TCT-498
Relationship between high platelet on clopidogrel treatment reactivity and sleep apnea syndrome in acute coronary syndromes

Zen-ko Nagaishimaa, Kengo Tsukaaharaa, Kazuo Kimuraab, Satoshi Umemurab, aYokohama City Hospital, Yokosuka, Japan, bYokohama City University Medical Center, Yokohama, Kanagawa, cYokohama City University Medical Center, Yokohama, Japan, dYokohama City University Graduate School of Medicine, Yokohama, Japan

Background: Sleep apnea syndrome (SAS) is often observed in patients with acute coronary syndromes (ACS). It is known that SAS is associated with an increased risk of cardiovascular events. However, it remains unknown that relationship between high on-clopidogrel treatment platelet reactivity (HPR) and SAS in patients with ACS undergoing stent implantation.

Methods: Sient implantation was performed in 62 patients with ACS receiving aspirin 100mg/day and clopidogrel 75mg/day. PY212 Reaction Unit (PRU) was determined on admission, 6 days(acute phase) and 18 days(chronic phase) after stenting with VerifyNow PY212 assay. HPR was defined as PRU ≥ 235. Sleep disturbance was evaluated with ApnoNonitoror. SAS was defined as apnea-hypopnea index (AHI) ≥ 15. Patients were divided into 2groups, SAS group (n=26) and non-SAS group (n=36).

Results: There were no significant differences in baseline characteristics between 2 groups. PRU levels were similar at baseline (271.60 vs 275.71, p=0.40). In acute phase, SAS group had a trend of higher PRU level (270.44 vs 243.56, p=0.06). And in chronic phase, SAS group had higher PRU level (249±44 vs 183.52, p=0.002) and the higher frequency of HPR (70% vs 21%, p=0.001).

Conclusions: SAS may be related with HPR in both acute and chronic phase of ACS. These results suggest that assessment of sleep disturbance might be required in patients with ACS receiving clopidogrel.

TCT-499
Comparable outcomes on single use of clopidogrel vs. dual antiplatelet therapy after coronary stenting in patients with acute myocardial infarction

Jun-Hyok Oh, Kwang Soo Cha, Da-sung Lee, Han Cheol Lee, Hye Won Lee, Taek Jong Hong, Donghan Shin, Jung Hyun Choi, aPusan National University Hospital, Busan, Korea, Republic of

Background: Dual antiplatelet therapy (DAP) with aspirin and a thienopyridine following coronary stenting is superior to aspirin alone in reducing cardiovascular events in both the acute coronary syndrome (ACS) and the elective setting. However, there is no consensus that DAP is more effective and safe to clopidogrel alone in secondary prevention. We investigate whether clopidogrel alone vs. DAP leads to an excess of adverse outcomes in acute myocardial infarction (AMI) patients after coronary stenting.

Methods: We studied a consecutive series of 13,348 AMI patients undergoing successful coronary stenting and evaluated data from patients were discharged on clopidogrel alone (n=85, 0.6%) and DAP (n=13,263, 99.4%) from Korea acute myocardial infarction registry. To eliminate biased estimates, a propensity score was used and two cohorts of 1.5 nearest neighbor matched patients were obtained.

Results: Propensity matching identified two cohorts of 85 patients on clopidogrel alone and 425 patients on DAP at a median follow-up period of 11.8 months, there was no difference in all-cause death (3.1 vs. 3.5%, p=0.82), cardiovascular death (2.1 vs. 2.4%, p=0.892) myocardial infarction (MI) (1.6 vs. 1.2%, p=0.75), revascularization (6.6% vs. 6.2%, p=0.833) and cumulative major adverse cardiovascular events (MACE) (11.3 vs. 12.9%, p=0.665). Patients with clopidogrel alone compared with DAP were not associated with increased all-cause death (HR 1.11, 95% CI 0.314-3.93, p=0.871), MI (HR 0.38, 95% CI 0.17-11.2, p=0.763), revascularization (HR 0.808, 95% CI 0.353-1.851, p=0.615) and MACE (HR 1.129, 95% CI 0.585-2.178, p=0.717) during follow up.

