Imaging in PE guidelines

or

the influence on radiologist’s detection performance

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Tokuda Hospital Sofia

Sofia, 23-24 April 2010
Guidelines/Expert consensus documents

- Their goal is to provide
  - Early diagnosis and adequate treatment policy
  - Reduction of the morbidity and mortality
  - Lowering cost

- The only way to safely implement new and better diagnostic and therapeutic tools, algorithms and pathways

- Active implementation of a consensus-based strategy
  - Increasing the number of correct diagnoses
  - Reducing the incorrect treatment
  - Inducing a rapid change in the diagnostic behaviour of physicians

Guidelines in the real world Examplified on the development of guidelines in Pulmonary Embolism; Prof. Dr. M. Oudkerk; ECSR meeting Leipzig 2009
Guidelines/Expert consensus documents

- Focuses on currently available and validated methods of diagnosis, prognostic evaluation and therapy
  - **Accuracy studies** - designed to establish the characteristics of a diagnostic test (sens. and specif.) by comparing test results with a reference diagnostic criterion (gold standard)
  - **Outcome studies** evaluate patient outcomes when a given diagnostic test or strategy is used for clinical decision-making
PE guidelines

Where is the radiologist?
1938-1940
Westermark, Hampton, Castelman

CXR

- Hypoperfusion of the affected lung
- Plate-like atelectasis
- Pleural effusion
- Elevation of the hemidiaphragm
1979
Ventilation-perfusion studies in suspected PE

- Classified into groups with low, intermediate and high probability of PE
- Based on the size and number of perfusion defects
- Comparison between perfusion defects and ventilatory defect with CXR findings

Biello et al. AJR 1979

### TABLE 4: Scheme for Interpretation of V-Q Imaging

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>Pattern</th>
<th>Frequency of Pulmonary Embolism (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Probability of pulmonary embolism:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>Normal perfusion</td>
<td>0*</td>
</tr>
<tr>
<td></td>
<td>Small V-Q mismatches</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Focal V-Q matches with no corresponding radiographic abnormalities</td>
<td>4.8</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Perfusion defects substantially smaller than radiographic abnormalities</td>
<td>7.7</td>
</tr>
<tr>
<td></td>
<td>Diffuse, severe airway obstruction</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Matched perfusion defects and radiographic abnormalities</td>
<td>27</td>
</tr>
<tr>
<td>High</td>
<td>Perfusion defects substantially larger than radiographic abnormalities</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>1 or more large, or 2 or more moderate-sized V-Q mismatches with no corresponding radiographic abnormalities</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td></td>
<td>92</td>
</tr>
</tbody>
</table>

* From [4, 6, 7].
Lung scan interpretation: effect of different observers and different criteria

<table>
<thead>
<tr>
<th>TABLE I: Diagnostic Schemes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>McNeil Criteria</strong></td>
</tr>
<tr>
<td>2. Multiple P defects, all with ventilation (V) match.</td>
</tr>
<tr>
<td>3. Single V/P mismatch—subsegment.</td>
</tr>
<tr>
<td>4. Single V/P mismatch—segment.</td>
</tr>
<tr>
<td>5. Mixed V/P match and mismatch.</td>
</tr>
<tr>
<td>6. P defect with matched density on chest radiographs.</td>
</tr>
<tr>
<td>7. Single V/P mismatch—lung.</td>
</tr>
<tr>
<td>8. Single V/P mismatch—lobe.</td>
</tr>
<tr>
<td>9. Multiple V/P mismatches, largest being subsegmental.</td>
</tr>
<tr>
<td>10. Multiple V/P mismatches, largest being lung.</td>
</tr>
<tr>
<td>11. Multiple V/P mismatches, largest being lobar.</td>
</tr>
<tr>
<td>12. Multiple V/P mismatches, largest being segmental.</td>
</tr>
<tr>
<td></td>
</tr>
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<td></td>
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<td></td>
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<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>* Small = &lt;25% of an anatomic segment; Moderate = 25–75% of an anatomic segment; Large = &gt;75% of an anatomic segment</td>
</tr>
<tr>
<td>† Small subsegmental = &lt; half of an anatomic segment; Moderate subsegmental = &gt; half, but &lt; full anatomic segment</td>
</tr>
</tbody>
</table>
1982
Sinner W. Computed tomography of pulmonary thromboembolism; Eur J Radiol 1982;2:8–13

- CT was able to visualize large pulmonary emboli as nonenhancing regions in enlarged PA
- CT as a useful adjunct to V/Q scan
- Slow scanning time

versus

- Standardized algorithm in the interpretation of V/Q scans
Clinical assessment combined with the VQ scan established the diagnosis or exclusion of PE only a minority of patients - those with clear and concordant clinical and VQ scan finding.

