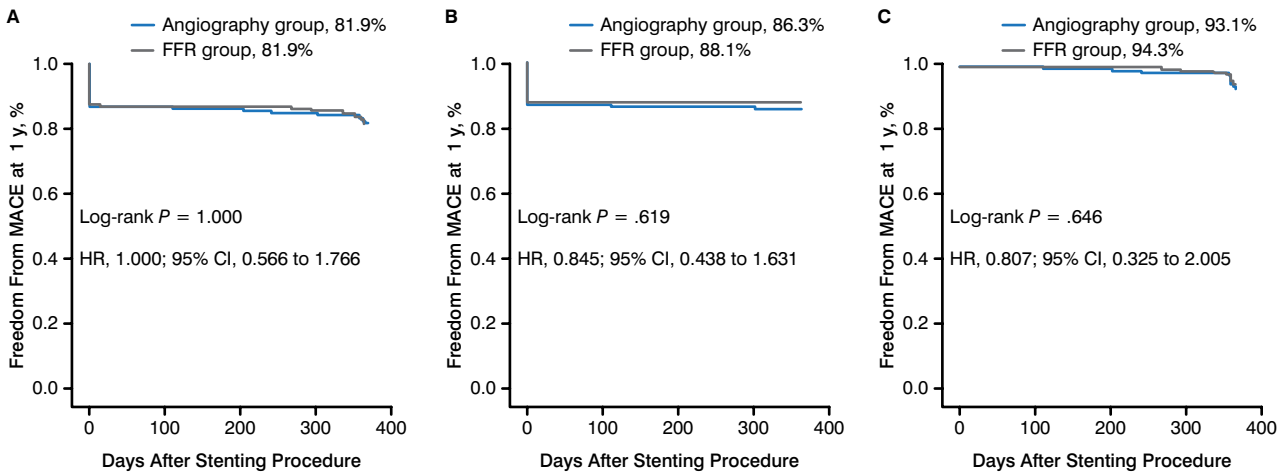
Figure 1. Kaplan-Meier Analysis for 1-Year Survival



FFR, fractional flow reserve; MACE, major adverse cardiac events; TVR, transcatheter valve replacement.
A, Composite MACE. B, Myocardial infarction. C, TVR.
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Table 1. Distribution of Restenosis[a]

Location	Angiography Group	FFR Group	*P* Value
Proximal MV	4 (3.4)	2 (1.7)	.68
Distal MV	11 (9.2)	2 (1.7)	.01
Side branch	14 (11.8)	25 (21.2)	.037

FFR, fractional flow reserve; MV, main vessel.
[a]Using a post hoc definition.

Lower 30-Day Mortality After Early Stent Thrombosis With Bivalirudin vs Heparin

Written by Toni Rizzo

The risk of subacute (≤30 days) stent thrombosis (ST) is high after primary percutaneous intervention (PCI) for STEMI. HORIZONS-AMI [The Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction; Dangas GD et al. *Circulation.* 2011], EUROMAX [European Ambulance Acute Coronary Syndrome (ACS) Angiography Trial; Clemmensen P et al. *J Am Coll Cardiol.* 2014], and HEAT-PPCI [How Effective Are Antithrombotic Therapies in Primary Percutaneous Coronary Intervention; Shahzad A et al. *Lancet.* 2014] trials demonstrated an increased risk of acute ST (<24 hours) in patients treated with bivalirudin vs heparin with or without a platelet glycoprotein IIb/IIIa inhibitor (GPI).

George D. Dangas, MD, PhD, Mount Sinai Medical Center, New York, New York, USA, presented the results of a pooled analysis of the international, open-label HORIZONS-AMI and EUROMAX trials. The aim of the analysis was to determine the independent predictors for subacute ST and evaluate mortality after ST according to the antithrombotic therapy used for primary PCI. Patient data from both trials were pooled and analyzed. In both trials, patients were randomized to either bivalirudin or heparin ± GPI.

A total of 5800 patients with STEMI treated with primary PCI was included in the analysis. The baseline and procedural characteristics were similar in the bivalirudin and heparin ± GPI groups. Early ST occurred in 100 patients (1.7%), 20 (20%) of whom died within 30 days. A 1-day landmark analysis of early ST incidence (within 30 days) found an ST event rate of 1.3% in the bivalirudin group vs 0.2% in the heparin ± GPI group during the first 24 hours ($P < .0001$). There were no statistically significant differences in the incidence of ST after the first 24 hours up to 30 days in those patients treated with bivalirudin (0.9%) when compared with heparin ± GPI (1.2%; $P = .271$) groups.

A 4-hour landmark analysis demonstrated that the ST event rate was only significantly higher in the bivalirudin

group (0.94%) vs the heparin ± GPI group during the first 4 hours ($P < .0001$). From 4 to 24 hours, the ST event rate was 0.32% in the bivalirudin group vs 0.17% in the heparin ± GPI group ($P = .2675$).

