platelets. Therefore, we postulate that the phosphorylation state of its substrate acetyl-coA carboxylase (ACC) could be considered as a valuable marker of the thrombin response in platelets from patients undergoing major surgery.
Methods: Twenty-nine consecutive patients scheduled for elective cardiac surgery with cardio-pulmonary bypass (CPB) were recruited in the department of cardiovascular surgery. The human platelets were isolated from citrated blood samples drawn during CPB (under high-dose UFH) and 4 hours after surgery. ACC phosphorylation was assessed by immunoblotting. Activated clotting time (ACT), thrombin time (TT) and activated partial thromboplastin time (aPPT) were measured in a coagulation device. In addition, an estimation of how each patient can generate thrombin during all steps of the protocol has been done, using a fluorogenic assay for the measurement of endogenous thrombin potential (ETP).
Results: Under CPB, mean ACT was 594±100 s, and aPTT and TT were over 180 s and 120 s, respectively. Normal capacity to coagulate was restored 4 hours after surgery (aPTT: 36.3±7.4 s; TT: 21.3±5.2 s). ETP values were characterized by a huge heterogeneity in post-operative status, reflecting the random ability of patients to generate thrombin after CBP. ACC phosphorylation was therefore evaluated in 2 extreme groups of patients, recovering more than 80% and less than 20%- of basal ETP, respectively. ACC phosphorylation was significantly higher in the platelets of patients preserving an intact ability to generate thrombin (ETP>80%).
Conclusion: ACC phosphorylation in platelets reflects (i) their activation by thrombin after major surgery and more importantly (ii) an intact ability to generate thrombin in this situation.

P4895 | BENCH
Acute effects of clopidogrel are predicted by integrity of prostacyclin signalling

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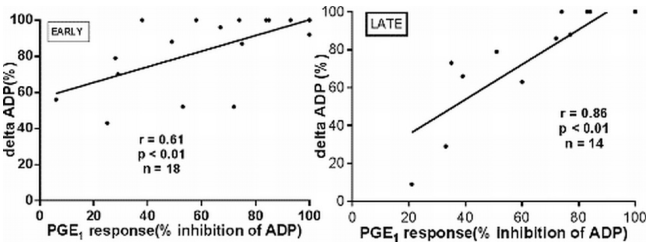
Purpose: Clopidogrel resistance (CR) is partially dependent on CYP2C19 genotype, but this does not completely explain CR in myocardial ischemia and diabetes: hence effects on intracellular signalling may be involved. Since clopidogrel limits ADP-induced inhibition of prostacyclin (PGI2)/cAMP signaling and its effects on vasodilator-stimulated phosphoprotein phosphorylation (VASP-P), this pathway is a potential site of CR. We therefore investigated the relationship between pre-clopidogrel platelet sensitivity to the PGI2 mimetic PGE1 (as an adenylate cyclase activator); changes in ADP induced aggregation and VASP-P before and after clopidogrel.
Methods: In two cohorts of patients with stable or unstable angina, platelet responses to PGE1 were determined via inhibition of ADP induced aggregation in whole blood before clopidogrel was given. Patients with CYP2C19 genotype defects were excluded. Clopidogrel effect (δ ADP [change between pre and post ADP (5μM) induced aggregation] and δ VASP-P) were measured either at 4 hours after 600mg loading dose of clopidogrel to evaluate early responses, or at 7 days post clopidogrel (late response).
Results: The relationship between pre-treatment PGE1 (30nM) response and parameters of clopidogrel effect (δ ADP) both early and late (early r = 0.61, p < 0.01 and late r = 0.86, p < 0.01) is shown in the Figure. The comparable data for δ VASP-P did not reach statistical significance (r = 0.5, p = 0.07)



Conclusion: 1.In the absence of loss-of-function CYP2C19 mutations, preclopidogrel response to PGE1 predicts both early (4 hours) and late (7 days) response to clopidogrel. 2. However early and late changes in δ VASP-P do not follow this relationship. 3. These data emphasise the importance of integrity of PGI2 signalling as a determinant of clopidogrel effect.

