Table. Rates of Stent Thrombosis

	Any post-PCI AC for routine prophylaxis (N=436)	No post-PCI AC for routine prophylaxis (N=1,009)	Adjusted HR [95% CI]	Adjusted p-Value
Acute (≤24 hour) stent thrombosis	3 (0.7)	10 (1.0)	0.65 [0.13, 3.18]	0.59
Thirty-day stent thrombosis	7 (1.7)	20 (2.1)	0.97 [0.37, 2.53]	0.95
	Post-PCI AC for routine prophylaxis with pre-PCI UFH (N=325)	Pre-PCI UFH with no post-PCI AC for routine prophylaxis (N=623)	Unadjusted HR [95% CI]	Unadjusted p-Value
Acute (≤24 hour) stent thrombosis	2 (0.6)	3 (0.5)	1.28 [0.21, 7.68]	0.78
Thirty-day stent thrombosis	5 (1.6)	8 (1.3)	1.20 [0.39, 3.65]	0.75
	Only post-PCI AC for routine prophylaxis with no pre-PCI UFH (N=111)	No pre-PCI UFH or post-PCI AC for routine prophylaxis (N=386)	Unadjusted HR [95% CI]	Unadjusted p-Value
Acute (≤24 hour) stent thrombosis	1 (0.9)	7 (1.9)	0.50 [0.06, 4.02]	0.50
Thirty-day stent thrombosis	2 (1.9)	12 (3.3)	0.57 [0.13, 2.55]	0.46

Values presented as n (%). Stent thrombosis was classified according to the Academic Research Consortium definition of definite or probable. AC = anticoagulation; PCI = percutaneous coronary intervention; UFH = unfractionated heparin.

TCT-464

Intracoronary Bivalirudin Bolus During Primary Angioplasty Improves Postprocedural Angiographic Flow and Myocardial Reperfusion Indexes

Alessandro Lupi[1], Andrea Rognoni[1], Gioel G. Secco[2], Angelo S. Bongo[1]
[1]AOU Maggiore della Carità, Novara, Italy, [2]University of Eastern Piedmont, Novara, Italy

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 infarct related artery. Thus we prospectively investigated the feasibility and safety of intracoronary bivalirudin bolus administration during primary percutaneous coronary interventions (PCI), comparing it with the standard intravenous route.
Methods: In 245 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 intravenous bivalirudin bolus plus infusion.
Results: Our study suggests safety similar bleeding episodes were observed in the two groups. However we observed better TIMI frame count values (14.7 vs 17.9, P=0.001), higher rates of ≥ 70% ST resolution (72.7 vs 60.0%, p=0.004) and lower postprocedural peak CK-MB levels (188.3 ± 148.7 vs 242.1 ± 208.1 Ui/dL, P=0.025) in the intracoronary bolus group. Acute stent thrombosis was observed only in 3 cases, all in the intravenous bolus group (P=NS). These results were substantially confirmed when the analysis was restricted to patients with evidence of an occluded infarct related artery before PCI.
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 GP2b3a inhibitors

Alessandro Lupi[1], Gioel G. Secco[2], Andrea Rognoni[1], Italo Porto[3], Maurizio Lazzero[1], Angelo S. Bongo[1]
[1]AOU Maggiore della Carità, Novara, Italy, [2]University of Eastern Piedmont, Novara, Italy, [3]San Donato Hospital, Arezzo, Italy

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 infarct 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 GP2B3A 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 70Ui/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±6.5 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=0.06). Moreover acute stent thrombosis (< 24h after PCI) was observed in 11 cases, all in 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

Carey D. Kimmelstiel[1], Duane Pinto[2], Andrew Weintraub[3], George Dangas[4], Weihong Fan[5], Jayne Prats[6], Efthymios N. Deliargyris[5], Barry T. Katzen[7]
[1]Tufts Medical Center, Boston, United States, [2]Beth Israel Deaconess Medical Center, Boston, United States, [3]Tufts Medical Center, Boston, MA, [4]Mount Sinai, New York, New York, NY, [5]The Medicines Company, Parsippany, NJ, [6]The Medicines Company, Parsippany, NJ, [7]Baptist Cardiac and Vascular Institute, Miami, FL

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 treatment included death , myocardial infarction (MI), transfusion, stroke, amputation, Major Adverse Cardiac Events (MACE: death, MI, stroke or amputation) and Net Adverse Cardiac Events (NACE: MACE and transfusion). Propensity score matching (PSM) was performed to control for selection bias.
Results: In-hospital outcomes for both the unadjusted population and the 3,649 PSM pairs are shown in the Table. After PSM, bivalirudin was still associated with significantly lower rates of death, transfusion, MACE and NACE compared with UFH. Linear regression modeling confirmed these findings. Subgroup analysis in the PSM population showed consistent treatment effect for all outcomes among subgroups.

