Venous Thromboembolic Disease: which Scores are Useful?

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21.03.2014
My talk today

- Why using CPR? The example of clinical probability scores
- How do the currently available CPRs compare with each other?
- Which CPRs are really useful in VTE management?

CPR: Clinical Prediction Rule
## Prevalence of PE according to lung scintigraphic probability*

<table>
<thead>
<tr>
<th>Clinical probability</th>
<th>Very low</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (&lt; 20%)</td>
<td>2%</td>
<td></td>
<td>28%</td>
<td>56%</td>
</tr>
<tr>
<td>Intermediate</td>
<td>40%</td>
<td>66%</td>
<td>88%</td>
<td></td>
</tr>
<tr>
<td>High (≥ 80%)</td>
<td></td>
<td></td>
<td></td>
<td>96%</td>
</tr>
</tbody>
</table>

* as compared with a composite reference standard

**PIOPED Investigators. JAMA 1990;263:2753**

Empirical assessment (compared to CPR)
- performs similarly
- cannot be easily transmitted
- is less reproducible
Reproducibility of clinical assessment

N=110

**Empirical pretest clinical probability**
- Any probability (<20, 20-80 >80%)
- Low clinical probability (<20%)
- High clinical probability (>80%)

- Kappa: 0.33
- Kappa: 0.41
- Kappa: 0.29

**Explicit pretest clinical probability**
- Wells model (three categories)
- Wells model (two categories)

- Kappa: 0.45
- Kappa: 0.62

Agreement
- Excellent > 0.6
- Good 0.4-0.6
- Fair 0.2-0.4
- Poor < 0.2

# PIOPED II: Results in relation to clinical probability assessment (explicit, Wells)

<table>
<thead>
<tr>
<th>Clinical probability</th>
<th>Prevalence of PE, n/n (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CT positive</td>
</tr>
<tr>
<td>Low</td>
<td>22/38 (58%)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>93/101 (92%)</td>
</tr>
<tr>
<td>High</td>
<td>22/23 (96%)</td>
</tr>
</tbody>
</table>

*as compared with a composite reference standard*
CPR: Influence on diagnostic or therapeutic strategy?

D-dimer
Initiate treatment

Low
Medium
High

Unlikely
Likely

Why using a validated diagnostic algorithm?

**Table 3. Patient Outcomes at 3 Months after Exclusion of Pulmonary Embolism***

<table>
<thead>
<tr>
<th>Diagnostic Work-up</th>
<th>Patients Receiving Appropriate Management (n = 418)</th>
<th>Patients Receiving Inappropriate Management (n = 506)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total thromboembolic events, n (%)</strong></td>
<td>5 (1.2)</td>
<td>39 (7.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Nonfatal thromboembolic event, n</strong></td>
<td>2</td>
<td>10</td>
<td>0.045</td>
</tr>
<tr>
<td><strong>Unexplained sudden death, n</strong></td>
<td>3</td>
<td>29</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Patients who received anticoagulation for reasons other than thromboembolic disease were excluded from follow-up analysis.

My talk today

- Why assessing prior clinical probability of VTE?
- How do the currently available CPRs compare with each other?
- Which CPR are really useful in VTE management?

CPR: Clinical Prediction Rule
Direct comparison between CPRs

[Graphs showing receiver operating characteristic curves for different CPRs and RGS cutoffs.]

The area under the receiving-operating characteristic curve was similar when 4 different RGS cutoff levels were applied: 0.67 (95% CI, 0.59 to 0.75) for a cutoff ≤ 4, 0.66 (CI, 0.58 to 0.75) for a cutoff ≤ 5, 0.65 (CI, 0.56 to 0.74) for a cutoff ≤ 6, and 0.65 (CI, 0.56 to 0.75) for a cutoff ≤ 7. RGS = revised Geneva score.

My talk today

• Why assessing prior clinical probability of VTE?

• How do the currently available CPRs compare with each other?

