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Left main coronary stenting in a non surgical octogenarian population: a possible approach

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Aims. Coronary artery bypass grafting is conventionally considered the standard treatment for significant left main coronary artery (LMCA) disease. The management of severe coronary artery disease in the octogenarians is still highly debated. The aim of this study was to appreciate safety and effectiveness of percutaneous coronary intervention (PCI) in octogenarians who were denied by the heart team for surgical revascularization.

Methods and Results. The study included 70 consecutive patients ≥80 years of age who had undergone PCI for the treatment of LMCA and who were primary denied by our center’s heart team for surgical revascularization. In our study mean age was 83.4 ± 2.6 years [range 80-89]. Mean Euroscore was 21.1 ± 16.7 and mean Syntax score was 28.6 ± 8.7. Ten (14%) were treated with LMCA PCI in the context of ST-segment Elevation Myocardial Infarction (STEMI). Overall in-hospital mortality was 11%. There were two cases of fatal stent thrombosis at 2 and 7 days respectively after DES implantation. Mean follow-up time was 27.2 ± 24.9 months [range 4-80 months]. Overall mortality at the end of follow-up was 28%. Cardiac death was found in 18 patients and 2 patients died from terminal renal insufficiency. 2 other patients (3%) presented with a new STEMI, 7 (10%) with a new non-STEMI 13 (19%) with heart failure and 2 (3%) had minor hemorrhage. There was a non-percutaneous target vessel revascularization in 7 (10%) patients. During follow-up, the total major adverse cerebral and cardiovascular event (MACCE) was 48.5%. Distal LMCA disease and male sex were independent factors predicting mortality [p<0.05].

Conclusions. Stent implantation was technically feasible and relatively safely applied for the treatment of LMCA disease in octogenarians who were refused for surgery and who represented a high risk population for PCI and coronary events. Despite a high rate of MACCE, the clinical long term outcome seems good for this specific population with heavy basal status.

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CYP2C19 but not PON1 genetic variants influence clopidogrel pharmacokinetics, pharmacodynamics and clinical efficacy in post-myocardial infarction patients

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Background: Reduced concentrations of clopidogrel active metabolite have been associated with diminished platelet inhibition and higher rates of adverse cardiovascular events. Paraoxonase-1 (PON1) has recently been proposed as a key enzyme for clopidogrel metabolic activation. We tested the effects of PON1 polymorphisms on clopidogrel pharmacokinetics (PK) and pharmacodynamics (PD), and the occurrence of cardiovascular outcomes in young post-MI patients treated with clopidogrel.

Methods and Results: We genotyped PON1 (Q192R and L55M) and CYP2C19 variants in 104 patients enrolled in the PK/PD CLOVIS-2 trial. Patients were randomly exposed to 300mg or 900mg clopidogrel loading dose in a cross-over study design. Clopidogrel active metabolite isomer H4 (clopi-H4) and platelet function testing were measured serially post-loading dose. There was no significant association between PON1 Q192R or L55M and clopi-H4 formation or antplatelet response to clopidogrel following either loading dose. Using multivariable linear regression analyses, the CYP2C19*2 allele was the only predictor of clopi-H4 generation and platelet response irrespective of the platelet function assay. CYP2C19 loss-of-function but not PON1 variants were significantly associated with increased risk of major cardiovascular events (death, myocardial infarction and urgent coronary revascularization) occurring during long-term clopidogrel exposure in 371 young post-MI patients (<45 years) enrolled in the AFUJ2 cohort: CYP2C19 loss-of-function allele carrier vs non carrier, HR 2.26 [95% CI [1.5-4.41]], p=0.02; PON1 Q192R vs QR/RR192, HR 1.03 [95% CI [0.50-2.11]], p=0.93; PON1 MM55 vs ML/LL55, HR 1.52 [95% CI [0.75-3.08]], p=0.24.

Conclusion: Our study does not confirm that PON1 Q192R or L55M can influence clopidogrel PK or PD in post-MI patients.

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Magnetocardiographic indices in assessment of patients with myocarditis and acute STEMI

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Aims: To assess ability of different magnetocardiographic (MCG) indices to discriminate between ischemic changes of electrophysiological properties of myocardium early after STE AMI and non-ischemic changes.

