Background: Incomplete P2Y12-inhibition during clopidogrel treatment is associated with increased cardiovascular events and mortality after coronary intervention.

The aim of this study was to evaluate the effect of high-dose clopidogrel continuation treatment on the development of MACCE in patients with Cytochrome P450 2C19*2 Loss-of-Function Allele.

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: The use of a double maintenance dose of clopidogrel (150 mg) was noted in 27% of cases, similarly in both study groups (28.6% in the non-mutated versus 21.7% in the mutant group (p=0.5).

This attitude was especially observed in diabetic patients, if drug-eluting stent is used and in case of complex angioplasty (77% of patients on double dose of clopidogrel are diabetics and 70% were implanted with a drug-eluting stent).

The use of a double dose of clopidogrel results in a non significant decrease in the occurrence of MACCE in the non mutated group (10.9% vs 0%, p=0.17) and has no effect in the mutated group (22% in a double dose of clopidogrel versus 20% p=0, 91).

Conclusion: Our study showed no relationship between the use of a double dose of clopidogrel and reduced occurrence of MACCE, irrespective of the genetic profile studied.

020

Prognostic value of persistent vs. transient fragmented QRS on a 12-lead ECG in patients with acute myocardial infarction

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Objective: To investigate the determinants and the prognostic capacity of fragmented QRS on a 12-lead ECG in patients with acute myocardial infarction.

Patients and methods: Prospective cohort of 307 consecutive patients with AMI. Main outcomes measure: in-hospital adverse outcomes, thirty-day and one year mortality.

Results: 163 (53%) were found without iQRS (No iQRS group). 144 (47%) presented a iQRS on the first 36 hours 12-lead ECG, which was persistent in 107 patients (persistent iQRS group) and non persistent in 37 patients (non-persistent iQRS group). Despite similar demographic features, clinical presentation and reperfusion strategies, patients with a fragmented QRS (transient or persistent) were older, more likely hypertensive and less smoker were found among these groups. If in-hospital adverse outcomes were similar between groups, interestingly we found a trend towards a greater likelihood of ventricular arrhythmias in the group without a fragmented QRS when compared with other groups (12% vs. 5% vs. 4%, respectively, p=0.054). An all-cause death at 30 days was similar in the three populations. At one year’s follow-up, 45 (14.6%) patients had died from all causes and 30 (9.7%) from cardiovascular cause. The Kaplan Meier analysis revealed that mortality was significantly higher in the iQRS group (persistent or not) than in the non-iQRS group (30% vs. 15(9.2%) respectively, p=0.007). By multivariate logistic regression analysis, age (p=0.008) and the presence of a family history of CAD (p=0.045) were independent predictors of iQRS occurrence. In multivariate analysis six variables were significant predictors of all-cause death at one year: age, DBP, glucose on admission, LVEF, treatment with beta-blockers at the acute phase and presence of a iQRS.

Conclusions: The iQRS is an independent predictor of 1 year all cause death after AMI, even after correction with age and LVEF, and it is associated with lower event-free survival.

021

Relation between clopidogrel discontinuation and early cardiovascular events after percutaneous coronary intervention with drug-eluting stents

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(1) CHRU Cardiologie, Centre Hémodynamique, Lille, France – (2) Washington Hospital Center, Washington DC, United-Sates – (3) AP-HM, CHU Nord, Marseille, France

Aims: Clopidogrel discontinuation after percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation has been reported to correlate with stent thrombosis. Whether these events are a consequence of the rebound phenomenon or a lack of protection in unhealed vessels is unclear. This study aimed to determine the link between clopidogrel cessation and cardiovascular events after PCI with DES.

Methods and results: The population included 1,903 patients who underwent PCI with DES implantation from 2003 to 2007. We compared patients who stopped their clopidogrel within the first month (group 1, n=97), from one to six months (group 2, n=344), from six to 12 months (group 3, n=468), and after 12 months (group 4, n=994) following the PCI. In each group, the composite of death, myocardial infarction and stent thrombosis at 30 days and between 31 and 60 days after clopidogrel cessation was indexed. Baseline characteristics were similar among groups. The event rate observed in the 0-30 day interval following cessation was higher only in group 1 (5.2%) compared to all other groups: 1.2% (group 2), 0.9% (group 3) and 0.6% (group 4) (p=0.004). The event rates from 31 to 60 days following cessation were low and similar among the four groups. When the elapsed time between the index PCI and the clopidogrel cessation was analysed as a continuous variable, the probability of events occurring within the first 30 days became similar to that observed in the 31-60 day interval following cessation after a minimum of 10.2 months.