The 30-day mortality rate for patients with acute ST was 2.8% in the bivalirudin group vs 16.7% in the heparin ± GPI group ($P = .14$). The 30-day mortality rate for patients with subacute ST was 12.0% in the bivalirudin group vs 44.1% in the heparin ± GPI group ($P = .01$). The 30-day mortality rate for all early ST was 6.7% with bivalirudin and 40% with heparin ± GPI ($P < .0002$).

Preprocedural TIMI flow of 0 or 1 predicted acute ST (OR 2.35; 95% CI 1.04 to 5.35; $P = .041$). Killip Class ≥ II during acute MI predicted subacute ST (OR 3.19; 95% CI 1.70 to 5.60; $P < .0003$).

The excess risk of ST associated with bivalirudin compared with heparin ± GPI occurred only in the acute phase on day 1 and more specifically during the first 4 hours after primary PCI. The mortality rate associated with subacute ST was higher than with acute ST. Thirty-day mortality after early ST was significantly lower in patients treated with bivalirudin than those treated with heparin ± GPI. These results were consistent for both acute and subacute ST.

Shorter Clopidogrel Therapy Not Superior Following Coronary DES Implantation

By Brian Hoyle

In the Triple Therapy in Patients on Oral Anticoagulation After Drug Eluting Stent Implantation trial [ISAR-TRIPLE; NCT00776633], 6 weeks of triple therapy including the oral antiplatelet compound clopidogrel is not superior to a 6-month regimen following implantation of a drug-eluting stent (DES). The results were reported by Nikolaus Sarafoff, MD, Technische Universität München, Munich, Germany.

Previous studies support the view that combined oral anticoagulant/antiplatelet therapy is advantageous in reducing adverse outcomes following cardiac surgeries [Connolly S et al. *Lancet.* 2006]. However, triple therapy comes with the drawback of increased risk of bleeding. The optimal length of therapy to maximize the benefits while minimizing bleeding risk following DES implantation is unknown.

The risk of stent thrombosis is greatest soon after percutaneous coronary intervention and declines thereafter. Also, bleeding risk depends on the length and intensity of oral anticoagulant therapy [Lip GYH et al. *Eur Heart J.* 2014]. Informed by this knowledge, the ISAR-TRIPLE prospective, randomized, open-label trial evaluated clinical outcomes of a 6-week and 6-month regimen of clopidogrel along with aspirin and oral anticoagulation following DES implantation in 614 patients [Fiedler KA et al. *Am Heart J.* 2014]. The hypothesis was that the shorter course of therapy is superior.

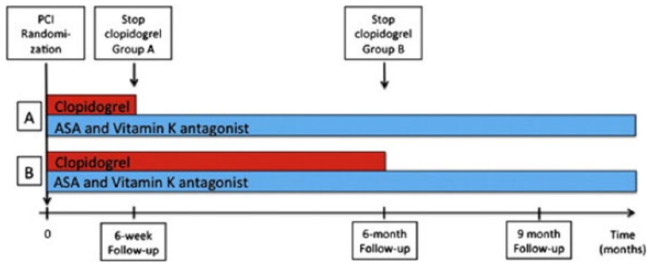
DES implantation and need for oral anticoagulation were the inclusion criteria. Exclusion criteria included prior stent thrombosis and DES implantation in the left main coronary artery. The primary end point was death, myocardial infarction (MI), confirmed stent thrombosis, stroke, or major bleeding at 9 months. Secondary end points included ischemic complications (cardiac death, MI, stent thrombosis, ischemic stroke) and major bleeding.

All patients received aspirin (75-200 mg QD) and vitamin K antagonist along with clopidogrel 75 mg QD for 6 weeks (n = 307) or 6 months (n = 307). Phenprocoumon or warfarin were used in patients with mechanical valves (5% and 9% of the 6-week and 6-month group, respectively) to achieve a target internal normalized ratio. Clinical follow-up was done after 9 months for most patients (n = 606 [98.7%]; Figure 1).

At baseline, the 2 groups were similar in age; sex; history of MI; prevalence of diabetes, acute coronary syndrome, and stable angina; and indication of oral anticoagulants. Compliance with all medications was excellent, with the exceptions of clopidogrel use by those in the 6-week group after 6 weeks (26% vs 87% in the 6-month group; $P < .001$) and at the 9-month follow-up (23% vs 35%; $P < .001$).

There were no significant differences between the 2 groups in either the primary end point (HR, 1.14; 95% CI, 0.68 to 1.91; $P = .63$) or the secondary end points of

Figure 1. ISAR-TRIPLE Design



ASA, aspirin; PCI, percutaneous coronary intervention.

A: 6-week group; B: 6-month group.

Reproduced from *American Heart Journal*, 167, Fiedler KA et al, Rationale and design of The Intracoronary Stenting and Antithrombotic Regimen—Testing of a six-week versus a six-month clopidogrel treatment Regimen In Patients with concomitant aspirin and oraL anticoagulant therapy following drug-Eluting stenting (ISAR-TRIPLE) study, 459-465, Copyright 2014, with permission from Elsevier.