Bivalirudin More Beneficial Than Heparin in Patients With AMI Undergoing PCI: The BRIGHT Trial

Written by Maria Vinall

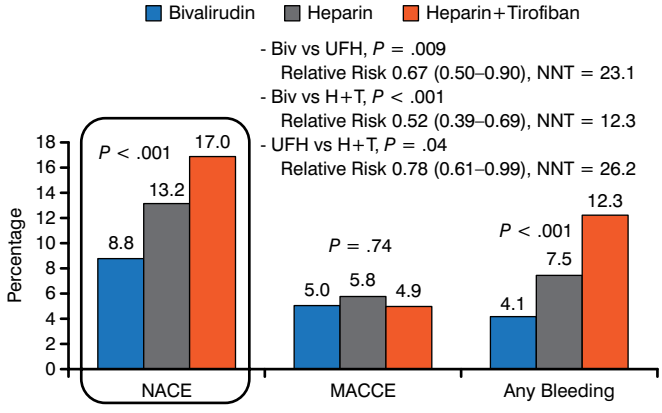
Although 2 studies [Stone GW et al. *N Engl J Med.* 2008; Steg PG et al. *N Engl J Med.* 2013] have documented the superiority of bivalirudin over heparin in patients with acute myocardial infarction (AMI) undergoing primary percutaneous coronary intervention (PCI), a third study showed heparin to be associated with fewer major adverse ischemic events with no increase in bleeding [Shahzad A et al. *Lancet.* 2014]. Yaling Han, MD, Department of Cardiology, General Hospital of Shenyang Military Region, Shenyang, China, presented the results of the Bivalirudin in Acute Myocardial Infarction vs Glycoprotein IIb/IIIa and Heparin trial [BRIGHT; NCT01696110] in which bivalirudin monotherapy led to better 30-day and 1-year outcomes in these patients compared with heparin monotherapy or heparin plus tirofiban.

Patients aged 18 to 80 years, with STEMI within 12 hours of symptom onset, NSTEMI within 72 hours of symptom onset, and planned emergency PCI were eligible for enrollment. Patients with thrombolysis within 72 hours, cardiogenic shock, or anticoagulant use 48 hours before randomization, and those with active bleeding/bleeding diathesis, hemoglobin < 100 g/L, platelet count $< 100 \times 10^9$/L, or creatinine clearance < 30 mL/min were excluded. Eligible subjects were randomized to bivalirudin (n = 735; 0.75 mg/kg bolus plus 1.75 mg/kg/h infusion followed by prolonged post PCI infusion for at least 30 minutes), heparin (n = 729; 100 U/kg bolus), or heparin plus tirofiban (n = 730; heparin 60 U/kg bolus and tirofiban 10 µg/kg bolus plus 0.15 µg/kg/min infusion for 18-36 hours). The primary end point was net adverse clinical events (NACE) at 30 days defined as a composite of death from any cause, reinfarction, ischemia-driven target vessel revascularization (TVR), stroke, or any bleeding. Secondary end points included NACE at 1 year, major adverse cardiac and cerebrovascular events (MACCE), and any bleeding (Bleeding Academic Research Consortium [BARC] definition) at 30 days and 1 year. Stent thrombosis (ARC definite or probable) at 30 days and 1 year and thrombocytopenia (nadir platelet count $< 100 \times 10^9$/L or drop > 50% from baseline) at 30 days were the safety end points.

Participants were mean age 58 years, 82% were men. The majority (88%) enrolled with STEMI within 7 hours of first symptom. Mean door-to-device time was 68 minutes. Almost all (99%) patients received drug-eluting stents; most stents (78%) were placed using transradial access. At 30 days, NACE ($P < .001$) and bleeding ($P < .001$) occurred significantly less often in bivalirudin-treated patients compared with the heparin therapies (Figure 1). Time-to NACE, but not MACCE, favored bivalirudin ($P < .001$) at 30 days.

Thrombocytopenia occurred in 0.1%, 0.7%, and 1.1% of bivalirudin-, heparin-, and heparin plus tirofiban-treated patients, respectively ($P = .02$, bivalirudin vs heparin plus tirofiban). No group differences for ischemic events or stent thrombosis (STEMI) were noted at 30 days. At 1 year, NACE and time-to-NACE also favored bivalirudin (Figure 2).

Figure 1. NACE, MACCE, and Any Bleeding at 30 Days



Biv, bivalirudin; H + T, heparin plus tirofiban; MACCE, major adverse cardiac and cerebrovascular events; NACE, adverse clinical events; UFH, unfractionated heparin.

