Impact of Clopidogrel Pretreatment on Ischemic Complications of PCI among Bivalirudin-Treated Patients: Results from the EVENT Registry

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Background
Although clopidogrel (CLO) pretreatment benefits PCI patients with acute coronary syndromes, these benefits are less well-established among elective PCI patients—particularly when treated with the direct thrombin inhibitor (DTI), bivalirudin. The effect of timing of CLO pretreatment on ischemic complications in these patients is also unknown.

Methods
We used data from the multicenter EVENT registry to assess the association of clopidogrel pretreatment (600 mg 2 hr pre-PCI, 300 mg 6 hrs pre-PCI, or 75 mg/d for 1 week) with PCI-related complications in patients undergoing elective PCI with a DTI as planned antithrombotic. The primary endpoint was the composite of in-hospital death or MI (peak CKMB > 3 x ULN).

Results
Between 01/05 and 12/07, 3568 pts underwent elective PCI and 1913 (54%) received DTI as planned anticoagulant (37% diabetics, age 65±10 y). Clopidogrel pre-treatment was used in 923 (48%). There were no differences in in-hospital or 1 year ischemic or bleeding events in relation to clopidogrel pretreatment in both unadjusted and adjusted analyses (see Table). There was a trend toward lower rates of death or MI with earlier pretreatment, however [Odds ratios vs. no pretreatment: >1 week 0.48 (95% CI 0.08 - 2.73); > 6 h OR 0.69 (95% CI 0.11 - 4.45) and 2-6 h OR 0.77 (95% CI 0.18 - 3.31)].

Conclusion
Among unselected patients undergoing elective PCI with DTI as the planned anticoagulant, clopidogrel pretreatment was common, but was not associated with a reduced risk of ischemic complications.

<table>
<thead>
<tr>
<th>Clopidogrel Pretreatment (n=923)</th>
<th>No Pretreatment (n=990)</th>
<th>Univariate P-value</th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>Multivariable P-value †</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In-Hospital Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death or MI</td>
<td>5.5%</td>
<td>5.8%</td>
<td>0.83</td>
<td>0.91 (0.60-1.39)</td>
</tr>
<tr>
<td>Death</td>
<td>0.3%</td>
<td>0.3%</td>
<td>1.00</td>
<td>Adjusted model not possible due to low event rate</td>
</tr>
<tr>
<td>MI</td>
<td>5.2%</td>
<td>5.7%</td>
<td>0.66</td>
<td>0.89 (0.57-1.35)</td>
</tr>
<tr>
<td>Composite Bleeding ‡</td>
<td>1.0%</td>
<td>1.0%</td>
<td>0.94</td>
<td>1.38 (0.49-3.91)</td>
</tr>
<tr>
<td><strong>One Year Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death or MI</td>
<td>7.5%</td>
<td>8.3%</td>
<td>0.26</td>
<td>0.82 (0.58-1.18)</td>
</tr>
<tr>
<td>Death</td>
<td>1.4%</td>
<td>1.9%</td>
<td>0.38</td>
<td>0.65 (0.31-1.35)</td>
</tr>
<tr>
<td>MI</td>
<td>6.4%</td>
<td>6.6%</td>
<td>0.88</td>
<td>0.84 (0.57-1.25)</td>
</tr>
<tr>
<td>Definite or Probable Stent Thrombosis</td>
<td>0.3%</td>
<td>0.3%</td>
<td>1.00</td>
<td>Adjusted model not possible due to low event rate</td>
</tr>
</tbody>
</table>

† Models adjusted for age, gender, baseline clinical and angiographic characteristics
‡ Bleeding complications included TIMI major or minor bleeding, vascular complication requiring intervention, or the need for transfusion.