1052-11

Serum Uric Acid Level Is an Independent Predictor of Restenosis After Successful Percutaneous Transluminal Coronary Stent Implantation

Kazuaki Kumagai, Masatake Fukunami, Tsuyoshi Shimonagata, Takahisa Yamada, Akio Hirata, Mitsutoshi Asai, Nobuhiko Makino, Hidetaka Kioka, Noritake Hoki, *Osaka Prefectural General Hospital, Osaka, Japan.*

Background: Inflammatory activities have been shown to be associated with an increased risk for ischemic coronary events after percutaneous transluminal coronary stent implantation (PTCS). Serum uric acid (UA), reflecting oxidative radical activity through xanthine oxidase, might be also a potent marker for chronic inflammation. However, it is not elucidated whether elevated UA levels would be related to target lesion restenosis (TLR) following PTCS. Therefore, we studied whether UA level might be one of predictors of TLR. This study included 217 consecutive patients following successful PTCS without renal dysfunction and without serum UA-lowering drugs. **Results**: During the follow-up period of 2 years, TLR occurred in 46 patients (21%). In patients with TLR, serum UA level just before PTCS were significantly higher than in patients without TLR (6.5±1.5 vs. 5.6±1.5mg/dl, p=0.0003). Patients with UA of >7.0mg/dl had a significantly higher TLR rate (43%) at 2 years after PTCS than that (28%) in patients with UA of 7.0mg/dl or less (p<0.0001, Kaplan-Meier analysis and log-rank test). Univariate analysis revealed that UA level (p=0.0003), sex (p=0.09), the diameter of stent (p=0.019), serum C-reactive protein level (p=0.093) and DM (p=0.044) were predictive of TLR, but that age, smoking, hypertension, hyperlipidemia, acute coronary syndrome, prior myocardial infarction or medications were not. Furthermore, Cox hazard model showed that UA level (hazard ratio; 1.34, 95% CI; 1.09-1.64, p=0.005), serum C-reactive protein level (hazard ratio; 1.62, 95% CI; 1.01-2.59, p=0.044) and the diameter of stents (hazard ratio; 0.35, 95%CI; 0.14-0.88, p=0.025) were independent predictors of TLR. **Conclusion**: This study indicates that elevated serum uric acid level just before PTCS would be a most powerful independent predictor of TLR following successful PTCS.

1052-12

Does Stent Design Affect Platelet Activation? Results of the Platelet Activation in Stenting (PAST) Study

Paul A. Gurbel, Kevin P. Callahan, Michele J. Buczkowski, Victor L. Serebruany, *Sinai Hospital, Baltimore, Maryland.*

BACKGROUND: Platelet activation induced by coronary artery stenting affects clinical outcomes and may be related to stent design. However, little is known about how platelet activation may be altered by the specific design of a stent. **METHODS:** Patients (n=53) were randomly assigned to stenting with a closed-cell (NIR, Boston Scientific) or open-cell (TETRA, Guidant) stent. Patients were treated with aspirin and were loaded with 300 mg clopidogrel in the cath lab and received 75 mg daily thereafter. All stents were deployed at > 12 atm. GPIIb/IIIa inhibitors were not used. Platelet aggregation (5μ mol ADP and 1μg/ml collagen); and flow cytometry (mean fluorescence intensity (MFI)) to multiple platelet receptors and platelet-leukocyte aggregates (CD 151 + 14) were serially determined at baseline, and at 2 hours (2h), 24 hours (24h), 5 days (5d) and 30 days (30d) post procedure.**RESULTS:** Stenting was successful in all patients. Markers of platelet activation were less following NIR implantation: 30d ADP aggregation (%) (32.3± 6.1 vs 44.5± 18.9, p=.02); 24h CD31 (136± 48 vs. 110± 48, p=.04); 24h (104± 45 vs 91± 31 p=.048) and 30 d CD 151 (99± 33 vs 81± 32, p=.03); 24h (93± 40 vs. 77± 24, p=.018) and 30d CD 151+14 (84± 35 vs. 72± 31, p=.045); 30d PAC-1 (88± 41 vs. 72± 30, p=.025); and 2h (22± 13 vs 18± 5, p=.045) and 24 h CD 107a (24± 12 vs. 17 ± 4, p=.03). **CONCLUSIONS:** In this randomized prospective trial, platelet activation; indicated by enhanced aggregation and expression of multiple receptors; was greater during the 30 days following implantation of an open-versus a closed-cell stent. Stent-dependent platelet activation may be relevant to the propensity for subacute thrombosis and restenosis associated with a particular stent design.