Conclusions: Cardiac events seen immediately after clopidogrel cessation are not related to a rebound phenomenon, but are more likely influenced by the lack of healing at the time of cessation, which decreases over time. This increased risk related to the lack of healing seems to disappear after 10.2 months.

022

One-year outcome of everolimus vs. paclitaxel-eluting stents for the treatment of unprotected left main lesions

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(1) Institut Hospitalier Jacques Cartier, Institut Cardiovasculaire Paris Sud, Massy, France – (2) Clinique Saint-Augustin, Bordeaux, France – (3) CHU Rangueil, Toulouse, France

Background: Coronary artery bypass surgery is recognised as the “gold standard” treatment for unprotected left main (LM) stenosis. However, advances in percutaneous coronary intervention techniques and the introduction of drug eluting stents have led to the acceptance of PCI as an alternative strategy for complex lesions including LM lesions.

Methods: We performed a matched comparison of patients in the French Left Main Taxus registry and the Left Main Xience registry undergoing unprotected LM stenting with Taxus paclitaxel-eluting (PES) and Xience sirolimus-eluting (SES) stents respectively, in 4 French centres. 172 patients were matched according to Syntax score, stenosis involving the distal LM, provisional side-branch T-stenting and use of one stent in the distal LM.

Results: Patients were aged 69.5±11.3 years, 76.5 % of patients were male. 25.3% of patients were diabetics and 27.3% had undergone previous PCI. Mean Syntax score was 25.5±9.6. The distal LM was involved in 82% and provisional SB T-stenting was performed in 91.1%.

The one-year follow-up results are shown in Table 1.

Patients were stratified according to the 3 SYNTAX score subgroups. Patients with low SYNTAX score had similar outcomes for MACCE at 1 year (9.6% vs. 6.8%, p=0.67) for PES and EES respectively. Intermediate and high
SYNTAX score subgroups demonstrated numerically higher MACE rates in patients with PES compared to EES (15.3% vs. 5.1%) and (30.0% vs. 15.4%) respectively.

Patients with low and intermediate SYNTAX scores had similar TLF outcomes at 1 year. However, the high SYNTAX score group had a significantly higher rate of TLF in the PES group (27.5% vs. 10.3%, p=0.01).

Cardiac death was higher in patients with an intermediate SYNTAX score in PES patients (6.8% vs.0.0%, p=0.04) as was TVMI (8.5% vs. 0.0%, p=0.02).

Conclusion: Unprotected LM stenting with EES is feasible, safe and more effective in the mid term, than with PES with a reduction in MACCE, TLF and cardiac death at one year.

Table 1 – One-year follow-up results

<table>
<thead>
<tr>
<th></th>
<th>EES</th>
<th>PES</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause death</td>
<td>2.9%</td>
<td>6.4%</td>
<td>0.13</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>1.2%</td>
<td>4.7%</td>
<td>0.05</td>
</tr>
<tr>
<td>Target vessel myocardial infarction</td>
<td>4.1%</td>
<td>8.7%</td>
<td>0.08</td>
</tr>
<tr>
<td>Clinically driven target-lesion revascularization</td>
<td>2.9%</td>
<td>5.8%</td>
<td>0.19</td>
</tr>
<tr>
<td>Clinically indicated target vessel revascularization</td>
<td>7.0%</td>
<td>13.4%</td>
<td>0.05</td>
</tr>
<tr>
<td>Target lesion failure</td>
<td>6.4%</td>
<td>14.0%</td>
<td>0.02</td>
</tr>
<tr>
<td>MACE</td>
<td>8.1%</td>
<td>16.3%</td>
<td>0.02</td>
</tr>
<tr>
<td>Device-oriented composite</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac death+MI-TLR</td>
<td>6.4%</td>
<td>16.3%</td>
<td>0.004</td>
</tr>
<tr>
<td>Steal thrombosis</td>
<td>1.2%</td>
<td>6.4%</td>
<td>0.01</td>
</tr>
</tbody>
</table>

HIV-infected status is associated with increased recurrence of acute coronary syndrome. Results of long term follow up of the PACS-HIV study

Franck Boccara [Orateur] (1), Mouhanna Mary-Krause (2), Emmanuel Teiger (3), Sylvie Lang (1), Pascal Lim (3), Karim Wahbi (4), Farzin Beygui (5), Olivier Milleron (6), Philippe Gabriel Steg (7), Christian Funck-Brentano (8), Ariel Cohen (1)

Objectives: The PACS-HIV study is designed to evaluate the 3-year prognosis of acute coronary syndrome (ACS) in HIV-infected patients (HIV+ vs. HIV-) as compared to HIV-uninfected patients (HIV-) in a prospective observational study. We aim to present the long term 3-year follow-up.