PIOPED I proposed new schema VQ categories:
- Normal (high NPV)
- High probability (two or more mismatched segmental perfusion defects; high PPV)
- Non high probability
Comparison of Biello, McNeil, and PIOPED criteria for the diagnosis of PE on lung scans

**Table 1: Sets of Criteria Used to Assess Radionuclide Scans for the Probability of Pulmonary Embolism on Angiograms**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1. Normal perfusion</td>
<td>1. Normal perfusion</td>
<td>1. Normal perfusion</td>
</tr>
<tr>
<td>Very low probability</td>
<td>2. Single ventilation/perfusion mismatch; segmental or subsegmental; chest radiograph clear</td>
<td>2. Small* ventilation/perfusion mismatch(es)</td>
<td>2. One to three small* perfusion defects; normal chest radiograph; ventilation irrelevant</td>
</tr>
<tr>
<td></td>
<td>4. Multiple ventilation/perfusion mismatches, subsegmental; chest radiograph clear</td>
<td>4. Perfusion defect substantially smaller than chest film density</td>
<td>4. Single moderate* perfusion defect; chest radiograph normal; ventilation irrelevant</td>
</tr>
<tr>
<td>Indeterminate or inter-</td>
<td>5. Mixed ventilation/perfusion match and mismatch</td>
<td>5. Severe diffuse obstructive pulmonary disease with perfusion defects</td>
<td>5. Any perfusion defect substantially smaller than chest film defect; ventilation irrelevant</td>
</tr>
<tr>
<td>mediate</td>
<td>6. Perfusion defect with matched density on chest radiograph</td>
<td>6. Perfusion defect same size as change on chest film</td>
<td>6. Ventilation/perfusion match ≤50% of lung including ≤75% of one lung zone* with normal or almost normal chest radiograph</td>
</tr>
<tr>
<td>High probability</td>
<td>7. Single ventilation/perfusion mismatch, lobe or larger, with normal chest film</td>
<td>7. Single medium* ventilation/perfusion mismatch</td>
<td>7. More than three small* perfusion defects; chest film and ventilation irrelevant</td>
</tr>
<tr>
<td></td>
<td>8. Multiple ventilation/perfusion mismatches, segmental or larger; chest film normal</td>
<td>8. Single large* ventilation/perfusion mismatch</td>
<td>8. Three or fewer small perfusion/chest film matches; ventilation irrelevant</td>
</tr>
<tr>
<td></td>
<td>9. Perfusion deficit substantially larger than density on chest film</td>
<td>9. Perfusion defect substantially larger than density on chest film</td>
<td>9. Abnormality that is not defined clearly by other criteria</td>
</tr>
<tr>
<td></td>
<td>10. Multiple medium or large* ventilation/perfusion mismatches without matched density on chest film</td>
<td>10. Two or more large* perfusion defects; ventilation and chest film normal</td>
<td>10. Two or more large* perfusion defects in which perfusion defect is substantially larger than either matching ventilation or chest film defect</td>
</tr>
<tr>
<td></td>
<td>11. Perfusion deficit substantially larger than density on chest film</td>
<td>11. Two or more moderate* perfusion defects and one large* perfusion defect; ventilation and chest film normal</td>
<td>11. Two or more moderate* perfusion defects and one large* perfusion defect; ventilation and chest film normal</td>
</tr>
<tr>
<td></td>
<td>12. Perfusion defect substantially larger than density on chest film</td>
<td>12. Four or more moderate* perfusion defects; ventilation and chest film normal</td>
<td>12. Four or more moderate* perfusion defects; ventilation and chest film normal</td>
</tr>
</tbody>
</table>

- PIOPED scale with the highest number of indeterminate results
- McNeil’s criteria demonstrate the least favorable likelihood for predicting PE on an angiogram
- The study suggests that the Biello scheme represents the best compromise of the sets of criteria studied

Webber et al. AJR 1990
1993 - 1999
US and deep venous thrombosis – two clinical presentation of the same disease

Jacques Cornuz, MD, MPH
Steven D. Pearson, MD
Joseph F. Polak, MD, MPH

Index terms:
Venous, extremities
Veins, thrombosis, 935.458, 935.751
Veins, US, 935.12981, 935.12983

Radiology 1999; 211:637-641

Deep Venous Thrombosis:
Complete Lower Extremity
Venous US Evaluation in
Patients without Known Risk
Factors—Outcome Study