• Which CPR are really useful in VTE management?

CPR: Clinical Prediction Rule
Useful CPRs

• Diagnostic CPRs (Wells rules, Geneva rule, etc.)
• Prognostic scores (PESI, Hestia rule, etc.)
• Bleeding risk scores (OBRI, RIETE…)
• PE exclusion scores (PERC rule)
• VTE recurrence scores (REVERSE rule, Vienna prediction model, etc.)
PESI and simplified PESI

0 points = low-risk
(30-day mortality <1.5%)

Jiménez et al. Arch Intern Med 2010

<table>
<thead>
<tr>
<th>Variable</th>
<th>Original PESI</th>
<th>Simplified PESI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 80 y</td>
<td>+10</td>
<td>1</td>
</tr>
<tr>
<td>Male sex</td>
<td>+20</td>
<td>1</td>
</tr>
<tr>
<td>History of cancer</td>
<td>+30</td>
<td>1</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>+10</td>
<td>1</td>
</tr>
<tr>
<td>History of chronic lung disease</td>
<td>+10</td>
<td>1</td>
</tr>
<tr>
<td>Pulse $\geq$ 110 beats/min</td>
<td>+20</td>
<td>1</td>
</tr>
<tr>
<td>Systolic blood pressure $&lt; 100$ mm Hg</td>
<td>+30</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory rate $\geq$ 30 breaths/min</td>
<td>+20</td>
<td>1</td>
</tr>
<tr>
<td>Temperature $&lt; 36^\circ$ C</td>
<td>+20</td>
<td>1</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>+60</td>
<td>1</td>
</tr>
<tr>
<td>Arterial oxyhemoglobin saturation level $&lt; 90%$</td>
<td>+20</td>
<td>1</td>
</tr>
</tbody>
</table>
Outpatient Treatment of PE: the OTPE study

Exclusion criteria:
1. Arterial oxygen saturation <90%
2. Systolic blood pressure <100 mm Hg
3. Severe chest pain
4. Elevated bleeding risk
5. Severe renal failure (creatinine clearance <30 ml/min.)
6. Psychosocial contraindications
7. PE diagnosed >23 h before screening

# OTPE study: comparison of medical outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Outpatient (N=171)</th>
<th>Inpatient (N=168)</th>
<th>1-sided P-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent VTE at 90 days</td>
<td>1 (0.6)</td>
<td>0</td>
<td>0.011</td>
</tr>
<tr>
<td>Major bleeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at 14 days</td>
<td>2 (1.2)</td>
<td>0</td>
<td>0.031</td>
</tr>
<tr>
<td>at 90 days</td>
<td>3 (1.8)</td>
<td>0</td>
<td>0.086</td>
</tr>
<tr>
<td>Overall mortality at 90 days</td>
<td>1 (0.6)</td>
<td>1 (0.6)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Non-inferiority margin= 4%

Useful CPRs

• Diagnostic CPRs (Wells rules, Geneva rule, etc.)

• Prognostic scores (PESI, Hestia rule, etc.)

• Bleeding risk scores (OBRI, RIETE…)

• PE exclusion scores (PERC rule)

• VTE recurrence scores (REVERSE rule, Vienna prediction model, etc..)
# Bleeding Risk scores for VTE

