

Bivalirudin Reduces Adverse Events During Primary Percutaneous Coronary Intervention for Acute Myocardial Infarction

Stone GW, Witzenbichler B, Guagliumi G, et al; HORIZONS-AMI trial investigators. Bivalirudin during primary PCI in acute myocardial infarction. *N Engl J Med* 2008;358:2218–30.

Study Overview

Objective. To evaluate the safety and efficacy of bivalirudin, a direct thrombin inhibitor, in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).

Design. Open-label, randomized, multicenter trial.

Setting and participants. 3602 patients with STEMI who presented within 12 hours of symptom onset and undergoing primary PCI were randomized to anticoagulation with heparin plus a glycoprotein IIb/IIIa inhibitor or bivalirudin alone.

Main outcome measures. Major bleeding and a composite of adverse clinical events (major bleeding, death, reinfarction, target-vessel revascularization for ischemia, and stroke) at 30 days.

Main results. Compared with heparin and a glycoprotein IIb/IIIa inhibitor, treatment with bivalirudin resulted in lower rate of major bleeding (4.9% vs. 8.3%; relative risk [RR], 0.60 [95% confidence interval {CI}, 0.46–0.77]; $P < 0.001$) and a reduced 30-day rate of adverse clinical events (9.2% vs. 12.1%; RR, 0.76 [95% CI, 0.63–0.92]; $P = 0.005$). In the bivalirudin group, there was an increased risk of acute stent thrombosis within 24 hours after PCI, but this was not significant at 30 days. Compared with the heparin and glycoprotein IIb/IIIa inhibitor

group, the bivalirudin group had significantly lower 30-day mortality from cardiovascular causes (1.8% vs. 2.9%; RR, 0.62 [95% CI, 0.40–0.95]; $P = 0.03$) and lower all-cause mortality (2.1% vs. 3.1%; RR, 0.66 [95% CI, 0.44–1.00]; $P = 0.047$).

Conclusion. In STEMI patients undergoing revascularization by primary PCI, anticoagulation with bivalirudin alone compared with heparin and a glycoprotein IIb/IIIa inhibitor resulted in significantly reduced 30-day rates of major bleeding and adverse clinical events.

Commentary

The primary objective in management of STEMI is to restore coronary blood flow by either primary PCI or fibrinolysis. This decision is usually driven by access to PCI at each institution. The next steps in management focus on the prevention of early reinfarction and reduction of adverse cardiac events. To this end, this study by Stone et al begins to examine adjunctive therapy in primary PCI. Currently, the most common adjunctive therapy in primary PCI is heparin and glycoprotein IIb/IIIa inhibitors [1]. However, bivalirudin, a short-acting direct thrombin inhibitor, has not been studied in these high-risk patients.

In this study of a clinically relevant population of STEMI patients, bivalirudin reduced major bleeding episodes (defined by more than 1 criteria) and adverse clinical events; however, a number of considerations should be taken into

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account. First, the open-label design introduces bias and could have influenced the endpoints. This was addressed by a clinical-event adjudication committee that used original source documentation for adverse event verification. Second, approximately two thirds of patients received heparin in the bivalirudin group, and as a result the impression that the patient received bivalirudin alone is not entirely true. However, interaction testing revealed that major bleeding was still reduced in the bivalirudin group. Third, there was a 1% incremental risk of stent thrombosis with bivalirudin within the first 24 hours after PCI, but this was not found to be significantly different than with heparin and glycoprotein IIb/IIIa at 30 days. Finally, mortality was a secondary endpoint and the study was underpowered to detect differences in low-frequency outcomes such as death.

Current guidelines [2] recommend that patients undergoing primary PCI receive aspirin, a loading dose (600 mg) of clopidogrel, and heparin. The glycoprotein IIb/IIIa inhibitor, abciximab, has been given a class IIa recommendation (ie, it is reasonable to administer treatment).

Applications for Clinical Practice

In patients presenting with STEMI, bivalirudin can be considered for ancillary antithrombotic therapy and may lead to

reduced major bleeding events and adverse clinical events (eg, death, reinfarction, target-vessel revascularization for ischemia, and stroke) when compared with heparin and a glycoprotein IIb/IIIa inhibitor. However, more studies will likely need to be performed before bivalirudin becomes a class I recommendation.

—Review by Robert L. Huang, MD, MPH

References

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