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TCT-205

High and low platelet reactivity on clopidogrel, prasugrel and ticagrelor in acute coronary syndrome patients: insight from a real-life large cohort

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BACKGROUND Dual antiplatelet therapy with a P2Y12 inhibitor is mandatory in acute coronary syndromes (ACS) undergoing angioplasty. New antiplatelet drugs prasugrel and ticagrelor offer more efficient inhibition compared to clopidogrel. Under P2Y12 inhibitor, platelet reactivity (PR) assessment can predict ischemic and bleeding events. The aim of our study was to compare PR in ACS patients on P2Y12 inhibitors in a real-world setting.

METHODS Platelet reactivity (PR) was prospectively assessed in consecutive patients with recurrent ACS or undergoing high-risk angioplasty. PR was measured 24hrs after last intake of clopidogrel (C) and prasugrel (P), and 12hrs for ticagrelor (T) by flow cytometry measured vasodilatator-stimulated phosphoprotein platelet reactivity index (VASP-PRI) and light transmission agregometry with ADP 20μM (LTA-ADP). High Platelet Reactivity (HPR) was defined as VASP-PRI>50% or LTA-ADP>65% (thresholds previously linked to clinical events). Low Platelet Reactivity (LPR) was defined as VASP-PRI<16% or LTA-ADP<40%.

RESULTS Six hundred and nineteen patients treated with aspirin and C (n=269), P (n=241) or T (n=109) were included from 01/2011 to 07/2013. Mean age was 62±13yrs., 80% were men and 63% had STEMI. Patients on C were older, more often women and admitted for NSTEMI. Inflammatory parameters were lower in this subgroup (C). Clinical and biological characteristics were similar between patients on P and those on T. HPR was more frequent with C compared to P and T and significantly more frequent with P compared to T (Table 1). At the opposite, LPR was significantly more frequent in patients treated with T. In multivariate analysis, the significant predictor of HPR with VASP was P (OR=0.13-CI[0.08-0.22]) or T (OR=0.01-[0.01-0.09]). The significant predictor of LPR with VASP was T (OR=3.37-[2.09-5.44]).

Table 1. Platelet reactivity assessment according to P2Y12 inhibitors and platelet function tests.

	HPR		LPR	
	VASP-PRI	LTA-ADP	VASP-PRI	LTA-ADP
Clopidogrel	48%	37%	7%	14%
Prasugrel	12%*	15%*	27%*	44%*
Ticagrelor	1%*§	2%*§	55%*§	72%*§

*p<0.05 vs clopidogrel; §p<0.05 vs prasugrel.

CONCLUSIONS This observational biological study confirms a more potent platelet inhibition of the new P2Y12 compared to clopidogrel, mainly ticagrelor. The very high rate of LPR found with ticagrelor does not match with the bleeding risk found in the PLATO trial.

CATEGORIES CORONARY: Pharmacology/Pharmacotherapy

KEYWORDS Acute coronary syndromes, Platelet aggregation, Platelet function testing

TCT-206

Effect of the α2A-Adrenergic Receptor Genetic Variants on Platelet Reactivity and Adverse Clinical Events in Chinese Patients with Dual Antiplatelet Therapy after Percutaneous Coronary Intervention

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BACKGROUND Platelet α2A-Adrenergic Receptor(ARs) potentiates epinephrine-induced platelet aggregation in response to sympathetic stimulation. Genetic variants of the α2A -ARs are associated with different antiplatelet reactivity. The effect of genetic variants of the α2A -ARs on platelet reactivity and clinical outcomes has not yet been reported in Chinese patients with dual antiplatelet therapy after percutaneous coronary intervention. The aim of this study was to investigate the effect of the α2A -ARs variants on platelet reactivity and clinical outcomes in these patients.

METHODS 1056 patients with dual antiplatelet therapy after percutaneous coronary intervention were enrolled in a single-center registry. All known α2A -ARs genetic variants including rs11195419, rs3750625, rs13306146, rs553668 were detected by the ligase detection reaction and the antiplatelet effect was assessed by thromboelastography. Primary clinical endpoints included cardiovascular death, nonfatal myocardial infarction, target vessel revascularization, and stent thrombosis. The secondary clinical endpoints were angina recurrence, readmission and in-stent restenosis. The follow-up periods were 6 months and 12 months.