<table>
<thead>
<tr>
<th>Score</th>
<th>Study Design</th>
<th>Score Variables</th>
<th>Risk of Major Bleeding</th>
</tr>
</thead>
</table>
| Outpatient Bleeding Risk Index | Retrospective 556 patients | Age ≥ 65 years (+1)  
History of GI bleeding (+1)  
History of stroke (+1)  
Recent myocardial infarction and/or hematocrit < 30% and/or diabetes mellitus and/or creatinine > 1.5 mg dL⁻¹ (+1) | Low: 0 points  
Intermediate: 1-2 points  
High: ≥ 3 points |
| Kuijer score           | Retrospective 246 patients | Age ≥ 60 years (+1.6)  
Female gender (+1.3)  
Malignancy (+2.2) | Low: 0 points  
Intermediate: 1-3 points  
High: ≥ 3 points |
| Kearon score           | Prospective 738 patients | Age ≥ 65 years (+1)  
Previous stroke (+1)  
Previous peptic ulcer (+1)  
Previous GI bleeding (+1)  
Renal impairment (+1)  
Anemia (+1)  
Thrombocytopenia (+1)  
Liver disease (+1)  
Diabetes mellitus (+1)  
Use of antiplatelet therapy (+1) | Low: 0-1 points  
Intermediate: 2-3 points  
High: ≥ 4 points |
| RIETE score            | Retrospective 13057 patients | Recent major bleeding (+2)  
Creatinine > 1.2 mg dL⁻¹ (+1.5)  
Anemia (+1.5)  
Cancer (+1)  
Clinically overt pulmonary embolism (+1)  
Age >75 years (+1) | Low: 0 points  
Intermediate: 1-4 points  
High: ≥ 4 points |
ROC Curves: Bleeding risk scores

Useful CPRs

• Diagnostic CPRs (Wells rules, Geneva rule, etc.)

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Assessment of clinical probability

Unresolved issues

**Clinical suspicion of PE**

- HR/SBP > 1.0 or age > 50 years?
  - No → Not high risk
  - Yes → Next step

**Unexplained hypoxemia?** SaO2 < 95%
- Non smoker, no asthma or COPD
  - Yes → High risk
  - No → Not high risk

**Unilateral leg swelling?**
  - Yes → High risk

**Recent surgery (within past 4 weeks)?**
  - Yes → High risk

**Hemoptysis?**
  - Yes → High risk
  - No → Not high risk

The PERC rule

(Kline et al., J Thromb Haemost 2004;2:1247-55)
## The PERC rule

<table>
<thead>
<tr>
<th></th>
<th>PE, %</th>
<th>PE in low-risk patients*, %</th>
<th>Sensitivity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Derivation</strong></td>
<td>11</td>
<td>1.4 (0.5 to 3)</td>
<td>96 (90 to 99)</td>
</tr>
<tr>
<td><strong>Validation</strong></td>
<td>26</td>
<td>6.7 (3 to 14)</td>
<td>97 (93 to 97)</td>
</tr>
</tbody>
</table>

*according to PERC rule

Kline et al., JTH 2004;2:1247-55.
Useful CPRs

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# VTE recurrence scores

<table>
<thead>
<tr>
<th>Prediction model</th>
<th>Items</th>
<th>Points</th>
<th>Development status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vienna Prediction model</td>
<td>Male sex, Proximal DVT, PE, D-Dimer (continuous value post VKAs)</td>
<td>N/A</td>
<td>Derived</td>
</tr>
<tr>
<td>Updated Vienna Prediction model</td>
<td>Male sex, Proximal DVT, PE, Multiple D-Dimer measurement (post VKA)</td>
<td>N/A</td>
<td>Derived and internally validated</td>
</tr>
<tr>
<td>HERDOO</td>
<td>Hyperpigmentation, edema, leg redness, D-Dimer ≥ 250 microgr/L (on VKA), BMI &gt;30 kg/m2, Age ≥65 y</td>
<td>1 1 1</td>
<td>Derived and internally validated. External validation pending.</td>
</tr>
<tr>
<td>DASH tool</td>
<td>D-dimer (normal/abnormal post VKA), Age ≤ 50 years, Male sex, Hormonal therapy</td>
<td>2 1 1 -2</td>
<td>Derived not validated</td>
</tr>
</tbody>
</table>
Summary

• Many scores for VTE (diagnosis, prognosis, bleeding, recurrence)

• Scores may improve patient prognosis

• But many scores still need prospective validation/impact analysis

• Still much work to increase their use (education, handheld computers)

• Two many scores kill the scores
Merci pour votre attention !