TABLE 3
Comparison of the Incidence of Venous Thrombosis in the Current Study
with the Incidence in Published Series

<table>
<thead>
<tr>
<th>Series</th>
<th>Method</th>
<th>Minimal Follow-up (mo)</th>
<th>Rate (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heijboer et al (3)</td>
<td>Serial US</td>
<td>6</td>
<td>1.5 (0.5, 3.3)</td>
</tr>
<tr>
<td>Heijboer et al (3)</td>
<td>Serial impedance plethysmography</td>
<td>6</td>
<td>2.5 (1.2, 4.6)</td>
</tr>
<tr>
<td>Hull et al (13)</td>
<td>Serial impedance plethysmography</td>
<td>8</td>
<td>1.9 (0.7, 4.2)</td>
</tr>
<tr>
<td>Vaccaro et al (17)</td>
<td>Single US†</td>
<td>8</td>
<td>0.5 (0.1, 1.86)</td>
</tr>
<tr>
<td>Birdwell et al (20)</td>
<td>Serial US</td>
<td>3</td>
<td>0.6 (0.07, 2.14)</td>
</tr>
<tr>
<td>Current study‡</td>
<td>Single US with calf vein evaluation</td>
<td>3</td>
<td>0 (0.4)</td>
</tr>
</tbody>
</table>

Note.—In all studies except that by Birdwell et al and the current study, the distribution and prevalence of risk factors were not reported.
* Numbers in parentheses are the 95% CI.
† Serial US was performed in a few patients.
‡ Study included patients without risk factors for DVT.

• DVT in 29% of pts with proven PE
• DVT in 13%–15% of pts with suspect PE
• specificity in the symptomatic group > 95%
• specificity in asymptomatic group < 80%

Lewis BD et all; Diagnosis of acute deep venous thrombosis of the lower extremities: prospective evaluation of color Doppler flow imaging versus venography. Radiology 1994;192:651-655
1993
Dutch PE consensus strategy (Arch Inter Med 1993)
Active implementation of a consensus strategy improves diagnosis and management in suspected pulmonary embolism

A. BERGHOUT¹, M. OUDKERK², S.G. HICKS*, T.H. TENG¹, M. PILLAY² and H.R. BÜLLER³

From the ¹Zuiderziekenhuis, Rotterdam, ²Dr Daniel den Hoed Cancer Center/University Hospital Rotterdam, Rotterdam, and ³Department of Internal Medicine, University of Amsterdam, Amsterdam, The Netherlands

Received 21 December 1999

Table 2  Outcome of diagnostic tests and subsequent treatment in patients with clinically suspected pulmonary embolism before and after the implementation of a consensus-based diagnostic strategy

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Perfusion lung scan performed*</td>
<td>618</td>
<td>250</td>
</tr>
<tr>
<td>Normal perfusion scan</td>
<td>223 (36%)</td>
<td>96 (38%)</td>
</tr>
<tr>
<td>Abnormal perfusion scan</td>
<td>395 (64%)</td>
<td>154 (62%)</td>
</tr>
<tr>
<td>Pulmonary embolism adequately confirmed</td>
<td>31 (8%)</td>
<td>41 (26.5%)</td>
</tr>
<tr>
<td>Pulmonary embolism adequately excluded</td>
<td>13 (3%)</td>
<td>49 (32%)</td>
</tr>
<tr>
<td>Pulmonary embolism diagnosis uncertain, but treated with anticoagulants</td>
<td>216 (55%)</td>
<td>20 (13%)</td>
</tr>
<tr>
<td>Pulmonary embolism diagnosis uncertain, but not treated with anticoagulants</td>
<td>135 (34%)</td>
<td>44 (28.5%)</td>
</tr>
</tbody>
</table>

Active implementation of a consensus-based strategy in the diagnosis of PE increases definitive diagnosis, and reduces the numbers treated with anticoagulants. It induces a rapid change in the diagnostic behavior of physicians.
Although active implementation of the guideline-based diagnostic work-up for pulmonary embolism increased the number of adequate diagnoses, the diagnostic work-up was not completed in half of the patients with inconclusive lung scans. The main reasons for this were the advanced age of the patients, alternative diagnoses, and a reluctance to perform invasive pulmonary angiography.