Methods: We enrolled consecutively 103 HIV-infected and 195 HIV-uninfected patients with a first episode of ACS matched for age (± 5 years), sex, and type of ACS. The primary endpoint was the rate of major adverse cardiac and cerebral events (MACCE), comprising cardiac death, recurrent ACS, recurrent coronary revascularization, and stroke.

Results: The mean age of the cohort was 49.0 ± 9.4 years and 94% were men. At baseline, coronary risk factors were well balanced and angiographic features were not different between both groups. MACCE at 3-year are depicted in Table. The rate of occurrence of first MACCE at 36-months was similar in both groups (univariate hazard ratio [HR]=1.4, 95% CI, 0.7-2.6). However, recurrent ACS was more frequent in HIV+ group as compared with HIV- group (univariate HR=3.4, 95% CI, 1.3-8.8). Stratified multivariate Cox model showed that the only factor associated with the recurrence of ACS was HIV status with HR 7.86 for HIV+ versus HIV- (95% CI, 1.2-50.6, p=0.03).

Conclusion: HIV-infected patients had higher recurrence of ACS despite similar coronary risk factors, clinical, and angiographic features at baseline of a first episode of ACS as compared to HIV-uninfected patients. Specific secondary prevention may be warranted to alleviate this risk.

Table – MACCE at 3-year

<table>
<thead>
<tr>
<th>HIV+ (n=103)</th>
<th>HIV– (n=195)</th>
<th>Univariate Hazard ratio [95% CI]*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major adverse cardiac events</td>
<td>17 (16.8%)</td>
<td>29 (15.1%)</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>2 (3.0†)</td>
<td>3 (1.6†)</td>
</tr>
<tr>
<td>Recurrent ACS</td>
<td>12 (11.9†)</td>
<td>11 (5.8†)</td>
</tr>
<tr>
<td>Target lesion revascularization</td>
<td>8 (7.8†)</td>
<td>17 (9.0†)</td>
</tr>
<tr>
<td>Target vessel revascularization</td>
<td>11 (10.8†)</td>
<td>20 (10.5†)</td>
</tr>
</tbody>
</table>

Long term prognosis value of heart rate in coronary artery disease

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Purpose: Our aim was to assess the long term prognosis value of resting HR in a contemporary large cohort of subjects with known CAD.

Methods: Among 834 consecutive male pts hospitalized in 2001-2004 for coronary artery disease, HR was measured in 778 pts. The median follow-up was 7.17 years. Total mortality was predicted with a Cox proportional hazard model.

Results: Mean age (SD) was 60.2 (8.1), 144 pts (18.4%) were diabetic, mean glycaemia was 5.9 mmol/L (2.1), 155 pts (19.8%) were smokers, mean blood pressure was 139 (20) / 84 (11) mmHg. Mean HDL cholesterol was 43 mg/dl (11), mean LDL cholesterol124 mg/dl (39) and median triglycerides were 147 mg/dl IQR [109-197]. Mean Cockcroft-Gault creatinine clearance was 87 ml/min and 11 pts (1.4%) had a severe chronic renal failure (lower than 30 ml/min). Mean left ventricular ejection fraction was 0.53 (0.13), 88.5% were on antiplatelet therapy, 75.2% on beta-blocker, 66% on statin therapy and 54.8% on ACE inhibitors or ARB.

-0.45% of pts had HR < 60 bpm, 32% HR between 60 and 69 bpm and 27.5% had HR ≥70 bpm. The cumulative seven-year total mortality rate was 17.8%. In the HR < 60 bpm group, mortality rate was 11.1%, whereas it was 17.3% in the group with HR ≥ 60 bpm and < 70 bpm and 28.5% in the HR ≥70 bpm group (p<.001).

We performed a multivariate analysis adjusted for age, diabetes, tobacco consumption (none; ≤40 pack-years; > 40 pack-years), left ventricular ejection fraction (>0.5; ≤0.5 and > 0.35; ≤0.35), duration of CAD, ankle-brachial index (>0.9; ≤0.9 and > 0.6; ≤0.6), history of chronic obstructive pulmonary disease or stroke, statin therapy and coronary revascularization. For every 5 bpm increase in resting heart rate, there was a significant 11% increase in all-cause death (95% CI [4%; 18%] p=0.002).

Conclusion: HR is a strong and independent long term predictor factor of all-cause death in CAD. A close control of HR should be promoted to improve long term prognosis in coronary pts.