Travel and Risk for Venous Thromboembolism

November 2009

Prof. P. HAINAUT
Médecine Interne
Maladie thromboembolique
Cliniques Universitaires St Luc
Travel and Venous Thromboembolism (VTE)

- Definition
- Myth or reality
- Analysis of the risk
- Absolute risk
- Associated risk factors
- Pathophysiology
- Prevention
Venous Thromboembolism: The third most frequent vascular disorder

<table>
<thead>
<tr>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT</td>
</tr>
<tr>
<td>145 / 100,000 $^{1,2}$</td>
</tr>
<tr>
<td>PE +/- DVT</td>
</tr>
<tr>
<td>23-69 / 100,000 $^{3}$</td>
</tr>
<tr>
<td>mortality: 11%/2 weeks</td>
</tr>
</tbody>
</table>

**ENDOTHELIAL INJURY**

Traumatism

Surgery

---

**VENOUS STASIS**

Venous insufficiency

Immobilisation, plaster

Heart failure

Stroke

---

**THROMBOPHILIA**

- Prot C, S, AT deficiency: 4-8x
- APC resistance (V Leiden): 2.5x
- Factor II 20210A: 2.8x
- Hyperhomocysteinemia: 2.5x
- Antiphospholipids
- Elevated factor VIII-c
- Cancer: 7x
- Oral Contraceptives: 4x
Travel and VTE risk
Definition

- Symptomatic and/or asymptomatic VTE
- Lower limbs venous thrombosis and/or pulmonary embolism
- In the first weeks after travel
- ≠ economic class: other than air travel
- 1986: PE occurred more often in the arrival than the departure hall
- 2000: sudden death of a young Australian woman travelling to London
Travel and Venous Thromboembolism (VTE)

- Definition
- Myth or reality
- Analysis of the risk
- Absolute risk
- Associated risk factors
- Pathophysiology
- Prevention
Travel and VTE risk
Evaluating the risk

- 2.5 $10^9$ air travellers in 2010
- PE (pulmonary embolism) potentially fatal
- Conflicting results
  - 50% studies: no relationship
  - 50% studies: positive relationship
Travel and VTE risk
Evaluating the risk

- 14 studies (out of 42) finally selected
- 7: statistically significant association
- 7: no association

Travel and VTE risk
Evaluating the risk

- 14 studies (out of 42) finally selected

<table>
<thead>
<tr>
<th>Design</th>
<th>Studies number</th>
<th>Participants number</th>
<th>VTE number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case-control</td>
<td>11</td>
<td>3980 + 5413 ctrl</td>
<td>3980</td>
</tr>
<tr>
<td>Cohorts</td>
<td>2</td>
<td>10932</td>
<td>29</td>
</tr>
<tr>
<td>Case-crossover</td>
<td>1</td>
<td>5408</td>
<td>46</td>
</tr>
</tbody>
</table>

Travel and VTE risk
Evaluating the risk

- Heterogenous

Design:

- 11 case-controls:
  - more VTE cases
  - does not allow to calculate absolute risk
  - selecting controls...the probability of travel must be equal to the general population from which the cases come from

- 2 cohorts:
  - large groups in specific populations
  - allow to calculate VTE risk in relationship to travel
  - few cases but few bias

Travel and VTE risk
Evaluating the risk

- Heterogenous
- Design:
  - 11 case-controls:
    - 5/11: condition of the controls is not related to travel (i.e respiratory infection)
    - 6/11: controls have been referred for suspicion of VTE but tested negative; the probability of travel is increased

Travel and VTE risk
Evaluating the risk

- Heterogenous
- Design:
  - 1 case-crossover:
    - Same people in different periods of time
    - Discard confounding factors

Travel and VTE risk
Evaluating the risk

- **Type of travels**:  
  - 5 : air only  
  - 9 : air or surface travel

- **VTE**:  
  - 7 : DVT (deep venous thrombosis) alone  
  - 5 : PE (pulmonary embolism) and DVT  
  - 2 : PE alone

- **Location**:  
  - 10 : Europe  
  - 2 : Europe + North America  
  - 2 : Australia + New Zealand

