Impact of sex and risk factors for venous thromboembolism on the clinical course of first acute venous thromboembolism. Insights from the PREFER in VTE.

Authors: M Giustozzi¹, S Barco², L Valerio², FA Klok², MC Vedovati¹, C Becattini¹, SV Konstantinides², G Agnelli¹, ¹Internal and Cardiovascular Medicine-Stroke Unit - Perugia - Italy, ²Center for Thrombosis and Hemostasis - Mainz - Germany,

Topic(s): Venous Thromboembolism

Citation: Funding Acknowledgements: This study was funded by Daiichi Sankyo.

Introduction
The interaction between sex and specific provoking risk factors for venous thromboembolism (VTE) may influence initial presentation and prognosis.

Purpose
We investigated the impact of sex on the risk of recurrence across subgroups of patients with first VTE classified according to baseline risk factors.

Methods
PREFER in VTE was an international, non-interventional registry (2013-2015) including patients with a first episode of acute symptomatic objectively diagnosed VTE. We studied the risk of recurrence in patients classified according to baseline provoking risk factors for VTE consisted of i) major transient (major surgery/trauma, >5 days in bed), ii) minor transient (pregnancy or puerperium, progestogen therapy, prolonged immobilization, current infection or bone fracture/soft tissue trauma); iii) unprovoked events, iv) active cancer-associated VTE.

Results
A total of 3,455 patients diagnosed with first acute VTE were identified, of whom 1,623 (47%) were women. The percentage of patients with a major transient risk factor was 22.2% among women and 19.7% among men. Minor transient risk factors were present in 21.3% and 12.4%, unprovoked VTE in 51.6% and 61.6%, cancer-associated VTE in 4.9% of women and 6.3% of men, respectively. The proportions of cases treated with Vitamin-K antagonists (VKAs) and direct oral anticoagulants (DOACs) were similar between sexes. Median length of treatment of VKAs was 181.5 and 182.0 days and of DOACs was 113.0 and 155.0 days in women and men, respectively. At 12-months of follow-up, VTE recurrence was reported in 74 (4.8%) women and 80 (4.5%) men. Table 1 shows the sex-specific proportion of recurrences by VTE risk factor categories.

Conclusions
The proportion of patients with recurrent VTE events after first acute symptomatic VTE provoked by transient risk factors was not negligible during the first year of follow-up during in both women and men. These results may have implications on the decision whether to consider extended anticoagulant therapy in selected patients with provoked events.

<table>
<thead>
<tr>
<th>Major Transient</th>
<th>Minor transient</th>
<th>Cancer-associated</th>
<th>Unprovoked</th>
</tr>
</thead>
<tbody>
<tr>
<td>(722)</td>
<td>(573)</td>
<td>(195)</td>
<td>(1965)</td>
</tr>
<tr>
<td>Women</td>
<td>Men</td>
<td>OR</td>
<td>Women</td>
</tr>
</tbody>
</table>
Impact of sex and risk factors for venous thromboembolism on the clinical course of first acute venous thromboembolism. Insights from the PREFER in VTE.

Authors: M Giustozzi 1, S Barco 2, L Valerio 2, FA Klok 2, MC Vedovati 1, C Becattini 1, SV Konstantinides 2, G Agnelli 1

1 Internal and Cardiovascular Medicine - Stroke Unit - Perugia - Italy, 2 Center for Thrombosis and Hemostasis - Mainz - Germany.

Topic(s): Venous Thromboembolism

Introduction
The interaction between sex and specific provoking risk factors for venous thromboembolism (VTE) may influence initial presentation and prognosis.

Purpose
We investigated the impact of sex on the risk of recurrence across subgroups of patients with first VTE classified according to baseline risk factors.

Methods
PREFER in VTE was an international, non-interventional registry (2013-2015) including patients with a first episode of acute symptomatic objectively diagnosed VTE. We studied the risk of recurrence in patients classified according to baseline provoking risk factors for VTE consisted of i) major transient (major surgery/trauma, >5 days in bed), ii) minor transient (pregnancy or puerperium, estroprogestinic therapy, prolonged immobilization, current infection or bone fracture/soft tissue trauma); iii) unprovoked events, iv) active cancer-associated VTE.

Results
A total of 3,455 patients diagnosed with first acute VTE were identified, of whom 1,623 (47%) were women. The percentage of patients with a major transient risk factor was 22.2% among women and 19.7% among men. Minor transient risk factors were present in 21.3% and 12.4%, unprovoked VTE in 51.6% and 61.6%, cancer-associated VTE in 4.9% of women and 6.3% of men, respectively. The proportions of cases treated with Vitamin-K antagonists (VKAs) and direct oral anticoagulants (DOACs) were similar between sexes. Median length of treatment of VKAs was 181.5 and 182.0 days and of DOACs was 113.0 and 155.0 days in women and men, respectively. At 12-months of follow-up, VTE recurrence was reported in 74 (4.8%) women and 80 (4.5%) men. Table 1 shows the sex-specific proportion of recurrences by VTE risk factor categories.

Conclusions
The proportion of patients with recurrent VTE events after first acute symptomatic VTE provoked by transient risk factors was not negligible during the first year of follow-up in both women and men. These results may have implications on the decision whether to consider extended anticoagulant therapy in selected patients with provoked events.

<table>
<thead>
<tr>
<th>One-year follow-up, n(N%)</th>
<th>361</th>
<th>361</th>
<th>(95%CI)</th>
<th>346</th>
<th>227</th>
<th>(95%CI)</th>
<th>79</th>
<th>116</th>
<th>(95%CI)</th>
<th>837</th>
<th>1128</th>
<th>(95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent VTE,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding,</td>
<td>21</td>
<td>10</td>
<td>0.46</td>
<td>9</td>
<td>12</td>
<td>2.09</td>
<td>6</td>
<td>5</td>
<td>0.54</td>
<td>38</td>
<td>53</td>
<td>1.03</td>
</tr>
<tr>
<td>All-cause death,</td>
<td>37</td>
<td>31</td>
<td>0.82</td>
<td>14</td>
<td>26</td>
<td>2.21</td>
<td>49</td>
<td>33</td>
<td>1.49</td>
<td>30</td>
<td>0.66</td>
<td>0.66</td>
</tr>
</tbody>
</table>

One-year follow-up, n(N%)

| Recurrent VTE,            |     |     |         |     |     |         |    |     |         |     |       |         |
| Major bleeding,           | 21  | 10  | 0.46    | 9   | 12  | 2.09    | 6  | 5   | 0.54    | 38  | 53    | 1.03    |
| All-cause death,          | 37  | 31  | 0.82    | 14  | 26  | 2.21    | 49 | 33  | 1.49    | 30  | 0.66  | 0.66    |