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Letters

Re-Examination of the Antithrombotic Regimen in the STEMI-RADIAL Trial

In the STEMI-RADIAL (ST Elevation Myocardial Infarction treated by RADIAL or femoral approach) trial (1), the primary endpoint of the cumulative incidence of major bleeding and vascular access site complications at 30 days was lower with transradial intervention than with transfemoral intervention (1.4% vs. 7.2%, p = 0.0001). There was no difference in death, myocardial infarction, and stroke. However, this trial included suboptimal antithrombotic regimens, including high doses of heparin and a high percentage of patients treated with glycoprotein IIb/IIIa inhibitors. In patients with ST-segment elevation myocardial infarction (STEMI) being referred for primary percutaneous coronary intervention, the American College of Cardiology Foundation/American Heart Association guideline recommends a bolus of 50 to 70 IU/kg to achieve an activated clotting time of 200 to 250 s when treatment with a glycoprotein IIb/IIIa inhibitor is planned and 70 to 100 IU/kg to achieve an activated clotting time of 250 to 300 s (as measured by the HemoTec device, HemoTec Inc., Englewood, Colorado) when no treatment with a glycoprotein IIb/IIIa inhibitor is planned (2). Doses of heparin in excess of this have not been associated with improved pre-procedural patency or post-procedural outcomes. Patients who underwent transfemoral intervention received an average dose of heparin of 105 IU/kg, despite nearly half of the patients being treated with glycoprotein IIb/IIIa inhibitors.

Bivalirudin, a direct thrombin inhibitor shown to decrease bleeding and improve outcomes compared with heparin and glycoprotein IIb/IIIa inhibitors in patients undergoing an invasive strategy, was not used in the STEMI-RADIAL trial (3). The HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial, which compared patients with STEMI randomized to treatment with heparin plus glycoprotein IIb/IIIa inhibitors or bivalirudin, reported a 34% reduction in mortality in patients treated with bivalirudin (p = 0.047), driven by a reduction in major bleeding of 40% (p < 0.001).

The applications of the trial findings are suspect given the suboptimal antithrombotic regimens and the liberal use of potent parenteral antiplatelet agents (4). This is an important consideration especially for patients with acute coronary syndrome, in whom the negative implications of major bleeding are even greater. Ultimately, a trial comparing transradial with transfemoral intervention in patients treated with bivalirudin, with potent antiplatelet therapy, and without adjunctive glycoprotein IIb/IIIa inhibitors as well as possibly incorporating ultrasound guidance for vascular access is needed (5,6).

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REPLY: Re-Examination of the Antithrombotic Regimen in the STEMI-RADIAL Trial

We are pleased to address Dr. Lee's comments on the results of the STEMI-RADIAL (ST Elevation Myocardial Infarction treated by RADIAL or femoral

approach) trial published in the *Journal* (1). First, this letter has already been published twice with almost identical content (2,3). Second, responses to Dr. Lee's comments are already included in our report. In brief, Dr. Lee contends that unfractionated heparin was not used in accordance with guideline recommendations and that bivalirudin should have been used instead. As explained in the Methods section and in accordance with the most recent guidelines, an initial unfractionated heparin bolus dose of 70 IU/kg or a maximum dose of 5,000 IU was given (sometimes in the ambulance). Further adjustments were made according to the activated clotting time results, leading to a mean total dose of 104 ± 32 IU/kg with no difference between groups. Platelet glycoprotein IIb/IIIa receptor inhibitors were used in 45% of the cases when required during percutaneous coronary intervention as judged by the operators (provisional use). This rate is similar to the current experience with ST-segment elevation myocardial infarction (STEMI) in the United States (4,5). As explained in the Study Limitations section, bivalirudin was not used because it is not available in the Czech Republic. Furthermore, the recent results of the HEAT-PPCI (How Effective Are Antithrombotic Therapies in Primary Percutaneous Coronary Intervention) trial cast serious doubt on the claimed overwhelming superiority of bivalirudin over heparin in patients with STEMI undergoing primary percutaneous coronary intervention (6). Further studies such as SAFARI-STEMI (The Safety and Efficacy of Femoral Access Versus Radial for Primary Percutaneous Coronary Intervention in ST-Elevation Myocardial Infarction), which will evaluate the benefits of a radial compared with a femoral approach in patients with STEMI on a background of bivalirudin, and EASY-B2B (EArly Discharge After Transradial Stenting of CoronarY Arteries in High-Risk Patients of Bleeding), which will compare bivalirudin with heparin monotherapy in all comers at high risk for bleeding undergoing transradial percutaneous coronary intervention, should provide new insight into the interaction between anticoagulation and access site in the near future.

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