Need of a new diagnostic method

- High sensitivity and specificity
- Noninvasive
- Reproducible
- Low cost
1992 up to now

- different scanning protocols
- different injection protocols
- difference in pretest clinical probability

Perfusion scan

- normal
- subsegmental
- segmental

MDCT

- positive

Angiography

- negative
- positive

No ac therapy

Ac therapy

- Low mortality
- Low morbidity
- Moderate cost
- No overtreatment
Moores et al; Meta-analysis: outcomes in patients with suspected PE managed with CTA; AnnInternMed 2004;141:866-874

- assessment the safety of withholding anticoagulation in pts with suspected PE and negative CTA
- twenty three studies/ 4657 pts
- 3 months of follow-up
- VTE 1.4% (95% confidence interval); fatal PE 0.51% (95% cof.interval)

“...it’s seems that at last, we have a non-invasive technique that compares favorably than the previous gold standard of conventional angiography”

Rathbum SW et al; Ann Int Med 2000;132:227-232
Wittram C et al; Radiographics 2004;24:1219-1238
Acute PE - direct and indirect signs

- Intraluminal filling defects
- Filling defect with acute angle with the arterial wall
- Complete arterial occlusion
- Enlarged diameter of the affected vessel

- Lack of vessels enhancement
- Hypoperfusion areas
- Pulmonary infarct
- Flat atelectases
- Pleural effusion

• NPV of MDCT alone is similar to that of conv. pulmonary angiography

Simon M AJR 2001; 177: 195-198
Inadequacy in the assessment of subsegmental vessels...

When are they of importance?

- bad cardiopulmonary reserve
- concomitant DVT
- patients with recurrent BTE and suspected trombophilia

MDCT replaces conventional angiography and becomes “gold standard” technique.

MDCT could be used as a single diagnostic method in 98,5% of patients and to define the therapeutic algorithm in 97,9%.

Fatal recurrent PE

<table>
<thead>
<tr>
<th>In negative pulmonary angiography</th>
<th>(0.53%) (PIOPED; JAMA 1992)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FU &gt; 6 months</td>
<td>3/1050 (0.3%) (Van Beek et al; Clin Radiol 2001)</td>
</tr>
<tr>
<td>FU &gt; 12 months</td>
<td>2/524 (0.4%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In negative Spiral CTA</th>
<th>(0.9%) (Ferretti et al, Radiology 1997)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FU 3 months</td>
<td>1/112 (1.6%) (Tillie-Leblond et al, Radiology 2002)</td>
</tr>
<tr>
<td>FU 12 months</td>
<td>3/185 (0.5%) (Moores et al; AnnIntMed 2004)</td>
</tr>
<tr>
<td>FU 3 months</td>
<td>0.51% (Revel et al; Radiology 2005)</td>
</tr>
<tr>
<td>FU 3 months</td>
<td>7/1505 (1.8%) (Christopher study, JAMA 2006)</td>
</tr>
</tbody>
</table>
1998-2004
PE and DVT as a different presentation of the same disease

RD Hull et al; Pulmonary angiography, ventilation lung scanning, and venography for clinical suspected PE with abnormal perfusion lung scan; Ann Int Med 1998;129:1044


- PIOPE II - 711 CT venograms showed 95% concordance between US and CT venography
- The corresponding increase in NPV is not clinically significant
- Addition CT venography to the CTA increase the percentage of pts requiring anticoagulation by 5-27%
- High radiation exposure

Cham MD et al; Radiology 2005;234:591-594
2007
Management of Suspected Acute Pulmonary Embolism in the Era of CT Angiography: A Statement from the Fleischner Society

“The question now no longer concerns demonstrating its (MDCTA) clinical value but optimizing its use in various categories of patients”

- fast, noninvasive
- additional information for whole chest structures
- high radiation exposure

- reassessment of isolated subsegmental PE (frequency 1.5 - 5.4%)
- combine CTA and CT phlebography

optimal patients selection
Recommendations can now be formulated on the basis of the results of the (PIOPED) II trial and other studies, albeit with continued reliance on the physician’s judgment. The following recommendations include both evidence-based recommendations and opinions based on information available at this time. Both are subject to revision as further data become available.

The imaging diagnostic test choice depends on the:

- Clinical probability
- Patient’s condition
- Estimation of the CM induced complications
- Estimation of the radiation exposure risk
- Cost

Allergy to iodinated contrast material or impaired renal function

- D-dimer and clinical test
- Doppler US of lower legs; positive result – active treatment
- V/Q scintigraphy in negative Doppler US
- Serial Doppler US of lower legs
- MRA?

Pregnancy

- D-dimer test
- Doppler US of lower leg
- V/P scintigraphy
- MDCT ???

