Clopidogrel vs. aspirin in the chronic maintenance period following percutaneous coronary intervention in high thrombotic and high bleeding risk patients: sub-analysis of the HOST-EXAM Extended study

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Background: The HOST-EXAM Extended study evaluated the long-term follow-up results of the original HOST-EXAM trial, which demonstrated that clopidogrel monotherapy was associated with a lower risk of thrombotic and bleeding events compared to aspirin monotherapy. However, the optimal single antiplatelet agent during the chronic maintenance period in patients with high thrombotic risk and/or high bleeding risk has not been assessed.

Purpose: This study aimed to compare the efficacy of clopidogrel versus aspirin monotherapy in patients with high thrombotic risk and/or high bleeding risk who were stabilized after percutaneous coronary intervention (PCI) with drug-eluting stents (DES).

Methods: A post-hoc subgroup analysis of the HOST-EXAM Extended study was conducted. High thrombotic risk was defined as patients who had at least one of the following procedural features: 3 vessels treated, ≥3 stents implanted, ≥3 lesions treated, bifurcation with 2 stents implanted, total stent length >60 mm, or chronic total occlusion. High bleeding risk was defined according to the Academic Research Consortium for High Bleeding Risk (ARC-HBR) criteria. The primary endpoint was a composite of all-cause death, non-fatal myocardial infarction, stroke, readmission due to acute coronary syndrome, and Bleeding Academic Research Consortium bleeding type 3 or 5. Clinical outcome was analyzed according to the patients’ initial thrombotic and bleeding risk.

Results: Among the total population, 28.2% had high thrombotic risk and 27.0% had high bleeding risk. Patients with high thrombotic risk was not associated with a higher risk of primary endpoint, whereas those of high bleeding risk was associated with a increased risk of the clinical event (Hazard ratio [HR] 2.70, 95% Confidence interval [CI] 2.29-3.18, Log-rank p < 0.001). Clopidogrel consistently reduced the risk of primary endpoint, regardless of the presence of high thrombotic risk or high bleeding risk (Absolute risk difference [ARD] 7.5%, 95% CI 2.7-12.3, HR 0.59, 95% CI 0.43-0.82, Log-rank p=0.001 vs ARD 4.1%, 95% CI 1.5-6.7, HR 0.78, 95% CI 0.66-0.92, Log-rank p=0.004 with or without high thrombotic risk, respectively. P-interaction=0.133; ARD 9.2%, 95% CI 2.4-16.0, HR 0.71, 95% CI 0.55-0.92, Log-rank p=0.008 vs ARD 4.0%, 95% CI 1.6-6.4, HR 0.74, 95% CI 0.60-0.90, Log-rank p=0.003 with or without high bleeding risk, respectively. P-interaction=0.860; Figure 1). The beneficial effect of clopidogrel was consistent across patients divided into four groups based on the presence or absence of high thrombotic risk and high bleeding risk (Figure 2).

Conclusion: In chronic maintenance period of patients who received PCI with DES, the beneficial effect of clopidogrel was maintained in patients regardless of the presence or absence of high thrombotic risk and high bleeding risk.

Figure 1. Cumulative incidence of primary endpoint according to high thrombotic risk (HTR) or high bleeding risk (HBR)

A

B

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A

B

Figure 1. Cumulative incidence of primary endpoint according to high thrombotic risk (HTR) or high bleeding risk (HBR)
**Figure 2. Cumulative incidence of primary endpoint according to high thrombotic risk (HTR) and high bleeding risk (HBR)**

<table>
<thead>
<tr>
<th></th>
<th>Aspirin</th>
<th>Clopidogrel</th>
<th>HR (95% CI)</th>
<th>(P)</th>
<th>(P_{\text{int}})</th>
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<tbody>
<tr>
<td>HTR(-)HBR(-)</td>
<td>14.7</td>
<td>10.7</td>
<td>0.74 (0.59-0.93)</td>
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<tr>
<td>HTR(+)HBR(-)</td>
<td>14.1</td>
<td>10.2</td>
<td>0.68 (0.42-1.10)</td>
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<td>HTR(-)HBR(+)</td>
<td>34.1</td>
<td>28.1</td>
<td>0.80 (0.59-1.07)</td>
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<td>HTR(+)HBR(+)</td>
<td>38.8</td>
<td>21.9</td>
<td>0.53 (0.32-0.88)</td>
<td>0.015</td>
<td>0.248</td>
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