Cancer-Associated Thrombosis

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Thrombosis and Cancer

- Malignant tumor
- Thromboembolism

Diagram showing the relationship between malignant tumor and thromboembolism.
Cancer-Associated Thrombosis: Challenges

- Prognostic
- Diagnostic
- Therapeutic
VTE & Cancer: A mortal link

VTE & Cancer: A mortal link

• Thromboembolism is the second leading cause of death in patients with cancer

• Very high mortality of patients with CAT at 6 months

• Prophylaxis of VTE: no impact on mortality

Incidence of cancer in patients with DVT

Incidence of cancer in patients with DVT

Incidence of occult cancer detection in the different studies

1 in 10 patients

1 in 25 patients

Cancer detection

2008 Annals

2011 Trousseau

2016 MVTEP

2016 SOME
Occult cancer screening in VTE patients

Why?
• Earlier detection
  – Curable cancer
  – $\uparrow$ survival
  – $\downarrow$ morbidity

Why not?
• unnecessary invasive procedures
  – “incidental findings”
• No impact on outcome
• Anxiety
• Costs
Limited vs. extensive occult cancer screening strategy

SOMIT
Trousseau
SOME
MTVEP
Patients with unprovoked VTE should undergo:

• Medical history and physical examination
• Basic laboratory investigations
• Chest X-ray
• Age- and gender- specific cancer screening (i.e. cervical, breast, prostate and colon).

Take home messages

• The prevalence of occult cancer in patients with a unprovoked VTE seems to be lower (~4%) than previously reported (10%)

• The risk of occult cancer is similar to the general population after the initial 6 to 12 months of follow-up.

• Limited cancer screening + clinical vigilance
Cancer-Associated Thrombosis: Challenges

• Prognostic
• Diagnostic
• Therapeutic
CLOT: A Landmark

Recurrence of VTE (%)

VKA, 16% (53 events) (TTR 46%)

Dalteparin, 8% (27 events)

Days post-randomization

RR=52%
HR=0.48
(95% CI 0.30–0.77)

NNT = 13

Main outcomes at 6 months from Hokusai-VTE Cancer, SELECT-D and Caravaggio

**Recurrent VTE**

<table>
<thead>
<tr>
<th>Study</th>
<th>DOAC agent</th>
<th>DOAC Patients</th>
<th>DOAC Event</th>
<th>LMWH Patients</th>
<th>LMWH Event</th>
<th>Risk Ratio</th>
<th>RR</th>
<th>95%-CI</th>
<th>Weight</th>
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</thead>
<tbody>
<tr>
<td>Hokusai VTE Cancer</td>
<td>edoxaban</td>
<td>522</td>
<td>34</td>
<td>524</td>
<td>46</td>
<td>0.74</td>
<td>[0.48; 1.14]</td>
<td>45.4%</td>
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<tr>
<td>SELECT-D</td>
<td>rivaroxaban</td>
<td>203</td>
<td>7</td>
<td>203</td>
<td>17</td>
<td>0.41</td>
<td>[0.17; 0.97]</td>
<td>11.2%</td>
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<tr>
<td>Caravaggio</td>
<td>apixaban</td>
<td>576</td>
<td>32</td>
<td>579</td>
<td>46</td>
<td>0.70</td>
<td>[0.45; 1.08]</td>
<td>43.4%</td>
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<td><strong>Random effects model</strong></td>
<td></td>
<td>1301</td>
<td>73</td>
<td>1306</td>
<td>109</td>
<td>0.68</td>
<td>[0.39; 1.17]</td>
<td>100.0%</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $I^2 = 0\%$, $\tau^2 < 0.0001$, $p = 0.48$

**Major bleeding**

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<tbody>
<tr>
<td>Hokusai VTE Cancer</td>
<td>edoxaban</td>
<td>522</td>
<td>29</td>
<td>524</td>
<td>17</td>
<td>1.71</td>
<td>[0.95; 3.08]</td>
<td>40.3%</td>
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<tr>
<td>SELECT-D</td>
<td>rivaroxaban</td>
<td>203</td>
<td>11</td>
<td>203</td>
<td>6</td>
<td>1.83</td>
<td>[0.69; 4.86]</td>
<td>18.0%</td>
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<tr>
<td>Caravaggio</td>
<td>apixaban</td>
<td>576</td>
<td>22</td>
<td>579</td>
<td>23</td>
<td>0.96</td>
<td>[0.54; 1.71]</td>
<td>41.7%</td>
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<tr>
<td><strong>Random effects model</strong></td>
<td></td>
<td>1301</td>
<td>62</td>
<td>1306</td>
<td>46</td>
<td>1.36</td>
<td>[0.55; 3.35]</td>
<td>100.0%</td>
<td></td>
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</tbody>
</table>

Heterogeneity: $I^2 = 15\%$, $\tau^2 = 0.0379$, $p = 0.31$
Major bleeding events in patients with Cancer-Associated VTE

GI cancers

Non-GI cancers

HR 4.0 (95% CI 1.5–10.6)

\( p = 0.005 \)

Organ-specific bleeding patterns of anticoagulant therapy: lessons from clinical trials

Thomas Vanassche; Jack Hirsh; John W. Eikelboom; Jeffrey S. Ginsberg
Population Health Research Institute, Thrombosis and Atherosclerosis Research Institute, McMaster University and Hamilton Health Sciences, Hamilton, Ontario, Canada
What is important for patients?
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1. No interference with cancer treatment 39%
What is important for patients?

1. No interference with cancer treatment 39%
2. Efficacy / recurrent VTE 24%
3. Major bleeding 19%
4. Route of Administration 13%
5. Monitoring 2%
6. Minor bleeding 2%
7. Frequency of administration 1%

Simon Noble et al. Haematologica 2015;100:1486-1492
Managing daily challenges

◆ Low platelets
◆ Renal function
◆ Extremes of body weight
◆ Drug-drug interactions

Optimal dosing?
Managing daily challenges

- Low platelets
- Renal function
- Extremes of body weight
- Drug-drug interactions
- Recurrent TE
- Incidental VTE
- Port-a-cath & UE DVT
- Arterial TE
- Management post-bleeding
Which Patients Should Receive Long-Term Anticoagulation?

- Acute
- Long term

3 Months
Which Patients Should Receive Extended Anticoagulation?

1) Persistent Risk Factors
   - Major (e.g., cancer)
   - Minor (e.g., Immobile, FVL)

2) No known risk factors (unprovoked)
   And Low bleeding risk
   And Patient Preference
APICAT STUDY*

Active cancer with symptomatic or incidental proximal DVT and/or PE

Any anticoagulant for ≥ 6 months

Apixaban n=861
5 mg BID
12 months

Apixaban n=861
2.5 mg BID

* NCT03692065
Managing daily challenges

◆ No ‘One size fits all’ approach

◆ Patient selection is key:
  tumor type
  bleeding risk/renal function/thrombus burden…
  drug–drug interactions
  patient preferences
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