Pulmonary Embolism: Evidence for Overdiagnosis on CT
Linda B. Haramati, MD

What is overdiagnosis?
- Definition: diagnosis of clinically unimportant disease
- Overdiagnosis does not mean that the diagnosis is wrong

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

<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>N (Total No.)</td>
<td>Value (95% CI)</td>
<td>N (Total No.)</td>
</tr>
<tr>
<td>Positive predictive value of CTA or CTPA</td>
<td>21 (38)</td>
<td>96 (90-99)</td>
<td>89 (55)</td>
</tr>
<tr>
<td>Negative predictive value of CTA or CTPA</td>
<td>9 (15)</td>
<td>86 (66-97)</td>
<td>128 (111)</td>
</tr>
</tbody>
</table>

-PPV 58% - low clinical probability, 56% - VQ in PIOPED I
- Anticoagulation subjects patients to serious risk of bleeding: morbidity 7.5% in the elderly, mortality 1%
- Rx algorithm preceded CT as dominant imaging modality (2001)

PIOPED II

- Anderson et al. JAMA 2007;298:2743-2753
- CTPA vs VQ
- Randomized patients with Wells score > 4.5 or positive D-dimer assay to CTPA or VQ
  - 17.7% (123/694) CT vs 11.7% (83/712) VQ group dx PE
  - CT detected ~50% more PE than VQ,
- Similar outcomes on follow-up for CT vs VQ
  - False negatives
  - Mortality

Growing evidence for overdiagnosis of PE on CT
- Paradox of detailed, excellent CT images
- CT frequently depicts “pathology” of uncertain significance
- Lung nodules, atherosclerosis, pulmonary emboli, pancreatic, liver, kidney, adrenal

"...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

Editorial re: Anderson et al
JAMA 2007;298: 2788-2789

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 dx after introduction of CTPA, increase in presumed complications of anticoagulation, minimal change in mortality

Evidence for Overdiagnosis: Clinical Series

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


Evidence for Overdiagnosis: Imaging of Pulmonary Embolism

Too Much of a Good Thing?

PE: Pulmonary Embolism
CTPA: Computed Tomography Pulmonary Angiography
V/Q: Ventilation/Perfusion
OR: Odds Ratio
CI: Confidence Interval
Evidence for Overdiagnosis: Clinical Series

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


Evidence for Overdiagnosis: Clinical Series

- Asymptomatic patients have incidental PE in 1-1.5% contrast-enhanced CTs
- Wide range of isolated subsegmental PE -5-15% with suspected PE, depending on population
- PIOPED II-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: Clinical Series

- Summarized by Goodman
  - Radiology 2005;234:654-658
- At autopsy PE present in 20% & >50% if pulmonary arteries carefully scrutinized - pts died of other causes
- “Normal function of the pulmonary capillary bed is to filter small clots and protect the systemic circulation”

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


Practical Implications

Radiology 2014; 270

Montefiore experience

- 1962 ED and inpatients with suspected PE 7/1/11 - 6/30/12
Outcomes

<table>
<thead>
<tr>
<th></th>
<th>&quot;Definitive&quot; Negative%</th>
<th>&quot;Limited Negative&quot;</th>
<th>OR (95% CI)</th>
<th>OR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>False negative rate (readmission for PE/DVT)</td>
<td>1.8%</td>
<td>1.6%</td>
<td>0.89 (0.42 - 1.88)</td>
<td>1.07* (0.49 - 2.33)</td>
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<tr>
<td>Additional Imaging (CT Thorax, V/Q, LE Doppler)</td>
<td>2.1%</td>
<td>3.8%</td>
<td>1.03 (0.63 - 1.65)</td>
<td>1.77 (1.03 - 3.05)</td>
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<td>Anticoagulation (Dalteparin or IV Heparin)</td>
<td>15%</td>
<td>19%</td>
<td>1.38 (1.07 - 1.76)</td>
<td>1.30 (1.01 - 1.69)</td>
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<td>Bleeding Events</td>
<td>2.7%</td>
<td>4.2%</td>
<td>1.59 (0.96 - 2.63)</td>
<td>1.43 (0.85 - 2.39)</td>
</tr>
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Adjusted for age, Charlson comorbidity score, anticoagulation use, and metastatic malignancy.

Adjusted for previous DVT/PE, comorbid DVT on current admission, heart rate, and d-dimer.

Ambiguity: Cohort study

CT Findings and Long-Term Mortality After Pulmonary Embolism

Michael J. Maron, MD
Bruce M. Maron, MD
Bradley J. Maron, MD
William M. Thompson, MD
Walter E. Stewart, MD
Philip A. Aronson, MD

OBSERVATIONS: The utility of CT imaging in predicting outcome in patients with acute pulmonary embolism (PE) is uncertain. The purpose of this study was to investigate the relationship between CT scan findings and long-term mortality in patients with PE. The study included 1105 patients who underwent CT imaging within 24 hours of PE diagnosis. The CT findings evaluated included size of the embolus, degree of perfusion deficit, and presence of right heart strain. The results showed that larger clot burden and severe perfusion deficit were associated with increased mortality. The study concluded that CT findings can be useful in predicting long-term mortality in patients with PE.

AJR 2012;199:1396-1402

Review

- Overdiagnosis is defined as diagnosis of clinically unimportant disease
- Represents real, but clinically insignificant pathology
- CT demonstrates a less severe disease spectrum
- Complexity and ambiguity remain

The Diagnosis and Treatment of Pulmonary Embolism

A Metaphor for Medicine in the Evidence-Based Medicine Era

Yvonne F. Paul, MD
Max Lin, MD
Alok Gupta, MD

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

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

Results: Pulmonary embolism is a diagnostic category that is defined as an acute event leading to death of the patient. Initially, PE was recognized as a life-threatening condition, with the diagnosis based on right heart failure. Anticoagulation was established as the cornerstone of PE management with a single anticoagulant treatment called oral anticoagulants. In the past decade, advances in imaging technology have allowed for earlier detection of PE, resulting in more effective treatment options. The article discusses the evolution of the treatment of PE and highlights the importance of evidence-based medicine in patient care.

AJR 2012;198:1346-1352

Thank you