RESULTS The frequencies of the α2A -ARs variants were respectively 18.09%, 17.17%, 25.43%, 43.71%. Genotypic distributions of all the variants were in conformity with Hardy-Weinberg equilibrium except rs13306146. Platelet ADP inhibition were significantly different among wild type, heterozygote and homozygote mutated groups carrying rs11195419 genetic variant (53.86±29.78% vs. 50.72±27.80% vs. 39.28±19.53%, P=0.012) or rs3750625 genetic variant (53.71±29.84% vs. 50.93±27.55% vs. 37.524±18.60%, P=0.007) and the homozygote mutated groups have the lowest ADP inhibition of the three groups variants. However, there were no significant differences in ADP inhibition among the rs553668 genotype groups (50.20±27.83% vs. 54.09±29.41% vs. 52.11±30.00%, P=0.158). At the multivariable analysis, the presence of the rs11195419 (95%CI: -0.062- -2.070, P=0.039) or rs3750625 (95%CI: -0.068- -2.281, P=0.023) genetic variants was an independent predictor of the ADP inhibition. However, there were no significant differences in the composite clinical outcome across the rs11195419, rs3750625, rs553668 genotype groups at both 6 and 12 months follow-up period(P>0.05).

CONCLUSIONS The presence of mutated alleles of α2A -AR genetic variants (rs11195419, rs3750625) except rs553668 is associated with decreased ADP-induced platelet reactivity in Chinese patients with DAPT after percutaneous coronary intervention. However, none of the α2A -AR genetic variants significantly influenced the clinical outcomes of DAPT in these patients.

CATEGORIES OTHER: Genomics / Proteomics

TCT-207

Comparative efficacy & safety of Prasugrel, Ticagrelor, standard & high dose Clopidogrel in patients undergoing percutaneous coronary intervention (PCI): A network meta-analysis

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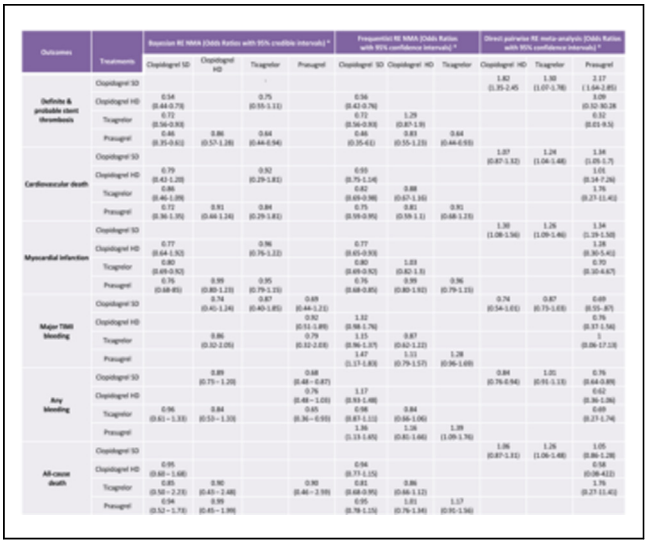
BACKGROUND Higher loading and maintenance dose Clopidogrel overcomes delayed and often variable effect of standard dose Clopidogrel in majority of the patients. However, data comparing this strategy with potent alternatives such as Ticagrelor & Prasugrel are scarce.

METHODS We aimed to compare efficacy & safety of Prasugrel, Ticagrelor, standard & high dose Clopidogrel in patients undergoing PCI. PubMed, EMBASE, CENTRAL and clinicaltrials.gov were searched for studies comparing Prasugrel, Ticagrelor, standard dose (SD) & high dose (HD) Clopidogrel in patients undergoing PCI. Frequentist and Bayesian random effect network meta-analyses were performed besides random effect direct pairwise comparisons. Statistical analysis was conducted using WinBugs and Stata software. Ranking of treatments are based on surface under cumulative ranking curves (SUCRA) derived from Bayesian analysis. SUCRA values provide chances of being best drug in form of percentage (%).

