Conclusions: In the population studied intracoronary bivalirudin bolus during primary PCI is safe and might improve results obtained through the standard intravenous route over postprocedural coronary flow and clinical myocardial reperfusion.

TCT-465

Safety and efficacy of intracoronary bivalirudin administration during primary angioplasty in comparison with a standard treatment with heparin and provisional GPIb3a inhibitors

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Background: Bivalirudin efficacy in the very first hours after primary PCI has been questioned, due to increased acute stent thrombosis rates. Intracoronary administration of the bivalirudin bolus might furnish an extremely high local drug concentration without changing the global dose administered to the patient, with a potential favorable effect over the pro-thrombotic milieu of the infant related artery. We prospectively investigated the feasibility and safety of intracoronary bivalirudin bolus administration during primary percutaneous coronary interventions (PCI), comparing this strategy with the standard treatment based upon unfractionated heparin (UFH) with provisional GPIb3a inhibitors (GPI) given through the intravenous route.

Methods: In 273 consecutive patients treated with primary PCI we administered intracoronary bivalirudin bolus followed by standard intravenous infusion. Postprocedural coronary blood flow indexes and clinical reperfusion markers of these patients were compared with a propensity score-matched cohort of primary PCI patients treated with standard treatment with intravenous UFH 70U/kg (eventually with supplementary boluses to achieve an ACT≥250sec) plus provisional GPI.

Results: In the intracoronary bivalirudin group we observed better TIMI frame count values (14.8±4.6 vs 16.9±9.3, P=0.002), higher rates of ≥70% ST resolution (72.1 vs 44.5%, p=0.001), lower incidence of no-reflow (7.0 vs 13.5%, p=0.011) and a trend for lower postprocedural peak CK-MB levels (140.0 [53.7-235.5] vs 159.2 [64.3-269.9] UI/dL, p=0.08). Moreover acute stent thrombosis (<24 after PCI) was observed in 11 cases, in all the UFH/GPI group (p=0.009). Intracoronary bivalirudin administration was safe, with less internal bleedings (3.7 vs 11.2%, p=0.001) and less need for transfusion (4.6 vs 1.1, p=0.012). The results were substantially confirmed when the analysis was restricted to patients with an occluded infarct related artery before PCI.

Conclusions: In the population studied intracoronary bivalirudin during primary PCI was safe and might improve postprocedural coronary flow, clinical myocardial reperfusion and acute stent thrombosis rates, in comparison with the UFH plus provisional GPI treatment.

TCT-466

Bivalirudin Is Associated With Improved In-Hospital Outcomes After Peripheral Arterial Interventions: An Observational Analysis On 23,934 Patients From The PREMIER Hospital Database

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Background: Bivalirudin has been shown to reduce bleeding complications and improve clinical outcomes in percutaneous coronary interventions but has not been well studied in peripheral arterial interventions (PAI). We sought to evaluate the efficacy and safety of bivalirudin as compared with unfractionated heparin (UFH) in patients undergoing PAI by evaluating in-hospital outcomes from a large, real-world, US hospital database of over 600 hospitals.

Methods: We identified all patients (n=23,934) entered from 1/08-12/12 in the PREMIER hospital database following PPI of the extremities and who were treated with bivalirudin or UFH. In-hospital outcomes that were compared according to the Academic Research Consortium definition of definite or probable. AC – anticoagulation; PCI – percutaneous coronary intervention; UFH – unfractionated heparin.

Results: In the population studied intracoronary bivalirudin bolus during primary PCI was safe and might improve bleeding complications and improve clinical outcomes in percutaneous coronary interventions but has not been well studied in peripheral arterial interventions (PAI). We sought to evaluate the efficacy and safety of bivalirudin as compared with unfractionated heparin (UFH) in patients undergoing PAI by evaluating in-hospital outcomes from a large, real-world, US hospital database of over 600 hospitals.

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Background: Controversy exists regarding the optimal choice of anticoagulation regimen for percutaneous coronary intervention (PCI). We performed a meta-analysis of randomized controlled trials (RCT) to compare bivalirudin (bival) versus heparin with provisional or routine glycoprotein IIb/IIIa inhibitor (GPI) use on 30-day outcomes following PCI.

Methods: Medline/Pubmed and Cochrane CENTRAL were searched along with recent abstract presentations at national meetings for all RCTs comparing BIV with heparin with provisional or routine GPI use for PCI. Pooled estimates of 30-day outcomes were generated for with random-effect models to compare the treatment groups. Data is presented as odds ratios (OR) [95% confidence intervals]

Results: Our analysis included 14 studies with 30,446 patients that were randomized to either bivalirudin with provisional GPI use (n=14,869) or heparin with provisional GPI use (n=6,451) or heparin with routine GPI use (n=9,126). There was no significant difference between anticoagulation with bival compared with heparin for 30 day death (OR 0.94 [0.78-1.14]) or myocardial infarction (OR 1.11 [0.97-1.27]). Early stent thrombosis was significantly greater with bivalirudin compared with heparin (OR 1.62 [1.18-2.23], p=0.003), especially when comparing bivalirudin versus heparin with provisional GPI use (OR 2.09 [1.26-3.47], p=0.005) or among STEMI patients (OR 2.17 [1.15-4.10], p=0.002). However, bivalirudin reduced the risk of major bleed (OR 0.58 [0.40-0.80], p<0.0001) and TIMI major bleeding (OR 0.58 [0.47-0.71], p<0.0001) compared with heparin. Meta-regression analysis demonstrated that bleeding risk with use of heparin significantly increases with increasing GPI use (p=0.02).

