1.29; 95% CI, 0.48 to 3.47; p=0.61). Definite or probable stent thrombosis occurred in 0.8% of patients with the zotarolimus-eluting stent compared with 0.5% of patients with the biolimus-eluting stent (HR, 1.73; 95% CI, 0.68 to 4.38; p=0.25).

The results of the SORT-OUT VI trial demonstrate that both zotarolimus-eluting stents and biolimus-eluting stents are associated with similar rates of cardiac death, MI, or TLR. The zotarolimus-eluting stent met the criteria for noninferiority compared to the biolimus-eluting stent in patients treated with PCI.

Prehospital Bivalirudin Improved Outcomes Versus Heparin in Patients With Myocardial Infarction

Written by Toni Rizzo

The HORIZONS AMI trial showed that bivalirudin therapy in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous intervention (PCI) reduced mortality and bleeding for up to 3 years compared with heparin plus a glycoprotein IIb/IIIa inhibitor [Stone GW et al. *N Engl J Med* 2008]. According to Philippe Gabriel Steg, MD, Universite Paris-Diderot, Paris, France, who presented the results of the European Ambulance Acute Coronary Syndrome Angiography Trial [EUROMAX; Steg PG et al. *N Engl J Med* 2013], several issues remain, including the role of bivalirudin in the ambulance for patients triaged to primary PCI; the potential for reducing the risk of acute stent thrombosis with a prolonged bivalirudin infusion post-PCI; and the impact of contemporary practice (frequent use of radial arterial access and novel oral P2Y12 inhibitors) on the efficacy and safety of bivalirudin.

The objective of the EUROMAX trial was to examine whether bivalirudin, initiated in patients with STEMI while being transported in the ambulance for primary PCI, was superior to heparin and provisional use of glycoprotein IIb/IIIa inhibitors.

Patients with STEMI who presented within 12 hours after the onset of symptoms and were scheduled for primary PCI (n=2218) were randomized in the ambulance or at a non-PCI hospital to treatment with bivalirudin (0.75 mg/kg bolus followed by 1.75 mg/kg/hour infusion; n=1089) or to unfractionated heparin with or without a glycoprotein IIb/IIIa inhibitor (n=1109). To address prior concerns for increased acute stent thrombosis seen in patients treated with bivalirudin in the HORIZONS AMI trial, bivalirudin infusion in EUROMAX was continued post-PCI for at least 4 hours. Bailout use of a glycoprotein IIb/IIIa inhibitor was also allowed in the bivalirudin group if needed. During the course of the trial, the primary endpoint was changed. The original primary endpoint was the composite endpoint of death, reinfarction, or major bleeding. After a change in the study protocol, the primary and secondary endpoints were switched so that the primary endpoint was the composite of all-cause mortality or major bleeding at 30 days and the key secondary endpoint was mortality, reinfarction, or major bleeding at 30 days. The change in the primary endpoint was made in order to reduce the necessary sample size and occurred while the investigators were still unaware of study outcomes. Major bleeding was defined as intracranial, retroperitoneal, or intraocular bleeding; access-site hemorrhage requiring radiologic or surgical intervention; a reduction in the hemoglobin level of more than 4 g/dL (2.5 mmol/L) without an overt source of bleeding or a reduction in the hemoglobin level of more than 3 g/dL with an overt source of bleeding; reintervention for bleeding; or use of any blood-product transfusion that was not related to coronary artery bypass surgery.

Baseline characteristics were similar between the two groups, with the exception of diabetes (bivalirudin, 11.7% vs heparin, 15.3%; p<0.05) and prior MI (bivalirudin, 7.4% vs heparin, 10.2%; p<0.05). The primary endpoint occurred in 5.1% of patients treated with bivalirudin compared with 8.5% of those treated with heparin (RR, 0.60; 95% CI, 0.43 to 0.82; p=0.001).

The secondary endpoint occurred in 6.6% of the bivalirudin group versus 9.2% of the heparin group (RR, 0.72; 95% CI, 0.54 to 0.96; p=0.02). There was no significant difference between the bivalirudin and heparin groups in cardiac deaths (2.5% vs 3.0%; RR, 0.83; 95% CI, 0.50 to 1.38; p=0.48) and noncardiac deaths (0.5% vs 0.1%; RR, 5.09; 95% CI, 0.60 to 43.51; p=0.12). Major bleeding was reported in 2.6% of the bivalirudin groups versus 6.0% of the heparin group (RR, 0.43; 95% CI, 0.28 to 0.66; p<0.001). The composite endpoint of death, reinfarction, ischemia-driven reinfarction, stroke, and major bleeding was reported in 7.8% of the bivalirudin group compared with 10.6% of the heparin group (RR, 0.73; 95% CI, 0.56 to 0.96; p=0.02). The benefits of bivalirudin were consistent across the reported subgroups.

The rate of definite stent thrombosis within 24 hours was higher in the bivalirudin group (1.1%) compared with the heparin group (0.2%; RR, 6.11; 95% CI, 1.37 to 27.24; p=0.007).

The EUROMAX trial had several limitations, including its open-label design. Additionally, the trial was not powered to assess 30-day mortality.