	Unadjusted population			PSM population		
	Bivalirudin N = 4370	UFH N = 19,564	p	Bivalirudin N = 3649	UFH N = 3649	p
	%	%		%	%	
Death	0.3	1.0	<0.0001	0.3	0.7	0.01
Stroke	0.1	0.3	0.054	0.2	0.3	0.22
MI	0.6	1.2	0.0004	0.5	0.8	0.25
Amputation	1.3	4.5	<0.0001	1.5	2.0	0.09
Transfusion	3.4	10.0	<0.0001	4.0	5.3	0.009
MACE	2.2	6.6	<0.0001	2.3	3.5	0.003
NACE	5.4	14.8	<0.0001	5.9	7.9	0.0009

Conclusions: This analysis from a very large US hospital database suggests that the use of bivalirudin anticoagulation for PAI may confer significant clinical benefits over heparin. These results require confirmation in a prospective randomized trial.

TCT-467

Bivalirudin versus Heparin for Percutaneous Coronary Intervention: An Updated Meta-Analysis of Randomized Controlled Trials

Michael J. Lipinski[1], Thibault Lhermusier[1], Ricardo O. Escarcega[1], Nevin C. Baker[1], Marco A. Magalhaes[2], Rebecca Torguson[3], William O. Suddath[4], Lowell F. Satler[5], Augusto Pichard[6], Ron Waksman[1]
[1]Medstar Washington Hospital Center, Washington, DC, [2]MedStar Washington Hospital Center, Washington, DC, [3]Washington Hospital center, Washington, DC, [4]Medstat Washington Hospital Center, Washington, DC, [5]Washington Hospital Center, Washington, United States, [6]washsington hospital center, Washington, United States

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 provisional GPI use versus 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=0.02). However, bivalirudin reduced the risk of major bleed (OR 0.58 [0.49-0.69], 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 EUROMAX trials

George Dangas[1], Philippe G. Steg[2], Roxana Mehran[3], Arnoud van 't Hof[4], Mikkel Schoos[5], Jayne Prats[6], Debra Bernstein[7], Efthymios N. Deliargyris[7], Gregg W. Stone[8]
[1]Mount Sinai, New York, New York, NY, [2]Hopital Bichat, Paris, France, Paris, France, [3]Icahn School of Medicine at Mount Sinai, New York, NY, [4]Isala Klinieken, Zwolle, Netherlands, [5]Mount Sinai Medical Center, New York, NY, USA, Copenhagen, Denmark, [6]The Medicines Company, Parsippany , NJ, [7]The Medicines Company, Parsippany, NJ, [8]Columbia University Medical Center and the Cardiovascular Research Foundation, New York, United States

Background: The risk of early (≤30 day) stent thrombosis (ST) is considerable after primary PCI for 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 EUROMAX 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 100 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 4/2,889 bivalirudin-treated patients died within 30 days after early ST compared to 16/2,911 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.

30-day Mortality in Patients with Early ST

Timing of ST	Bivalirudin (n=2,889)	Heparin ± GPI (n=2,911)	Relative risk [95% CI]	P-Value*
Acute (≤24 hrs)	1/36 (2.8%)	1/6 (16.7%)	0.17 [0.01, 2.16]	0.14
Subacute (1-30d)	3/25 (12.0%)	15/34 (44.1%)	0.29 [0.10, 0.88]	0.01
Early (≤30d)	4/60 (6.7%)	16/40 (40.0%)	0.19 [0.07, 0.52]	0.0002

*Cochran-Mantel-Haenszel χ^2 test stratified by study

TCT-469

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

Naveen Rajpurohit[1], Mayank K Mittal[2], Adam Stys[3], Arashk Motei[4], Mandeep Singh[4], Rajiv Gulati[5], Ryan Lennon[4], Charanjit Rihal[5], Shahyar M Gharacholou[6]
[1]University of South Dakota, Sanford Cardiovascular Institute, Sioux Falls, SD, [2]University of Missouri, Columbia, MO, [3]Sanford Heart Hospital, Sioux Falls, SD, [4]Mayo Clinic, Rochester, MN, [5]Mayo Clinic, Rochester, United States, [6]Mayo Clinic, La Crosse, WI

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)	p value	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/TLR	0.97 (0.94, 1.00)	0.07	0.99 (0.96, 1.03)	0.57

Abbreviations: MI, myocardial infarction; TLR, target lesion revascularization
Models 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