RESULTS Thirty trials, with 34, 563 person years of follow up data after PCI, were included in the analysis. Prasugrel (86%) emerged as best drug to prevent definite or probable stent thrombosis, followed by Clopidogrel HD (66%) and Ticagrelor (44%), with Clopidogrel SD being the worst. Myocardial infarction was least likely to be prevented by Clopidogrel SD (0%) after PCI, and rest three were superior to it (Prasugrel 74%; Clopidogrel 70%; Ticagrelor 56%). Clopidogrel SD (18%) was least effective in preventing cardiovascular deaths after PCI. Prasugrel (73%) was likely most effective in preventing cardiovascular deaths followed by Ticagrelor (62%) and Clopidogrel HD (47%). Ticagrelor (68%) reduced all-cause mortality by a small margin compared to rest of treatments (Prasugrel 50%; Clopidogrel 48%; Clopidogrel 34%). Clopidogrel SD (79%), followed by Clopidogrel HD (53%) and Ticagrelor (48%), resulted in significantly lower TIMI major bleeding complications compared to Prasugrel. Analysis of any bleeding revealed similar trend. Clopidogrel HD performed better than Prasugrel in terms of bleeding complications. Results of direct pairwise comparison and network meta-analysis were consistent in the direct of overall effect (Figure).



CONCLUSIONS Prasugrel is most effective drug to prevent post PCI ischemic events but at the expense of higher bleeding. Ticagrelor followed by Clopidogrel HD appears to strike the right balance between efficacy & safety.

CATEGORIES CORONARY: Pharmacology/Pharmacotherapy

KEYWORDS Antiplatelet therapy, Percutaneous coronary intervention

TCT-208

Comparison Of Antithrombotic Regimens For Primary Angioplasty In Patients > 75 Years With ST Elevated Myocardial Infarction: The ESTROFA-MI+75 Study

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BACKGROUND Primary angioplasty is the best reperfusion treatment in ST elevated myocardial infarction. The number of elderly patients (> 75 years) undergoing primary angioplasty is progressively increasing as population is ageing. The optimal antithrombotic therapy during the procedure (bivalirudin vs. unfractioned heparin with or without abciximab) is not defined for this important subgroup of patients.

METHODS Retrospective consecutive registry conducted in 31 centers of patients > 75 years with ST elevation myocardial infarction undergoing primary angioplasty.

RESULTS A total of 3,126 pts have been included, 2,029 (64.9%) treated only with UFH, 750 (24%) with UFH+abciximab, 319 (10.2%) with bivalirudin only and 28 (0.9%) with bivalirudin+abciximab. Three groups were defined: BIV (319), UFH (2.029) and UFH-A (750) with mean ages 81.2±5, 81.6 ±4.7 and 79.6 ±4.3 years respectively (p<0.001).. Outcomes at 12 months were the following: survival free of cardiac death and MI was 85.6%, 80% and 83.4% (p=0.01) in BIV, UFH and UFH-A groups and TLR was 2.7%, 3% and 1.4% (p=0.1) respectively. Incidences of definite or probable stent thrombosis were 2.8%, 2.5% and 2.3% (p=0.2) and incidences of bleeding BARC > 2 were 0.8%, 1.3% and 1.5% (p=0.1) respectively.

CONCLUSIONS The most common antithrombotic treatment in primary angioplasty of the very elderly is based on UFH (89%) with the use of abciximab in a 24% of cases. The use of bivalirudin was associated with the lowest incidence of cardiac death and MI with no increase in stent thrombosis. The rate of severe bleeding (BARC >2) was comparable.

CATEGORIES CORONARY: Pharmacology/Pharmacotherapy

KEYWORDS Acute myocardial infarction, Antithrombotic therapy, Elderly

TCT-209

Safety and efficacy of policosanol in patients with high on-treatment platelet reactivity after drug-eluting stent implantation

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BACKGROUND Some patients have high residual platelet reactivity on clopidogrel after coronary intervention and risk of thbombotic events is high. The aim of the study was to investigate safety and efficacy of policosanol in patients with high on-treatment platelet reactivity after drug-eluting stent implantation.