This trial showed that in patients with STEMI who were being transported for primary PCI, the initiation of bivalirudin prior to hospital admission reduced the primary endpoint of death or bleeding and the secondary endpoint of death, bleeding, or reinfarction when compared with heparin. However, the rate of acute stent thrombosis was higher with bivalirudin compared with heparin-treated patients. The investigators attributed the benefits of bivalirudin to the

substantial reduction in major bleeding. Prof. Steg concluded that these results support the use of bivalirudin for the prehospital management of STEMI prior to primary PCI.

Similar Outcomes With Two-Stent and Provisional Stenting Techniques in Large Side Branch Bifurcation Lesions

Written by Toni Rizzo

Bifurcation lesions occur at the point where one coronary artery branches from another. Currently, provisional side-branch stenting is the preferred strategy for treating most bifurcation lesions. This type of stenting involves stenting the main branch, reserving further stent placement in the side branch only if it is compromised. However, it is not known if provisional stenting provides the best outcomes in bifurcation lesions involving a large side branch.

The aim of the Nordic-Baltic Bifurcation Study IV [NCT01496638], presented by Indulis Kumsars, MD, Pauls Stradins Clinical University Hospital, Riga, Latvia, was to compare provisional stenting with a two-stent techniques for the treatment of true coronary bifurcation lesions involving a large side branch. The study investigators hypothesized that a two-stent technique would be superior to provisional stenting in this setting.

This open-label trial randomized 450 patients with bifurcation lesions involving a large side branch to either provisional stenting (n=221) or a two-stent technique (n=229). Patients with bifurcation stenosis involving both the main vessel and the side branch were eligible. The patients could have stable angina, unstable angina, or non-ST-segment elevation myocardial infarction (NSTEMI), but were excluded if they had STEMI, cardiogenic shock, other critical illnesses, or if the side branch lesion was >15 mm long. The first 225 patients were treated with a sirolimus-eluting stent and the last 225 patients received an everolimus-eluting stent. The primary endpoint was major adverse cardiac events (MACE), defined as the composite of cardiac death, non-index procedure-related MI, target lesion revascularization, and definite stent thrombosis.

Baseline demographics and clinical characteristics were well balanced between the two groups. Lesion characteristics were similar between the provisional stent and two-stent groups, with the exception of the main vessel reference diameter (3.5 vs 3.4 mm; p=0.04) and the side branch lesion length (7.4 vs 8.0 mm; p<0.0001; Table 1).

Of the 450 randomized patients, 220 in the provisional stent group and 227 in the two-stent group were stented and completed 6 months of follow-up. The side branch was dilated in 64.3% of the provisional group and in 78.0% of the two-stent group. Final kissing balloon stent dilation was performed in 36.1% of the provisional group and in 91.2% of the two-stent group. Side branch stenting was performed in 3.7% of the provisional group and 96.0% of the two-stent group. When defining success as residual stenosis of <30% in the main vessel plus TIMI Grade III flow in the side branch, 97.7% of the provisional group and 99.1% of the two-stent group had successful procedures.

Table 1. Lesion Characteristics

	Provisional (n=221)	Two-Stent (n=229)	p Value
LAD/diagonal(%)	74.1	76.7	ns
CX/obtuse marginal (%)	16.8	17.6	ns
RCA POA/PLA (%)	6.4	4.0	ns
LM/LAO/CX (%)	2.7	1.3	ns
Ref. diameter main vessel (mm)*	3.5	3.4	0.04
Ref. diameter side branch (mm)*	2.9	2.9	ns
Lesion length SB (mm)*	7.4	8.0	<0.0001
Angulation >60-70° (%)*	50.9	51.1	ns

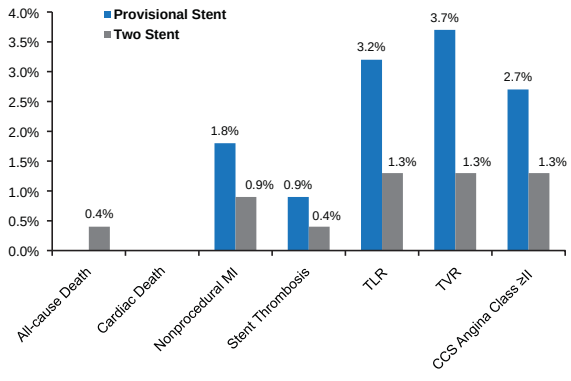
*visual estimation.

CX=circumflex; LAD=left anterior descending; LAO= left anterior oblique; LM=left main; POA=primitive olfactory artery; PLA=posterolateral artery; RCA=right coronary artery; SB=side branch.

At 6 months, the primary endpoint of MACE had occurred in 4.6% of patients in the provisional stent group compared with 1.8% of patients in the two-stent group (p=0.09).

No differences between the provisional stent group and the two-stent group achieved statistical significance for the following secondary endpoints (Figure 1).

Figure 1. Secondary Endpoints



CCS=Canadian Cardiovascular Society; MI=myocardial infarction; TLR=target lesion revascularization; TVR=target vessel revascularization.

At 6 months, there were no statistically significant differences in the rate of MACE between patients treated with provisional stenting and those treated with a two-stent technique for bifurcation lesions involving a large side