POSTER SESSION

1053 Adjunctive Drug Therapy in Percutaneous Interventions

Sunday, March 17, 2002, 3:00 p.m.-5:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1053-1

Early and Sustained Survival Benefit Associated With Statin Therapy at the Time of Percutaneous Coronary Intervention

Albert W. Chan, Deepak L. Bhatt, Derek P. Chew, Martin J. Quinn, David J. Moliterno, Eric J. Topol, Stephen G. Ellis, *The Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: Long-term administration of statin therapy has been shown to reduce major coronary events and cardiac mortality in clinical trials. Beyond lipid lowering, statins favorably affect platelet adhesion, thrombosis, endothelial function, inflammation, and plaque stability, which may potentially improve outcome after PCI. Therefore, we hypothesized that statin therapy has an early beneficial effect in patients undergoing PCI. **Methods:** Each year from 1993 through 1999, we prospectively collected data and followed our first 1,000 patients undergoing PCI. Baseline, procedural, and 6-month data of statin-treated and non-statin-treated patients were compared. Propensity score and multivariate survival analysis were used to adjust for heterogeneity between the 2 groups. **Results:** Of 6,647 patients with completed follow-up, 23.5% were treated with statin at the time of the procedure. Statin therapy was associated with a 60% lower mortality at 30 days (1.0% vs 2.5%, p = 0.0007) and a 37% reduction at 6 months (3.1% vs 4.9%, p = 0.003). After adjusting for the propensity to receive statin therapy prior to the procedure and for other confounders, statin therapy remained an independent predictor for survival at 6 months following PCI (HR 0.66, 95% C.I. 0.46-0.93, p = 0.017). The mortality benefit was independent of peri-procedural MI, recurrent MI, and target vessel revascularization. **Conclusion**: Statin therapy among PCI patients was associated with a significant mortality lowering at early and intermediate term follow-up. The mechanism of survival benefit of statin beyond lipid-lowering needs further elucidation.

1053-2

A Blinded Multicenter Dose Escalation Phase IIa Study of the Factor VIIa/Tissue Factor Inhibitor Recombinant Nematode Anticoagulant Protein c2 in Patients Undergoing Elective Percutaneous Coronary Intervention

Arno H. Moons, N. R. Bijsterveld, H. R. Büller, M. H. Prins, W. E. Rote, G. P. Vlasuk, R. J. Peters, *Academic Medical Center, Amsterdam, The Netherlands, Corvas International, San Diego, California.*

Introduction: A multicenter, randomized, double-blind, placebo controlled, dose escalation study in patients undergoing elective percutaneous coronary intervention (PCI) evaluated the safety of recombinant Nematode Anticoagulant Protein c2 (rNAPc2), a potent inhibitor of the factor VIIa/tissue factor (FVIIa/TF) complex.
Methods: Patients received either placebo or rNAPc2 from one of 4 dose groups as a single SC administration 2-6 hours before PCI, as well as aspirin and IV unfractionated heparin (activated clotting time > 250 sec). The primary endpoints were femoral compression time (FCT) after sheath removal, and incidence of major and minor bleeding. Secondary endpoints included the plasma concentration of prothrombin activation fragment 1+2 (F1+2) over time.
Results:

