Clopidogrel Response Stability over Time in Patients after an Acute Myocardial Infarction

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Background: High on-treatment platelet reactivity (HTPR) despite clopidogrel therapy is associated with adverse cardiac events after acute myocardial infarctions (AMI). Most studies to date assessed clopidogrel response at a single time point before or after percutaneous coronary intervention (PCI). It is unclear, however, whether the HTPR phenotype is stable over time after an AMI. Accordingly, we aimed to examine response to clopidogrel in patients with AMI treaed with primary PCI over a 6 month period.

Methods: Patients with AMI treated with primary PCI were assessed for response to clopidogrel at 3 time points: in-hospital, 30-days and 6-months after the index hospitalization. Response to clopidogrel was determined by the VerifyNow P2Y12 assay (reported as P2Y12 response units, PRU) and multiple electrode aggregometry (MEA ADP test, reported as aggregation units, AU). HTPR was defined as PRU≥235 or AU≥47, respectively.

Results: Fifty-seven patients were recruited. The mean age was 54.5±10.9 years, 91% were male, 19% had diabetes and 74% were admitted with ST-elevation MI. HTPR based on MEA was observed in 22.8% of patients in-hospital, 26.8% at 30-days and 18.0% at 6-months (P=NS). HTPR based on the VerifyNow assay was observed in 37.9% of patients in-hospital, 28.0% at 30-days and 33.3% at 6-months (P=NS). Mean MEA and VerifyNow results were relatively stable over time, except for a decrease in MEA values between 30 days and 6 months (in-hospital: 31.6 ±2.2 AU, 30 days: 32.8±2.7 AU, 6 months: 27.5±2.3 AU, P=NS for the first 2 time points, P=0.004 for 30 days vs. 6 months). The individual HTPR phenotypic assignment at baseline was stable in 71.9% (based on MEA) and 78.9% (based on VerifyNow) of patients at 6 month follow-up.

Conclusions: The rates of HTPR to clopidogrel therapy appear to be relatively stable up to 6 months after an AMI.

Dynamic Response to Aspirin in Patients with ACS, Clinical and Prognostic Implications

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Background: Increased platelet reactivity and reduced response to anti-platelet drugs may result in recurrent ischemic events after acute coronary syndrome (ACS).
Aim: To evaluate the laboratory response to aspirin in patients with ACS before and after percutaneous coronary intervention (PCI) and assess its effect on major adverse clinical events.
Methods and Results: Sixty three consecutive patients with ACS were tested for the response to aspirin by light transmittance aggregometry (LTA) and the IMPACT-R test (both with arachidonic acid- AA) before and 2-4 days after PCI and clopidogrel loading. Patients were followed for clinical events up to 15 month from PCI. Response to aspirin improved significantly after PCI and clopidogrel treatment: mean AA-induced LTA decreased from $34.9\pm3.35\%$ before PCI to $15.2\pm2.2\%$, and surface coverage increased from $2.2\pm0.27\%$ to $6.2\pm 0.6\%$ ($p<0.0001$ for both methods). The improved response to aspirin after PCI correlated with the response to clopidogrel (LTA and IMPACT-R, $p<0.01$). Patients with good laboratory response to aspirin before but not after PCI had significantly lower major cardiovascular event rate during 15 months follow up, in multivariate analysis.
Conclusion: The laboratory response to aspirin is highly dynamic in patients with ACS. The improved response to aspirin following PCI may result from stabilization of coronary artery disease and/or clopidogrel treatment. The laboratory response to aspirin before PCI and clopidogrel loading is a sensitive marker for platelet reactivity that correlates with clinical outcome in patients with ACS.

Transient Atrial Fibrillation in Acute Myocardial Infarction: Implications for Future Risk of Stroke

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Background: Atrial fibrillation (AF) is a frequent complication of acute myocardial infarction (AMI). In the AMI setting, transient AF is frequently attributed to acute hemodynamic changes, inflammation or ischemia. Oral anticoagulation (OAC) is generally recommended for post-AMI patients with previously known AF, or AF at hospital discharge. However, it remains uncertain whether transient AF episodes are associated with a subsequent increased risk of ischemic stroke.
Methods: We studied the impact of transient new-onset AF on the 1-year risk of ischemic stroke and recurrent AF episodes in 2484 consecutive patients with AMI (mean [SD] age, 64 ± 10 years; 74% men). Patients with previous AF or AF at hospital discharge were excluded.
Results: Transient AF was observed in 227 patients (9.1%) during their initial hospitalization for AMI. At hospital discharge, all patients were in sinus rhythm and had been prescribed single or dual-antiplatelet therapy (n=172; 75.8%) or oral anticoagulation (OAC) with or without antiplatelet agents (n=55; 24.2%). At 1-year follow-up, the incidence of ischemic stroke was higher in patients with transient AF than in those without transient AF (7.9% vs. 3.0%, respectively; $p < 0.001$), with higher stroke rates in patients receiving antiplatelet agents alone (Figure). Cox regression analysis demonstrated that the adjusted hazard ratio for ischemic stroke at 1-year was 1.9 (95% CI 1.1 to 3.2; $p = 0.03$). In addition, the incidence of recurrent AF was higher (20.7% vs. 1.3%, respectively; $p < 0.001$).
Conclusion: Most patients with AMI-related transient AF are discharged without OAC therapy. Transient AF complicating AMI is associated with an increased future risk of ischemic stroke in patients treated with antiplatelet agents alone. High AF recurrence rates in these patients also suggest that OAC should be considered.

