Bivalirudin in ST-segment-elevation myocardial infarction: for better or worse?

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Bivalirudin and heparin are the major available parenteral anticoagulants for percutaneous coronary intervention (PCI) in ST-segment-elevation myocardial infarction. Even though hard clinical outcomes are comparable with both drugs, bivalirudin appears to be safer (less bleeding events) at the expense of lower short-term efficacy (more acute stent thrombosis events). The selection of anticoagulation during PCI in ST-segment-elevation myocardial infarction should be individualized, taking into account the patient’s ischemic and bleeding risk. In patients with increased bleeding risk, bivalirudin might be preferable to heparin, whereas in complex PCI with increased risk for stent thrombosis, heparin is preferable. Further clinical studies are needed to elucidate the role of these drugs in PCI for ST-segment-elevation myocardial infarction in the era of radial approaches, new potent antiplatelet agents and the use of glycoprotein IIb/IIIa inhibitors.

**KEYWORDS:** bivalirudin • bleeding • heparin • stent thrombosis • ST-segment elevation myocardial infarction

Bivalirudin, a direct thrombin inhibitor, is one of the available parenteral anticoagulants currently used during percutaneous coronary intervention (PCI) in ST-segment-elevation myocardial infarction. Even though hard clinical outcomes are comparable with both drugs, bivalirudin appears to be safer (less bleeding events) at the expense of lower short-term efficacy (more acute stent thrombosis events). The selection of anticoagulation during PCI in ST-segment-elevation myocardial infarction should be individualized, taking into account the patient’s ischemic and bleeding risk. In patients with increased bleeding risk, bivalirudin might be preferable to heparin, whereas in complex PCI with increased risk for stent thrombosis, heparin is preferable. Further clinical studies are needed to elucidate the role of these drugs in PCI for ST-segment-elevation myocardial infarction in the era of radial approaches, new potent antiplatelet agents and the use of glycoprotein IIb/IIIa inhibitors.

**KEYWORDS:** bivalirudin • bleeding • heparin • stent thrombosis • ST-segment elevation myocardial infarction
and bivalirudin group. Acute stent thrombosis rates did not differ between the study groups, but bleeding events were more common with heparin. The results were applicable in the STEMI subgroup.

Preliminary results from the MATRIX trial in patients with any acute coronary syndrome, recently presented at the American College of Cardiology Scientific Sessions 2015 in San Diego, showed a similar major adverse cardiovascular events rate with heparin and bivalirudin. However, stent thrombosis was more frequent with bivalirudin, whereas major bleeding events were more common with heparin \[6\].

The lower incidence of acute stent thrombosis in the BRIGHT trial, compared with the HORIZONS-AMI, EUROMAX and HEAT-PPCI trials, may be explained by the prolonged post-PCI bivalirudin administration (for 0.5–4 hours) at the dose of 1.75 mg/kg·h. In the first three trials, bivalirudin was stopped at the end of PCI (HORIZONS-AMI and HEAT-PPCI) or continued at a lower dose (0.25 mg/kg·h for 0.5–4 h in EUROMAX). A post hoc analysis of the EUROMAX trial \[7\] also supports this observation that needs to be confirmed in further clinical trials.

Two recent meta-analyses, published before BRIGHT and MATRIX studies, shed further light on the efficacy and safety of bivalirudin versus heparin (Table 1). The first one (including patients undergoing elective or urgent PCI) was in favor of heparin concerning the major adverse cardiovascular events rate at 30 days, mostly driven by an increase in myocardial infarction and ischemia-driven revascularization in the bivalirudin arm \[8\].

Is there clinical equipoise regarding the use of bivalirudin and heparin in STEMI? Composite hard clinical outcomes appear to be comparable with both drugs. Current evidence suggests that bivalirudin is associated with a safety benefit (less major bleeding events) at the expense of lower short-term efficacy (more acute stent thrombosis events) (Figure 1). Therefore, anticoagulation choice during PCI in STEMI should be individualized taking into account patient’s ischemic and bleeding risk. In patients with increased bleeding risk, bivalirudin appears to be preferable to heparin, whereas in complex PCI with increased risk for stent thrombosis, heparin might be preferable. The significantly higher cost of bivalirudin compared with heparin should also be taken into account. Further clinical studies are needed to elucidate the role of these drugs in STEMI PCI in the era of radial approach, new potent antiplatelet agents and provisional glycoprotein IIb/IIIa inhibitors use.

**Expert commentary & five-year view**

On the basis of current evidence, bivalirudin is associated with a safety benefit (less bleeding) at the expense of lower short-term efficacy (more ischemic events) in STEMI PCI. In the following years, as radial approach becomes even more widespread and new stents and potent antiplatelet agents come on board, a personalized anticoagulation management is anticipated to further reduce major adverse cardiovascular events and bleeding complications post PCI.

**Financial & competing interests disclosure**

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**Table 1. Ischemic and bleeding risk of bivalirudin versus heparin in STEMI PCI across clinical trials and meta-analyses.**

<table>
<thead>
<tr>
<th>Clinical trials</th>
<th>More acute stent thrombosis</th>
<th>Less bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>HORIZONS-AMI</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>EUROMAX</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>HEAT-PPCI</td>
<td>✓</td>
<td>–</td>
</tr>
<tr>
<td>BRIGHT</td>
<td>–</td>
<td>✓</td>
</tr>
<tr>
<td>MATRIX</td>
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</table>

**Meta-analyses**

<table>
<thead>
<tr>
<th></th>
<th>More acute stent thrombosis</th>
<th>Less bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lancet 2014</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>BMJ 2014</td>
<td>✓</td>
<td>✓</td>
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</tbody>
</table>

**Figure 1. Risk-benefit ratio of bivalirudin versus heparin in percutaneous coronary intervention for STEMI.**
Key issues

- Composite hard clinical outcomes appear to be comparable with both drugs. Current evidence suggests that bivalirudin is associated with a safety benefit (less major bleeding events) at the expense of lower short-term efficacy (more acute stent thrombosis events).
- Anticoagulation management during PCI in STEMI should be individualized, taking into account patient’s ischemic and bleeding risk. In patients with increased bleeding risk, bivalirudin appears to be preferable to heparin, whereas in complex PCI with increased risk for stent thrombosis, heparin might be more preferable. The significantly higher cost of bivalirudin compared with heparin should be also taken into account.
- Further clinical studies are needed to elucidate the role of these drugs in STEMI PCI in the era of radial approach, new potent antiplatelet agents and provisional glycoprotein IIb/IIIa inhibitors use.

References

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