Conclusions: Meta-analysis of 14 RCTs with 30,446 patients demonstrated that bivalirudin is associated with higher risk of stent thrombosis but lower risk of major bleeding compared with heparin.

TCT-468

Predictors Of Stent Thrombosis After Primary Percutaneous Coronary Intervention And Risk for 30-Day Mortality: Analysis from the HORIZONS-AMI and EURONAX trials

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Background: The risk of early (≤30 day) stent thrombosis (ST) is considerable after primary PCI at STEMI. We sought to determine the independent predictors of early ST and evaluate the risk of mortality after ST according to antithrombotic therapy used during the index primary PCI.

Methods: In a patient-level pooled analysis from the HORIZONS-AMI and EURO-MAX trials, we studied 5,800 patients undergoing primary PCI at 188 sites, randomized to either bivalirudin or heparin ± a glycoprotein IIb/IIIa inhibitor (GPI). Predictors of ST were determined by multivariate logistic regression, and 30-day mortality was evaluated according to timing of ST and antithrombotic treatment received.

Results: Of 101 patients (1.7%) who developed early ST, 20 (20%) died within 30 days of enrollment. By logistic regression, independent predictors of early ST were pre-PCI TIMI grade flow 0-1 and Killip class ≥2 at presentation. Bivalirudin was associated with higher rates of early ST (2.1% vs. 1.4%, RR=1.51, adj. p-value=0.07) driven by a higher incidence of acute ST (1.2% vs. 0.2%, RR=6.04, p<0.0001) with similar rates of subacute ST (0.9% vs. 1.2%, RR=0.74, p=0.24) in comparison to heparin ± GPI. However, 30-day mortality rates among patients with ST were lower in the bivalirudin-treated subset; this was consistent for both acute and subacute ST (Table). As a result, only 42,889 bivalirudin-treated patients died within 30 days after early ST compared to 16,523 heparin ± GPI treated patients (0.14% vs. 0.56% respectively, p<0.01).

Conclusions: Killip class ≥2 during acute MI presentation and pre-procedure TIMI grade flow 0-1 are independent predictors of early ST after primary PCI. Although the risk of ST within 30 days is higher among patients treated with bivalirudin due to a greater hazard of acute ST, death attributable to early ST is substantially less common in patients having received bivalirudin compared to heparin ± GPI.

TCT-469

Association Between Activated Clotting Times During Percutaneous Coronary Intervention and Clinical Outcomes

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Background: Monitoring the intensity of anticoagulation with heparin during percutaneous coronary intervention (PCI) using the activated clotting time (ACT) is one of the most frequently used tests in invasive cardiology. However, despite its ubiquitous use, controversy remains regarding the association of ACT with ischemic and bleeding events.

Methods: We reviewed all PCI procedures performed at Mayo Clinic (Rochester, MN) between 2001 - 2012 and evaluated the association between the ACT value at the time of PCI and in-hospital and 1-year outcomes. For descriptive purposes, ACT values were grouped into tertiles. We used logistic and Cox proportional hazards regression models to estimate the association of ACT, modeled continuously, with outcomes while accounting for baseline characteristics.

Results: Of 12,059 patients studied, 3,978 (33.0%) had ACT < 227, 4,047 (33.6%) had ACT ≥227-285, and 4,034 (33.4%) had ACT >285. Groups were similar regarding baseline and procedural characteristics. In univariate analysis, ACT had associations with in-hospital and 1-year clinical events; however, after multivariable adjustment, ACT at the time of device activation was not independently associated with outcomes (Table).

Association Between Activated Clotting Time (per 50 sec increase) and Clinical Outcome

Unadjusted OR (95% CI) Adjusted OR (95% CI) p value

In hospital overt bleeding 0.94 (0.88, 1.01) 0.09 1.00 (0.93, 1.08) 0.96

In hospital death 0.79 (0.71, 0.88) 0.0001 1.01 (0.89, 1.15) 0.85

In hospital death/MI 0.98 (0.93, 1.04) 0.51 1.01 (0.95, 1.08) 0.77

1 year cardiac death/MI 0.97 (0.93, 1.01) 0.16 1.00 (0.95, 1.04) 0.81

1 year cardiac death/MI/TRL 0.97 (0.94, 1.00) 0.07 0.99 (0.96, 1.03) 0.57

Abbreviations: MI, myocardial infarction; TLR, target lesion revascularization; p value, p value of the univariable model adjusted for age, sex, body mass index, hypertension, diabetes, heart failure, smoking, cholesterol level, prior PCI/CABG, shock at presentation, MI at presentation, stent type (drug eluting vs bare metal), glycoprotein IIb/IIIa use.