Conclusions: In this observation study, clopidogrel alone therapy after coronary stenting did not increase the mortality and MACE compared with DAP therapy. However, larger trials are needed to support these observations.

TCT-500
Prasugrel Is A More Potent Platelet Inhibitor Than Clopidogrel In Bivalirudin-Treated Patients. Comparative Effects of Two Thienopyridines On ADP And Thrombin Receptor Antagonism As Assessed By Aggregometry

Carey D. Kimmelstiel, a, Athan Kaloupolous, b Vilma Castaneda, c Ryan Stevenson, d Andrew Weintraub, e, Navin K. Kapoor, f 1Tufts Medical Center, Boston, United States, 2Tufts Medical Center, Boston, MA, 3Tufts University, Boston, Massachusetts

Background: Early stent thrombosis has been noted with increased frequency in acute coronary syndrome patients undergoing coronary intervention when treated with bivalirudin and clopidogrel. We hypothesized that treatment with the more potent thienopyridine prasugrel would lead to significantly greater inhibition of platelet aggregation (PA) than clopidogrel following termination of bivalirudin treatment.

Methods: 24 patients referred for intervention with planned bivalirudin therapy, not previously treated with a PY212 inhibitor and not receiving heparins or GP IIb/IIIa inhibitors were randomized to treatment with either clopidogrel (600 mg) or prasugrel (60 mg). PA was measured by light transmission aggregometry (LTA) of platelet-rich plasma in response to PY212 and PAR1 and PAR4 thrombin receptor agonists at baseline and at 1, 2, 4 and 16 h following the cessation of bivalirudin infusion. Platelet response to agonists: 20 μM ADP, 5 μM SFFLRN, and 160 μM AYPGKF (PY212, PAR1 and PAR4 receptors respectively) was performed. The magnitude of inhibition of PA for each agonist was calculated as the mean final change from baseline in LTA at each time point.

Results: As compared to clopidogrel, prasugrel led to significantly earlier and more potent inhibition of PA following the discontinuation of bivalirudin. Prasugrel-mediated inhibition of PA was significantly greater than that of clopidogrel at all time points for ADP as well as PAR1 and PAR4 peptide agonists (Table).

TCT-501
Dual Antiplatelet Therapy Interruption For Surgery: Insights From The PARIS (Patterns Of Non-adherence To Anti-Platelet Regiments In Stented Patients) Registry

Mikkel Schoos, a Aarti Bhasin, b Samantha Sartori, c Melissa Aquino, d Jennifer Yu, e Timothy D. Henry, f David Cohen, g David J. Moliterno, h Cono Ar trio, i Rosana Melman, j 1Mount Sinai Medical Center, New York, NY, USA, Copenhagen, Denmark, 2Mount Sinai Medical Center, New York, NY, USA, New York, NY, 3Mount Sinai School of Medicine, New York, NY, 4The Icahn of Medicine at Mount Sinai, New York, NY, 5Mount Sinai Medical Center, New York, NY, 6Cedars-Sinai Medical Center, Minneapolis, United States, 7Saint Luke’s Mid America Heart Institute, Kansas City, United States, 8University of Kentucky, Lexington, United States, 9London school of hygiene and tropical medicine, london, United Kingdom, 10Mount Sinai Hospital, New York, United States

Background: Surgery is a frequent cause of dual antiplatelet therapy (DAPT) interruption. From patients following percutaneous coronary intervention (PCI). However, the specific types of surgery leading to interrupting DAPT have not been described. Methods: PARIS is a multinational registry of 5018 patients prescribed DAPT following successful PCI. Pre-specified categories of DAPT cessation were physician recommended discontinuation, brief interruption (< 14 days) for a surgical procedure of discontinuation due to bleeding or noncompliance. We examined the patterns and types of procedures leading to DAPT interruption.

Results: Over 2 years there were 594 DAPT interruptions involving 491 (9.8%) patients, with 42% occurring within 1 year. Among known recommenders (57.1%), non-cardiologists (primary care physicians, surgeons, clinical practitioners) frequently recommended interruption. Among cases where the specific type of surgery was reported (69.7%), minor procedures comprised the majority (68.4%), compared to major surgery (31.6%) (figure). Interruption of only one antiplatelet was more common (57.2%) (clopidogrel (32.3%), aspirin (24.9%), with similar patterns seen for minor and major surgery. Crude rates of cardiac death, MI or ST from interruption to follow-up were higher after major surgery (7.6% vs 2% P< 0.001) but did not differ significantly when correcting for disruption (4.2% vs 2% P=0.08).