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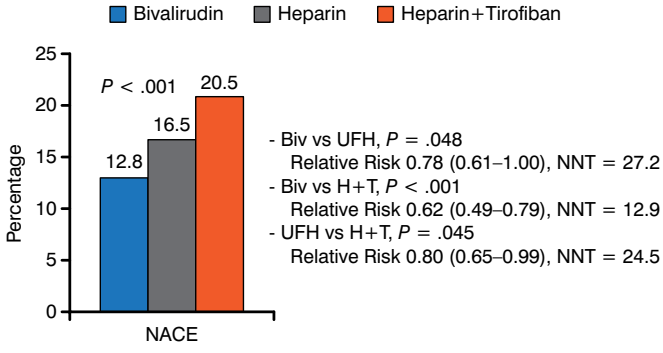
Figure 2. NACE at 1 Year



Biv, bivalirudin; H + T, heparin plus tirofiban; NACE, adverse clinical events; UFH, unfractionated heparin.

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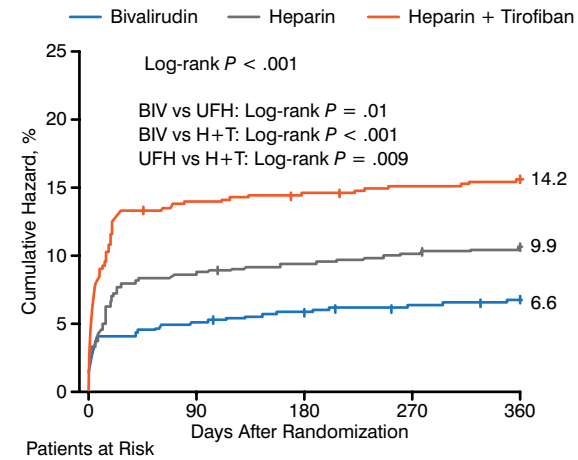
Figure 3. Treatment-Related Bleeding



Biv, bivalirudin; H + T, heparin plus tirofiban; UFH, unfractionated heparin.
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There were no significant differences as to major ischemic events at 1 year; however, bleeding risk favored bivalirudin (Figure 3).

The open-label trial design limits interpretation of these findings, as does the unequal number of STEMI and NSTEMI participants. In addition, Chinese domestic bivalirudin was used in this study. Prasugrel and ticagrelor were not used, as they were not available in China at the time of enrollment.

Six-Month DAPT Noninferior to 12-Month Regimen Following Stent Implantation

Written by Brian Hoyle

Results from the Second Generation Drug-Eluting Stents Implantation Followed by Six Versus Twelve Month Dual Antiplatelet Therapy trial [SECURITY; Colombo A et al. *J Am Coll Cardiol*. 2014. In press] have demonstrated the noninferiority of postprocedural dual antiplatelet therapy (DAPT) for 6 months as compared with 12 months in non-high-risk patients undergoing percutaneous coronary intervention (PCI) with a second-generation drug eluting stent (2G-DES). The trial findings were described by Antonio Colombo, MD, Centro Cuore Columbus, Milan, Italy.

The SECURITY trial was a prospective, randomized, non-inferiority, investigator-driven trial. The main inclusion criteria were the presence of coronary artery disease with stable angina, unstable angina or asymptomatic documented ischemia as clinical manifestations. Additional inclusion criteria were patient age over 18 years, no other DES implanted before the target procedure, and no bare metal stent implanted in the 3 months before the target procedure. The main exclusion criteria were history of treatment for venous or arterial graft lesions, in-stent restenosis, unprotected left main lesions, STEMI within 48 hours of surgery, non-STEMI in the prior 6 months. Additional exclusion criteria were left ventricular ejection fraction (LVEF) ≤ 30%; hypersensitivity or allergy to study drug or devices; chronic renal insufficiency; diagnosed life expectancy < 24 months; and current participation in another study involving a drug or device.

The primary end point was a composite of cardiac death, MI, stroke, stent thrombosis, or Bleeding Academic Consortium Criteria (BARC) type 3 or 5 bleeding at 12 months. Conversely, secondary end points included the composite of cardiac death, MI, stroke, definite/probable stent thrombosis or BARC type 2, 3, or 5 bleeding at 12 and 24 months, and the occurrence of MI, ischemia-driven revascularization (with PCI or coronary artery by-pass graft), all bleeding events, and all-cause mortality at 30 days and 6, 12, and 24 months.

The analysis was carried out according to the intention to treat principle. Additionally, it was prespecified as a per-protocol analysis including only patients fulfilling all major inclusion criteria and treated according to the assigned randomization arm.

Overall, 1399 patients were randomized to the 6-month (n = 682) or 12-month (n = 717) DAPT regimen. The randomization arms were well balanced in terms of baseline clinical and angiographic characteristics. Use of medication during the trial was similar at 6 months. Conversely, more than 30% of patients in the 6-month group were on DAPT regimen at 12 months.

There were no statistically significant differences between the 6- and 12-month regimens concerning the primary and secondary composite end points at 12 months (Figure 1).

Moreover, no differences in the secondary end points incidence at 24 months were observed between the study groups.

Rates of the single end points are reported in Table 1. Again, no differences were observed across the different outcomes between 6- and 12-month regimens. Of note, only 6 cases of definite/probable stent thrombosis occurred at follow-up.

Multivariable analysis revealed a significant association between the primary end point and age, type of