ACUTE CORONARY SYNDROMES

Bivalirudin improves 1-year survival in patients with STEMI undergoing PCI

Anticoagulation with bivalirudin during primary percutaneous coronary intervention (PCI) reduces the incidence of major bleeding and adverse cardiac events, and improves survival at 1 year in patients with acute ST-segment elevation myocardial infarction (STEMI). These results from the international, prospective, HORIZONS-AMI trial will be important in optimizing treatment in this patient population.

Procedural anticoagulation with unfractionated heparin and glycoprotein IIb/IIIa inhibitors during angioplasty was standard in the late 1990s and the early years of this decade. These agents reduce the risk of thrombosis and early ischemic events, but were associated with increased bleeding and thrombocytopenia. "High doses [of heparin] were required in acute coronary syndromes in which thrombin generation was upregulated, often resulting in high serum heparin levels and frequent bleeding" explains investigator Roxana Mehran, "heparin also directly binds to and activates the glycoprotein IIb/IIIa integrin receptor resulting in a procoagulant effect, necessitating glycoprotein IIb/IIIa receptor antagonists for maximal protection against ischemic complications." By contrast, bivalirudin can be used without the need for additional anticoagulants, and its reversible action and short half-life reduce the risk of bleeding.

In 2008, early outcome data from the HORIZONS-AMI trial demonstrated, for the first time, that bivalirudin reduced bleeding complications and improved survival at 30 days in patients with STEMI undergoing PCI. This new analysis confirms that the early beneficial effects persist at 1 year. All patients also received dual antiplatelet therapy with aspirin and clopidogrel.

A total of 3,602 patients with acute STEMI were randomly assigned to receive bivalirudin alone or a glycoprotein IIb/IIIa inhibitor with unfractionated heparin (control group).

At 1 year after PCI, the rates of net adverse clinical events (major bleeding or a composite of death, reinfarction, target lesion revascularization, and stroke), major bleeding, and cardiac-related and all-cause mortality were significantly lower in the bivalirudin group than in the control group. The use of bivalirudin prevented 17 cardiac deaths and 13 deaths from any cause per 1,000 patients and was an independent predictor of survival in a multivariate analysis. The incidence of stent thrombosis was similar for both treatment strategies.

The HORIZONS-AMI investigators will continue to work towards optimizing anticoagulation therapy in patients with STEMI. "Whether the newer thienopyridines will reduce ischemic complications without increasing bleeding ... has not yet been evaluated in acute MI patients" says Mehran. "The future will be choosing the right patient for the right therapy. This will be our goal."

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Original article Mehran, R. *et al*. Bivalirudin in patients undergoing primary angioplasty for acute myocardial infarction (HORIZONS-AMI): 1-year results of a randomised trial. *Lancet* **374**, 1149–1159 (2009).