JACC Vol 64/11/Suppl B | September 13–17, 2014 | TCT Abstracts/Pharmacotherapy - Aspirin, Thienopyridines and other Platelet Inhibitors B147
Conclusions: One in 25 patients underwent surgery in the first year after PCI requiring DAPT interruption, frequently recommended by non-cardiologists and most commonly due to minor surgery.

TCT-502
Efficacy and safety of switching from clopidogrel to prasugrel in diabetic patients with acute coronary syndromes treated with drug-eluting stents: results of the ESCAPADA study

Armando Pérez de Prada1, Bilen Çiçek2, Pilar Carrillo Saez2, Alejandro Diego2, Carlos Cuellas2, Diego Lopez-Otero2, Alberto Cordero1, María López-Benito1, Raymundo Ocaranza-Sanchez2, Tania Rodriguez-Gabella4, Araceli Frutos3, Carlos Cuellas1, Diego Lopez-Otero2, Alberto Cordero1, María López-Benito1, Rodrigo Estevez-Loureiro4, Soraya Merchan Gomez4, Ramon Lopez Palop3, Felipe Fernández-Vázquez4

1Hospital Universitario de Salamanca, Salamanca, Spain, 2Hospital Universitario de Canarias, Las Palmas de Gran Canaria, Spain, 3Hospital Universitario de Canarias, Las Palmas de Gran Canaria, Spain, 4Hospital Universitario de Canarias, Las Palmas de Gran Canaria, Spain

Background: Prasugrel demonstrated superior efficacy in the reduction of events of acute coronary syndrome (ACS), clopidogrel-naïve, patients treated with percutaneous coronary intervention (PCI), especially in the diabetic (DM) subgroup. The objective of this study is to assess the efficacy and safety of switching from dual antiplatelet treatment with clopidogrel to prasugrel in ACS DM patients being treated with everolimus-eluting stents.

Methods: Prospective, observational study conducted in 4 different centers. Patients were included if they met the ADA criteria for established or increased risk for DM. Platelet reactivity was measured before PCI and 1 month after with 2 different analyzers (VerifyNow P2Y12 test and Multiplate ADP-HS test); high on-treatment platelet reactivity (HTPR) was defined as according to PLATO definition. The aim of this analysis is to evaluate the bleeding risks of new oral antiplatelet agents

Results: Ninety-six patients were included: 63±8 years mean age, 77% male, 72% hypertensive, 66% hyperlipidemic, 32% smokers (plus 23% ex-smokers), 80% ACS with positive biomarkers, 38% multivessel disease. Only 16% of patients received insulin. 15% of patients were diagnosed with diabetes and 21% with increased risk for DM in the index admission. 10% of patients were previously treated with prasugrel and 5% were changed back to clopidogrel by their treating physicians. Before the PCI, 71 patients (74%) showed HTPR (67% met the VerifyNow criteria, 37% according to Multiplate results). At 1 month only 14% of patients showed HTPR, 3 of the 4 patients on clopidogrel treatment (75%) still showed HTPR. After 1 month follow-up only 5 bleeding events were recorded: one caused by coronary perforation after PCI, one significant groin hematoma, 3 minor bleedings (epistaxis, skin hematoma), without need of subsequent changes in treatment.

Conclusions: Switching from clopidogrel to prasugrel after stent treatment in ACS diabetic patients is associated with a significant reduction in platelet reactivity without a relevant increase in bleeding complications.

TCT-503
Prevalence of CYP2C19 Variants and Associated Stent Thrombosis in Patients Undergoing Percutaneous Coronary Intervention

Janarthanan Sathananthan1, Sefi El-Jack1, Ali Khan1, Gay Armstrong1, Jonathan Christiansen1, Tony Scott1, Mehran Zareian1, Kevin Smith1, Lifeng Zhou1, Patrick Gladding1

1Department of Cardiology, North Shore Hospital, Waitakere District Health Board, Auckland, New Zealand, 2Department of Cardiology, North Shore Hospital, Waitakere District Health Board, Auckland, New Zealand

Background: CYP2C19 gene polymorphisms affect clopidogrel metabolism resulting in variability in response. We sought to assess the frequency of CYP2C19 variants and association of stent thrombosis (ST) in a series of individuals undergoing percutaneous coronary intervention (PCI).