P4896 | BEDSIDE
Enhanced platelet reactivity in pediatric depression: an observational study

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Depression is associated with poor prognosis for Cardiovascular Disease (CVD) including mortality. Among multiple mechanisms linking depression and CVD, changes in platelet reactivity are known to be one of the major confounders of such adverse association. However, there are very limited data in children. Thus, we evaluated some conventional hemostatic indices including whole blood platelet aggregation in patients with documented pediatric depression and compared these data with those obtained from healthy children. The pediatric patients fulfilled criteria for major depression with a minimum score of 19 on the 21-item Beck Depression Inventory Scale. Plasma fibrinogen, D-dimer, platelet count, mean platelet volume, and platelet aggregation induced by Adenosine Diphosphate (ADP) and collagen were measured in 67 pediatric patients with depression and matched by age and sex with 78 healthy controls. As expected, the depressed children had significantly higher BECK scales (p=0.001) compared to the normal subjects. Platelet aggregation induced by ADP and collagen (p=0.0001 for both) was significantly higher in depressed children. BECK scale scores correlated significantly with platelet aggregation induced by ADP (r = 0.3, p=0.001) and collagen (r =0.4, p=0.01). In contrast, platelet counts, fibrinogen, D-dimer, mean platelet volume and antithrombin- III levels were almost identical between both groups. Children with depression exhibit mostly intact hemostatic parameters, with the exception of significantly higher platelet activity when compared with healthy controls. These data match well with prior evidence from depressed adults supporting the hypothesis that platelets participate in the pathogenesis of depression. However, beyond pure assessment of platelet activity, other elements including serotonin content, and cell receptor changes in pediatric depression should be elucidated before randomized trial(s) can be justified.

P4897 | BEDSIDE
Long-term outcomes in patients with early, late and very late stent thrombosis after bare metal stenting

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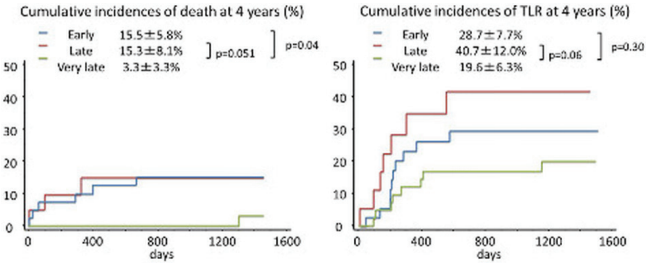
Purpose: We previously reported that very late stent thrombosis (VLST) occurred with progressive neoatherosclerotic changes within the stents, even after the bare metal stent (BMS) implantation. The main purpose of this study was to clarify the impact of timing of the stent thrombosis on the long-term outcomes.
Methods: From September 2002 to September 2010, a total of 102 definite BMS ST according to the Academic Research Council definition were screened in this study. There were 40 patients with early ST (EST, within 30 days), 20 patients with late ST (LST, between 31–365 days), and 42 patients with very late ST (VLST, >1 year). At the time of stent thrombosis, 2 patients underwent emergency coronary artery bypass grafting, 48 patients underwent balloon dilation only, 70 patients underwent additional stent implantation, and one patient underwent thrombolysis. The endpoints of this study were death and target lesion revascularization (TLR).
Results: Median follow-up duration was 1203 days. There were 10 deaths (7 of which were cardiac) and 25 TLR. The cumulative incidences of death at 4 year were significantly lower in patients with VLST (3.3±3.3%) as compared with those with EST (15.5±5.8%, p=0.04) and tended to be lower as compared with those with LST (15.3±8.1%, p=0.051). The cumulative incidences of TLR tended to be lower in patients with VLST than those with LST (19.6±6.3% versus 40.7±12.0%, p=0.06), while there was no significant difference between patients with VLST and EST (28.7±7.7%, p=0.29).



Cumulative incidence of Death and TLR

Conclusion: Patients with EST were associated with higher mortality as compared with those with VLST, while the cumulative incidence of death tended to be higher in patients with LST as compared with VLST.

P4898 | BEDSIDE
Onset of antiplatelet effect of prasugrel and ticagrelor is delayed in patients with acute coronary syndromes

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Introduction: A more rapid onset of antiplatelet effect following loading with prasugrel and ticagrelor compared to clopidogrel was demonstrated for healthy subjects and patients with stable coronary artery disease. These results have endorsed the clinical practice of delaying administration of P2Y12 antagonists until completion of angiography even in patients presenting with acute coronary syndrome (ACS). However, pharmacodynamic data supporting this procedure in patients with ACS are lacking.