Microvascular Obstruction Assessed by Cardiac MRI in Patients with STEMI Undergoing Primary PCI

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Background: Microvascular obstruction (MVO) occurring following percutaneous coronary interventions (PCI) may lead to myocardial injury, and is an independent predictor of adverse outcome in patients presenting with ST segment elevation MI (STEMI). Cardiac magnetic resonance (CMR) became the gold standard for assessment of microvascular obstruction (MVO). Recently CMR is being performed as part of the routine evaluation of STEMI patients undergoing angiographically successful (TIMI III) primary PCI (PPCI) in Sheba Medical Center. CMR was evaluated for the amount of delayed enhancement (DE) and MVO.
Methods: Gadolinium-enhanced CMR examination was performed in 26 consecutive patients undergoing PPCI for STEMI. CMR was performed 4 ± 1 days post PPCI, and evaluated using dedicated software for DE and MVO quantification.
Results: Ten patients had MVO > 2% (mean $6\pm3\%$) of LV mass (MVO group) and 16 patient had no or MVO extent < 2% (mean $0.56\pm0.66\%$) of LV mass (no MVO group). Patients in the MVO vs. no MVO group were more likely to be non-smokers (90% vs. 56%, P=0.074) and were two times more likely to be diabetic (30% vs. 12.5%, P=0.29). MVO was associated with larger myocardial damaged as assessed by CMR DE (24 ± 7 vs. $11\pm6\%$ of LV, P<0.005), peak CPK (4165 ± 2242 vs. 1202 ± 1010 IU/l, P=0.0001), peak troponin I (133 ± 108 vs. 39 ± 33, P=0.003) and echocardiographic left ventricular ejection fraction (38 ± 8 vs. $49\pm10\%$, P=0.01). Thrombus in the left ventricle was found in 3 patient in the MVO group and none in the no MVO group (P=0.02).
Conclusions: Routine early CMR, in patients undergoing PPCI for STEMI,can detect MVO, predicting larger myocardial damage and lower LVEF.

Plasugrel as Compared with Clopidogrel Has a More Potent Anti-Platelet Effect Early Post- STEMI

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Background: Prasugrel, as compared with clopidogrel, reduces ischemic complications in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). In patients with stable coronary artery disease plasugrel has a more potent and consistent anti-platelet effect than clopidogrel. While ACS is associated with increased platelet activation, the anti-platelet effect of prasugrel has not been sufficiently studied in this important patient subset.

Methods: The study comprised 120 consecutive ST-elevation ACS patients undergoing primary PCI. Patients older than 75 years, weight< 60 kg, or with a history of stroke were excluded. Sixty patients were treated with clopidogrel (600/75 mg) and 60 with prasugrel (60/10 mg). ADP-induced platelet aggregation (PA) was determined with light transmittance aggregometry 72 hours post loading. Patients were followed up for in-hospital thrombotic complications.

Results: Baseline characteristics and angiographic findings were comparable between the two study groups. Compared with clopidogrel, prasugrel treated patients had significantly lower ADP-PA ($29\pm13\%$ vs. $46\pm16\%$, $p< 0.001$). Accordingly, patients treated with prasugrel were less likely to be non- responders (ADP-PA >70%) or to show sub-optimal response (ADP-PA > 50%) as compared with clopidogrel (1.7% vs. 12%, $p=0.06$ and 12% vs. 40%, $p<0.001$ respectively). One patient who was treated with clopidogrel sustained early stent thrombosis.

Conclusion: In STE-ACS patients undergoing primary PCI prasugrel compared with clopidogrel results in greater platelet inhibition.

High Sensitive Troponin Assay - Helpful or Misleading?

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Background: Cardiac Troponin is considered a specific and sensitive marker for the diagnosis of acute coronary syndrome (ACS). In the last years, a high sensitive Troponin-T kit (HSTT) allows detection of very low levels of troponin, thus increasing test sensitivity. Nevertheless this test might detect elevated troponin in patients without ACS.
Aim: To evaluate the effect of the utilization of HSTT on the diagnostic accuracy of ACS.
Method: We assessed all consecutive patients with low positive HSTT levels (0.03-0.1ng/ml) during one month (8/9/2010-8/10/2010). Demographic and clinical data were collected and death at 1-year follow up was recorded. The main complaints on admission and final diagnoses on discharge for each patient were re-evaluated from computerized medical records. Positive predictive value (PPV) for ACS diagnosis was calculated.
Results: During the study period 302 low positive HSTT results were found in 179 patients. Mean age was 75.6 years, 102(57%) were males, 47% had history of CAD and 66.6% had renal failure. Only 43(24%) patients were admitted because of chest pain and no more than 24 had a final diagnosis of ACS, making the PPV of HSTT for the diagnosis of ACS only 0.13. In patients with chest pain the PPV of HSTT was 0.4 while in patients without chest pain the PPV was as low as 0.05! One year mortality in the study group was relatively high (35.5%), with no significant difference between patients with or without ACS.
Conclusion: The implementation of the high sensitive troponin assay results in high rate of positive troponin without evidence of ACS. The predictive value of low positive HSTT for the diagnosis of ACS is very low, particularly in patients who do not complain of chest pain. Low positive HSTT (<0.1ng/ml) might be misleading and clinicians should avoid using it as a screening tool when clinical presentation is not suggestive of ACS.