Methods: 32 pts with STE AMI (21 pts with ischemia on stress test – 1st group and 11 pts without ischemia – 2nd group examined on 7-10th day after STE AMI) , 32 pts with myocarditis (3rd group) and 34 healthy (4th group) were evaluated. All patients had neither conduction abnormalities, ischemic changes on resting ECG, nor LV hypertrophy, systolic dysfunction on EchoCG. Healthy and AMI pts had exercise test on the same day with MCG. Averaged deviations of largest vectors of current density distributions (CDD) on ST slope starting at 60 ms from J to Tapex (first half of this ST portion – D1), second half – D2, second portion of Ta-Te (D4) and differences in directions of vectors of CDD on R and Tapex (delta RTa), ratios between global CDD on peak R to that on Tapex (GCDD-RTa) were assessed.

Results: In 1st, 2nd, 3rd and 4th groups median D1 were 9.0, 5.0 ,3.0, and 2.25 grades respectively, p<0.05; median D2 were 11.9 , 5.3 , 3.5, and 1.60 grades, p<0.05; median D4 were 12.3, 6.3 , 7.3, and 5.0 grades, p<0.05; median delta RTa were 47.0, 32.5, 22.5 and 12.5 grades respectively, p<0.01. Best sensitivity (91%) and specificity (71% and 76%) in discerning patients with and without ischemia after MI were D2> 8.1 and delta RT>69.5 grades.

Of parameters consistent with myocarditis was ratio GCDD-RTa (In 1st, 2nd, 3rd and 4th groups median GCDD-RTa 3.4, 4.01, 7.13 and 5.0 respectively, p>0.01 between 3rd group and other study groups) which did not differ significantly in STEMI patients.

Conclusion: MCG is informative for assessment of patients with and without coronary artery disease. MCG is capable of detection changes in electrophysiological properties in myocardium susceptible to ischemia and may be used to select patients with STE MI who need revascularization.

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Evaluating in a “real-world” the performance of CRUSADE and MEHRAN bleeding risk scores to predict major bleeding complications among Tunisian patients with ACS

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Background: Bleeding is a major complication in patients treated for acute coronary syndromes (ACS) with antithrombotic and invasive therapies. Consequently, the benefit of such therapies should be balanced against the potential risk of hemorrhagic complications. CRUSADE and more recently...
MEHRAN models provide two risk scores that predict the likelihood of major bleeding in patients hospitalized with ACS.

The aim of this study: was to evaluate the performance of CRUSADE AND MEHRAN risk scores to predict in-hospital major bleeding in a contemporary cohort of patients hospitalized for ACS in Tunisia.

Methods and results: The study subjects were 205 consecutive patients admitted to our center between January 2010 and June 2010 with ACS. For each patient, we calculated both the CRUSADE AND MEHRAN risk score and evaluated its discrimination by the C statistic.

By CRUSADE and MEHRAN risk scores, our patients were classified as high or very high risk of major bleeding in 46.3%, 32.2% of cases, respectively.

The overall incidence of in-hospital bleeding events and major bleeding (TIMI major definition) was 19.5%, 3.9%, respectively. The major bleeding rate increased with the CRUSADE risk category: very low, 0%; low, 0%; moderate, 3.8%; high, 4.0%; and very high, 13.3% (P=0.004). A stepwise increase in rates of major bleeding with increasing MEHRAN score was also noted (0%, 0%, 4.2% vs 9.9%; P=0.01). CRUSADE and MEHRAN risk scores demonstrated a high performance for predicting in-hospital major bleeding (c-statistic=0.86 and 0.83, respectively).

Conclusions: In routine clinical practice, bleeding is a relatively frequent non-cardiac complication of contemporary therapy for ACS. These two scores discriminate major bleeding risk and are both potentially useful in clinical decision-making during ACS.

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Coronary stenting and surgery, a complex situation to manage. Usefulness of endothelial progenitor cells capture
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Background: Dealing with thrombotic risk of stent occlusion and hemorrhagic risk of surgery is not well documented in literature. Endothelial progenitor cells (EPCs), have been demonstrated to achieve a complete and functional reendothelialization of expended coronary stent in 48 hours in animal model. EPCs are captured by antibodies and immobilized on the stent surface of the Genous stent (Orbus Medical).