Relative Risks for travel-related VTE

All studies

Well designed

Inappropriate design
Relative Risks for travel-related VTE

<table>
<thead>
<tr>
<th>Study location</th>
<th>n</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>10</td>
<td>1.8</td>
<td>1.3 - 2.4</td>
</tr>
<tr>
<td>North America</td>
<td>2</td>
<td>2.2</td>
<td>1 - 4.5</td>
</tr>
<tr>
<td>Australia New Zeal</td>
<td>2</td>
<td>3.5</td>
<td>1.8 - 6.8</td>
</tr>
</tbody>
</table>

## Relative Risks for travel-related VTE

<table>
<thead>
<tr>
<th>VTE type</th>
<th>n</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT</td>
<td>7</td>
<td>1.5</td>
<td>1.1 - 2.2</td>
</tr>
<tr>
<td>PE</td>
<td>2</td>
<td>1.1</td>
<td>0.7 - 1.9</td>
</tr>
<tr>
<td>DVT or PE</td>
<td>5</td>
<td>3</td>
<td>2.1 - 4.2</td>
</tr>
<tr>
<td><strong>Mode of travel</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flight</td>
<td>11</td>
<td>2.2</td>
<td>1.4 - 3.2</td>
</tr>
<tr>
<td>Surface</td>
<td>6</td>
<td>1.4</td>
<td>1 - 2.1</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 3 weeks</td>
<td>3</td>
<td>2.5</td>
<td>1.4 - 4.7</td>
</tr>
<tr>
<td>&gt; 3 weeks</td>
<td>11</td>
<td>1.8</td>
<td>1.3 - 2.5</td>
</tr>
</tbody>
</table>

Travel and VTE risk
Evaluating the risk

- Previous metanalysis with negative results: inadequate selection of controls

- Dose-response:
  - 18% risk increase/2 h;
  - For air travel only, 26% risk increase/2 h;
  - Suggestive of causal relationship.

Travel and Venous Thromboembolism (VTE)

- Definition
- Myth or reality
- Analysis of the risk
- Absolute risk
- Associated risk factors
- Pathophysiology
- Prevention
Travel and VTE risk
Types of travel (MEGA study)

<table>
<thead>
<tr>
<th>Travel Characteristic</th>
<th>Subcategory</th>
<th>Patients (n = 1,906), Number</th>
<th>Controls (n = 1,906), Number</th>
<th>Matched OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Travel c</td>
<td></td>
<td>1,673</td>
<td>1,724</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>233</td>
<td>182</td>
<td>2.1 (1.5–3.0)</td>
</tr>
<tr>
<td>Air travel</td>
<td></td>
<td>1,673</td>
<td>1,724</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>86</td>
<td>72</td>
<td>1.7 (1.0–3.1)</td>
</tr>
<tr>
<td>Travel by bus</td>
<td></td>
<td>1,673</td>
<td>1,724</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>23</td>
<td>18</td>
<td>2.2 (0.8–6.3)</td>
</tr>
<tr>
<td>Travel by car</td>
<td></td>
<td>1,673</td>
<td>1,724</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>113</td>
<td>86</td>
<td>2.2 (1.3–3.7)</td>
</tr>
<tr>
<td>Travel by train</td>
<td></td>
<td>1,673</td>
<td>1,724</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>11</td>
<td>5</td>
<td>3.5 (0.8–16.8)</td>
</tr>
<tr>
<td>Duration of travel</td>
<td>No travel</td>
<td>1,673</td>
<td>1,724</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>4–8 h</td>
<td>93</td>
<td>62</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td>8–12 h</td>
<td>68</td>
<td>65</td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td>&gt;12 h</td>
<td>66</td>
<td>51</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Cannegieter et al. PLOS Medicine 2006; 3: 1258–65
Travel and VTE risk
Timing (MEGA study)

**Figure 1.** Frequency of the Occurrence of Events within the First 12 wk after Travel

The time window of analysis concerned the first 8 wk.

Cannegieter et al. PLOS Medicine 2006; 3: 1258-65