rNAPc2 (μg/kg)	n	FCT[a] (min)	F1+2 (nmol/L)[b]			Bleeding n(%)	
			8 hr[c]	24 hr[d]	36 hr[d]	Minor	Major
placebo	30	10 (10-27)	1.2 (0.8)	1.1 (0.6)	1.4 (0.9)	2 (7)	0 (0)
3.5	23	10 (10-16)	0.7 (0.3)[II]	0.7 (0.2)[III]	0.9 (0.3)[I]	1 (4)	0 (0)
5.0	24	10 (10-15)	0.8 (0.3)[I]	0.8 (0.3)[II]	1.0 (0.5)	1 (4)	3 (13)
7.5	27	10 (10-70)	0.7 (0.4)[II]	0.7 (0.2)[III]	0.7 (0.2)[II]	3 (11)	1 (4)
10.0	26	16 (10-50)[III]	0.8 (0.7)	0.7 (0.2)[II]	0.7 (0.2)[II]	8 (31)	0 (0)

[a]median (range) [b]mean (SD); [c]after PCI, [d]after rNAPc2;
P-value: rNAPc2 vs placebo: [I]<0.05 [II]<0.01 [III]<0.001

FCT and minor bleeding, but not major bleeding, demonstrated a dose-dependent increase. All three patients that developed major bleeding in the 5.0 μg/kg dose group also received a glycoprotein IIb/IIIa receptor antagonist. rNAPc2, regardless of dose, produced a prolonged, significant suppression of thrombin generation as measured by plasma F1+2 extending over 24 hours after the single SC administration.
Conclusions: These results suggest that FVIIa/TF inhibition with rNAPc2 is a safe and potentially effective strategy for prevention of thrombotic complications in patients undergoing coronary interventions. This study supports further investigation of rNAPc2 in patients suffering from acute coronary syndromes.

1053-3

The REPLACE 1 Trial: A Pilot Study of Bivalirudin Versus Heparin During Percutaneous Coronary Intervention With Stenting and GP IIb/IIIa Blockade

A. Michael Lincoff, John A. Bittl, Neal S. Kleiman, Dean J. Kereiakes, Robert A. Harrington, Ian J. Sarembock, J. Daniel Jackman, Sameer Mehta, Elizabeth F. Maierson, Derek P. Chew, Eric J. Topol, for the REPLACE Investigators, *Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: The direct thrombin inhibitor bivalirudin (previously "Hirulog") has been associated with improved efficacy and less hemorrhage than heparin during balloon angioplasty, but has not yet been widely tested with stenting or GP IIb/IIIa antagonists.
Methods: In a pilot study, 1056 pts undergoing elective or urgent coronary intervention (PCI) at 77 sites in the US were randomized in a central, open-label fashion to receive heparin (60-70 U/kg initial bolus) or bivalirudin (0.75 mg/kg bolus, 1.75 mg/kg-hr infusion during PCI). All pts received aspirin, and pretreatment with clopidogrel was encouraged. GP IIb/IIIa inhibitor use was per operator preference. Endpoints were death, MI, repeat revascularization, or major bleeding by hospital discharge or 48 hours.
Results: Stents were used in 85% of pts; 72% received a GP IIb/IIIa inhibitor. Activated clotting times were significantly higher among pts randomized to bivalirudin than heparin prior to device deployment (371 +/- 102 sec vs. 304 +/- 89 sec, p<0.001) and at procedure end (334 +/- 63 sec vs. 267 +/- 58 sec, p<0.001). Individual endpoints and the "Triple"(death, MI, revasc) and "Quadruple" composites (death, MI, revasc, major bleeding) are detailed in the Table (all p = NS).

	Heparin (n = 524)	Bivalirudin (n = 532)
Death (%)	0.6	0
MI (%)	5.2	4.9
Repeat Revascularization (%)	2.3	1.5
Major Bleeding (%)	2.7	2.1
"Triple" Composite (%)	6.9	5.6
"Quadruple" Composite (%)	8.8	7.1