Methods: A case-control study of 10 patients with stent thrombosis and 38 patients were routinely tested for CYP2C19 gene variants using the Verigene (Nanosphere Inc, Illinois) and iPlex assays (Sequenom Inc, San Diego). Patients were genotyped for three single-nucleotide polymorphisms of the CYP2C19 alleles (*2, *3, *17).

Results: Of 48 patients undergoing gene testing 31(65%), 95%CI:49%, 78% carried a loss-of-function (LOF) CYP2C19 allele. Call rate and concordance was 100% between the two assays. PCI was performed for acute coronary syndrome in 73% of patients. In patients with a variant allele, 17(35%) were *2, 11 (35%) were *3, and 1(10%) were both *2 and *17. No patient had the CYP2C19*3 variant. LOF alleles were present in 80% of patients with ST compared to 61% in patients without ST (OR=2.6, 95%CI: 0.5,14). Five patients with a LOF allele, had either a clopidogrel dose increase or were changed to prasugrel, with no in-stent thrombosis in these patients.

Conclusions: Carriage of a LOF CYP2C19 allele is associated with a higher odds ratio of in-stent thrombosis in patients on standard dose clopidogrel, highlighting the need for routine gene testing. Patients with a LOF allele should have alteration of P2Y12 inhibitor therapy with either a higher dose of clopidogrel or a switch to prasugrel or ticagrelor.

TCT-504
Bleeding risk in Acute Coronary Syndrome submitted to PCI with new oral antiplatelet agents

Gerardo Nau1, Pablo Lameiras2, Gustavo O. Pedernera1, Pablo Spalletri1, Lucio T. Padilla2, Alfonso Cardiello3, Jorge Belardi4, Fernando Curat3

1Instituto Cardiovascular de Buenos Aires, Buenos Aires, Buenos Aires, 2ICBA, Buenos Aires, Argentina, 3ICBA, BsAs, BsAs, 4ICBA, Bs As, Bs As, 5ICBA, Buenos Aires, Buenos Aires, 6Instituto Cardiovascular de Buenos Aires, Buenos Aires, Argentina

Background: The aim of this analysis is to evaluate the bleeding risks of new oral antiplatelet agents in real life.

Methods: All patients with ACS who underwent PCI during admission from September 2011 to December 2013 were included. Baseline characteristics and follow up were collected prospectively. Bleeding risk was stratified according to PLATO definition.

Results: 869 patients were included with a mean age of 62.7 (SD 10.8). Most were male (81%). Clinical admission: 46% were NSTEMI, 29.3% STEMI and 30.7% unstable angina. Median TIMI score was 3 pts, median GRACE score 124 pts and median CRUSADE 25.7 pts. Clopidogrel was received 54.5%, prasugrel 32.7% and ticagrelor 12.8%. CRUSADE score was lower in the prasugrel group (< 0.001), and ticagrelor (p=0.04) compared with clopidogrel. After a median follow up of 271 days, 92 (11.6%) bleeding events were detected: 6.6% minor bleeding, 4% major bleeding and 1.6% life threatening bleeding. On multivariate analysis STEMI (HR 2.25; CI95% 1.35-3.75; p=0.002), prasugrel (HR 2.31; CI95% 1.43-1.72; p=0.001), age (HR 1.036; CI95% 1.010-1.063; p=0.006) and reduced creatinine clearance (HR 1.74; CI95% 1.03-2.85; p=0.037) predicted bleeding events. After analyzing only major and life threatening events, prasugrel was not significantly associated with major bleeding events (HR 1.84; CI95% 0.89-3.80; p=0.097).

B148 JACC Vol 64/11/Suppl B | September 13–17, 2014 | TCT Abstracts/Pharmacotherapy - Aspirin, Thienopyridines and other Platelet Inhibitors