Method: 11 patients, 7 male, 4 female, 77.4±7.37 year old, presented an acute coronary syndrome with severe coronary artery lesions and an urgent surgical indication underwent PTCA with exclusive one or more Genous stent (Orbus Medical). Single unique bolus of 10 mg/kg of clopidogrel associated to 2 mg/kg of aspirin was given at least 6 hours prior PTCA. Surgery was planned to be performed at day 5 following half pool platelet renewal. Informed consent was obtained for all patients.

Results: 1.72±0.78 stent was implanted for a total length of 28±12 mm and a mean diameter of 3.0±0.5 mm. All target selected lesions included left main (n=1), LAD (n=9), CX (n=3), RCA (n=6) were treated with angiographic success. Mean ventricular ejection fraction was 55.0±0.5. Surgery was performed in average at day 5 under aspirin alone (2 mg/kg) with success of the planed surgical act (coleotony, prostestectomy, cholestelymey, mammectomy, gastrectomy, peripheral arterial graft) with no complication. Intra venous nitrate was used for patients presenting incomplete revascularization and distal lesions. Only one patient needed a blood transfusion. At one month no event was observed (death, myocardial infarction, repeat PTCA, cerebral event, stent thrombosis).

Conclusion: Single bolus of clopidogrel for high risk evolutive coronary artery lesions treated with Genous stent allow a surgical act at day 5 under aspirin alone in good condition with no complication in this short series. Those preliminary data can serve as an impetus for multi-center studies.

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Clopidogrel and statins: assessing a potential drug-drug interaction
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Background: Clopidogrel and statins are frequently administered in patients with ischemic heart disease or other atherothrombotic manifestations and are effective in the prevention of cardiovascular disease. Clopidogrel is a pro-drug metabolised in the liver to the active compound which inhibits the P2Y (12) ADP platelet receptor. The aim of this study was to assess the association between the loss-of-function cytochrome P450 2C19 (CYP2C19)*2 variant, the use of statins which are metabolized by the CYP3A4 system and ischemic outcomes (major adverse cardiovascular events [MACE]) in patients treated with clopidogrel.

Methods: Between May 2009, and September 2010, 100 patients who underwent a percutaneous coronary intervention (PCI) and were exposed to clopidogrel treatment for at least one month, were enrolled in our study. They underwent CYP2C19*2 determination. The primary endpoint was a composite of death, myocardial infarction, and urgent coronary revascularisation occurring during exposure to clopidogrel.

Results: 94% of our patients were on statins. Among these patients, 57% were on statins metabolized by CYP3A4 (simvastatin or atorvastatin) and 37% in statin not metabolized by CYP 3A4 (Rosuvastatin, Fluvastatin and Pravastatin). Statins metabolized by CYP3A4 have no effect on the occurrence of MACE under clopidogrel (p=0.18). In the group of patients on statins metabolized by CYP3A4, no statistically significant difference was observed regarding the occurrence of intra hospital MACE according to genetic profile (11% in the non mutated group versus 25% in the mutated group).

Conclusion: The results of our study are consistent with those of the literature and have not shown any association between major cardiovascular events and the use of statins metabolized by CYP3A4, this genotype.

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The C93T and G121A polymorphisms of the LPA gene is not associated with susceptibility to acute myocardial infarction
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Background: Acute myocardial infarction (AMI) is the clinical manifestation of the chronic development of coronary artery atheroma, with the final process of plaque rupture and coronary thrombosis. Plasma lipoprotein (a) (Lp(a)) levels are mainly genetically determined. The C93T and G121A polymorphisms are naturally occurring variant of the LPA gene that may influence Lp(a) concentration. The role of Lp(a) in the pathogenesis of myocardial infarction has not been established.

Methods: A one hundred sixty-eight AMI patients compared to 169 healthy controls.

Results: No association between LPA C93T genotypes and AMI was found. The frequencies of the GG, GA and AA genotypes of LPA G121A polymorphism were not significantly different in AMI patients and in healthy controls (45.2 %, 48.2 %, 6.6 % vs 41.7 %, 49.4 %, 8.9 %, P=0.880). In multivariate logistic regression analysis with covariates including traditional risk factors (diabetes, hypertension, smoking and cholesterol) and, The C93T and G121A polymorphisms, hypertension was independently associated with increased risk of AMI (OR=3.5, P=0.044).

Conclusion: The C93T and G121A polymorphisms of the LPA gene is not associated with susceptibility to acute myocardial infarction.