for Overdiagnosis: Clinical Trials

- Anderson et al.- CT Pulmonary Angiography vs Ventilation-Perfusion Lung Scanning in Patients With Suspected PE: A Randomized Controlled Trial. *JAMA* 2007;298:2743-2753

  Randomized patients with Wells criteria > 4.5 or a positive D-dimer assay to either CTPA or VQ
  17.7% in CT group diagnosed with PE
  11.7% (101/716) in VQ group diagnosed with PE

- CTPA detected 51% more PE than VQ
- Similar outcomes on follow-up for CT vs VQ
  - False negatives
  - Mortality
Evidence for Overdiagnosis

Editorial re: Anderson et al

JAMA 2007;298: 2788-2789

Imaging of Pulmonary Embolism
Too Much of a Good Thing?

Jeffrey Glassroth, MD

The study by Anderson and colleagues in this issue of JAMA convincingly demonstrates that computer tomographic pulmonary angiography can also

...is highly specific for pulmonary emboli, and eliminates some of the subjectivity and confusion associated with V/Q scan interpretation expressed in probabilities of PE. Computed tomographic pulmonary angiography can also
Evidence for Overdiagnosis: Cohort studies

- 24,871,131 New York State inpatients, 1994 - 2004
- PE diagnosis rate ~doubled
- PE death rate stable
- Increased PE diagnosis and mortality not associated
- Conclusion: Increased use of CT led to an increase in PE diagnosis without a corresponding decline in mortality

Burge et al. Increased diagnosis of PE without a corresponding decline in mortality during the CT era: Clinical Radiology 2008; 63:381-386
Evidence for Overdiagnosis: Cohort studies

Pulmonary Embolism Diagnosis and Mortality With Pulmonary CT Angiography Versus Ventilation-Perfusion Scintigraphy: Evidence of Overdiagnosis With CT?

Objective. The purposes of this study were to determine whether pulmonary emboli diagnosed with pulmonary CT angiography (CTA) represent a milder disease spectrum than those diagnosed with ventilation-perfusion (V/Q) scintigraphy, to determine the trends in incidence and mortality among patients with the diagnosis of pulmonary embolism from 2000 to 2007, and to correlate incidence and mortality trends with imaging modality trends.

Montefiore: 2087 patients with PE 2000-2007
Main outcome: PE mortality
CT vs VQ for diagnosis

Sheh et al AJR 2012;198:1340-5.
Evidence for Overdiagnosis: Cohort studies

Rate of PE diagnoses increased, 0.69 to 0.91 (p < 0.001). Mortality rate remained constant

Rate of CT- PE increased (< 0.001)
Rate of V/Q- PE decreased (p < 0.001)
Evidence for Overdiagnosis: Cohort studies

Overall PE case-fatality rate, 5.7% to 3.3% (p < 0.01)

CTPA case fatality rate vs VQ case fatality rate propensity adjusted - OR = 0.538 (95% CI 0.314 – 0.921)
Evidence for Overdiagnosis: Cohort studies

- Time Trends in Pulmonary Embolism in the United States: Evidence of Overdiagnosis
- Nationwide Inpatient and Cause-of-Death Databases
- 81% increase in PE diagnosis after introduction of CTPA, increase in presumed complications of anticoagulation, minimal change in mortality
Evidence for Overdiagnosis: Clinical Series

- Engleke et al. Radiology 2006
- Patients with small PE on CT that were missed and therefore not treated vs. patients whose PE were diagnosed and treated
- No difference in one-year survival

Engleke C, Rummeny EJ, Marten K. Pulmonary Embolism at Multi-Detector Row CT of Chest: One Year Survival of Treated and Untreated Patients. Radiology 2006;239:563-575
Evidence for Overdiagnosis: Clinical Series

- Suh et al. series of patients with PE on CTPA also evaluated with lower extremity US
- 58% with central PE had lower extremity DVT vs none with small peripheral PE

Evidence for Overdiagnosis: Clinical descriptions

- Summarized by Goodman
  Radiology 2005;234:654-658
- PE present in 20% at autopsy and >50% if pulmonary arteries are carefully scrutinized
  normal function of the pulmonary capillary bed is to filter small clots and protect the systemic circulation
- Technical advances: 1mm thick CT slices demonstrate 40% more subsegmental PE
Evidence for Overdiagnosis: Clinical descriptions

- Asymptomatic patients have incidental PE in 1-1.5% contrast-enhanced CTs
- Proportion with small, isolated subsegmental PE ranges 5-15% with suspected PE
- PIOPED I-lower mortality and risk of recurrent PE for small vs large clot burden
- Relationship between clot burden and VQ
  Cardiopulmonary reserve predict PE mortality
Evidence for Overdiagnosis: Meta-analysis

- 22 clinical trials
- Subsegmental PE diagnosis: 4.7% for single vs 9.4% for MDCT
- FN rate 0.9% vs 1.1%, respectively.
- **Conclusion:** MDCT increases dx of subsegmental PE without Δ in FN, **suggesting that subsegmental PE may not be clinically relevant**

The Diagnosis and Treatment of Pulmonary Embolism

A Metaphor for Medicine in the Evidence-Based Medicine Era

Vinay Prasad, MD; Jason Rho, MD; Adam Cifu, MD

Background: The history of pulmonary embolism (PE) provides a fascinating portrait of a well-established diagnosis and standard of care treatment moving into the age of evidence-based medicine.

Methods: We examined the history of PE and the practice of treating PE with anticoagulation.

Results: Pulmonary embolism is a diagnostic category whose definition and treatment have both changed in the past century. Initially, PE was recognizable only when massive, with the signs and symptoms of right heart failure. Anticoagulants were established as the cornerstone of PE management with a single randomized controlled trial of 35 patients in 1960 and based on commonsense pathophysiologic reasoning. Since then, the diagnostic category of PE has been broadened, and the advent of computed tomography pulmonary angiography has yielded nearly a doubling of the incidence of the disease, without a concordant decrease in mortality. Although anticoagulation remains the cornerstone of management, open questions remain: what end points are altered by anticoagulation? What is the number needed to treat?

Conclusions: Trials of newer anticoagulants and longer durations of anticoagulation have not yielded real improvements over heparin, inviting doubts regarding its efficacy. Thus, PE is the quintessential diagnosis of medicine not because it represents our greatest success, but because it captures all the complexity of medicine in the evidence-based era. It may serve as a metaphor for many other conditions in medicine, including coronary artery disease. New trials in the field continue to test trivialities, whereas fundamental questions are unanswered.

Review

- 2001: CT most common imaging modality for suspected PE in the USA
- Unsurpassed in depicting pulmonary artery anatomy and pathology
- Useful in demonstrating alternative diagnoses that explain symptoms
- Quick and easy
In addition to the risks of IV contrast and radiation, overdiagnosis is increasingly recognized as a potential risk of CT.

This is especially true when the pre-test probability is low (indication creep).

Overdiagnosis is defined as diagnosis of clinically unimportant disease.

Represents real, but clinically insignificant pathology.
Future directions

- Treatment for PE is based on diagnostic algorithms that preceded CT
- Strong evidence that CT demonstrates a less severe disease spectrum
- Randomized outcomes-based clinical trials to guide therapeutic choices for patients with good cardiopulmonary reserve and small PE on CT
Thank you