“the radiation dose to the fetus from 16-section CT angiography (0.24–0.47 mGy at 0 months and 0.61–0.66 mGy at 3 months) is of the same magnitude as that from a ventilation/perfusion scan (0.25–0.36 mGy at 0 months and 0.31–0.32 mGy at 3 months) or a perfusion scan alone (0.21 mGy at 0 months and 0.30 mGy 3 months)"
PE guidelines: what's new on diagnosis?

- Valid and accurate scores for assessing clinical probability
- More evidence on D-dimer
- Predominance of multidetector CT
- Definition of validated diagnostic criteria
- Different strategies for high-risk and non high-risk PE
Heart assessment

- Assessment of the after-load effect on the thin-walled RV
- Increased in-hospital mortality of pts who exhibit RVD in association with PE
- RVD is important for risk stratification
- CTA with heart assessment obviate the need for concomitant EchoCGr

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Principal markers useful for risk stratification in acute pulmonary embolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical markers</td>
<td>Shock</td>
</tr>
<tr>
<td></td>
<td>Hypotension(^a)</td>
</tr>
<tr>
<td>Markers of RV dysfunction</td>
<td>RV dilatation, hypokinesis or pressure overload on echocardiography</td>
</tr>
<tr>
<td></td>
<td>RV dilatation on spiral computed tomography</td>
</tr>
<tr>
<td></td>
<td>BNP or NT-proBNP elevation</td>
</tr>
<tr>
<td></td>
<td>Elevated right heart pressure at RHC</td>
</tr>
<tr>
<td>Markers of myocardial injury</td>
<td>Cardiac troponin T or I positive(^b)</td>
</tr>
</tbody>
</table>
- **Heart assessment**
  - Increase short axis dimension of the RV compared with LV
  - Increase dimension of RA
  - RA/RV thrombus
  - Leftward shift of the interventricular septum
  - RV dyskinesia
  - Decrease EF of the ventricles

*CT with sens. 91% and specif. 100%

Contractor S et al: Role of helical CT in detecting right ventricular dysfunction secondary to acute pulmonary embolism; J Comp Assist Tomogr 2002;26:587-591

Lim KE et al: Right ventricular dysfunction secondary to acute massive PE detected by helical CTA; JClinImaging 2005;29:16-21
CTA can be used with confidence as a first-line investigative tool in the diagnosis of PE.

Current guidelines suggest replacing potentially misleading terms such as “massive”, “submassive” and “non-massive” with the estimated level of the risk of PE-related early death.

Clinical assessment allows stratification into high-risk and non-high-risk PE.

Clinical assessment helps in the choice of the optimal diagnostic strategy.
Clinical Probability Score

Sy and signs of deep venous thrombosis  3.0
Heart rate > 100beats/min  1.5
Recent surgery (<4wk)  1.5
Previous deep vein thrombosis or PE  1.5
Hemoptysis  1.0
Cancer  1.0
PE more likely than alternative diagnosis  3.0

Low (<2) or intermediate (2-6) score

D-Dimer assay (highly sensitive)

negative

Do not treat

positive

High (>6) score

MDCT

No PE

Treat

PE confirmed
Multidetector CT: summary of outcome studies


3-month thromboembolic risk in patients left untreated based on a negative MDCT scan:

- **CTEP3 study** (n=756) 1.7% (0.7 to 3.9)
- **CHRISTOPHER study** (n=3306) 1.3% (0.7 to 2.2)
- **PEDS study** (n=694) 0.4% (0.1 to 1.3)
- **CTEP4 study** (n=1693) 0.3% (0.1 to 1.1)

A negative CT safely rules out PE at least in patients with a non high clinical probability
Conclusions

- The diagnostic workup for pts with suspected PE should begin with an assessment of the clinical probability on the basis of validated scores (Wells or Geneva’s)

- ECG and CXR have low sens and specif. They are helpful in weakening the clinical suspicion

- D-dimer test as a next step in low and moderate pretest probability group
Conclusions

- MDCT as an important test to diagnose or rule out PE
- Right heart evaluation as an important .....; PA diameter is no longer the main prognostic factor
- If MDCTA shows only subsegmental defects in pt with low clin probability, false positive result should be considered
Conclusions

- Combining MDCTA and MDCTV in a single procedure is generally not recommended, since increases the radiation exposure without significant increase of specificity or NPV

- VP scintigraphy remains an alternative to MDCTA when:
  - Injection of a CM is a concern
  - In inconclusive or sub-optimal results from MDCT

- DSA only in cases when catheter-based treatment is an option
Thank you for your attention