Atrial fibrillation is associated with a marker of endothelial dysfunction and oxidative stress in patients with acute myocardial infarction

Karim Stamboul (1), Julie Lorin (2), Luc Lorgis (2), Jean-Claude Beer (2), Claude Touszery (2), Luc Rochette (2), Catherine Vergely (2), Yves Cottin (2), Marianne Zeller (2)

(1) CHU Dijon, Bocage, Dijon, France – (2) Université de Bourgogne, INSERM U866, Dijon, France

Corresponding author: marianne.zeller@u-bourgogne.fr (Marianne Zeller)

Background Atrial fibrillation (AF), whether silent or symptomatic, is a frequent and severe complication of acute myocardial infarction (AMI). Asymmetric dimethylarginine (ADMA), an endogenous eNOS inhibitor, is a risk factor for endothelial dysfunction. We addressed the relationship between ADMA plasma levels and AF occurrence in AMI.

Methods 273 patients hospitalized for AMI were included. Continuous electrocardiographic monitoring (CEM) ≥48 hours was recorded and ADMA was measured by High Performance Liquid Chromatography on admission blood sample.

Results The incidence of silent and symptomatic AF was 39(14%) and 29 (11%), respectively. AF patients were markedly older than patients without AF (≥70y). There was a trend towards higher ADMA levels in patients with symptomatic AF than in patients with silent AF or no AF (0.53 vs. 0.49 and 0.49 μmol/L, respectively). After matching on age, we found that patients with symptomatic AF had a higher heart rate on admission and a higher rate of patients with LV dysfunction (28% vs. 3%, p<0.025). Patients who developed symptomatic AF had a higher ADMA level (0.53 vs. 0.43 μmol/L; p=0.001). Multivariate logistic regression analysis to estimate asymptomatic AF occurrence showed that ADMA was independently associated with symptomatic AF (OR: 2.46 [1.21-5.00], p=0.013) beyond history of AF, LVEF<40% and elevated HR.

Conclusion We show that high ADMA level is associated with the occurrence of AF. Although no causative role can be concluded from our observational study, our work further supports the hypothesis that endothelial dysfunction is involved in the pathogenesis of AF in AMI.

The author hereby declares no conflict of interest

Impact of thienopyridines on platelet CD40L biodisponability after an acute coronary syndrome in relation with bleeding events

Pierre Dharo (1), Charlotte Grosdidier (2), Thomas Cuisset (2), Marie Christine Alessi (2), Jean Louis Bonnet (2)

(1) APHM-CHU la Timone, Cardiologie, Marseille, France – (2) APHM-CHU la Timone, Laboratoire d'hématologie, Marseille, France

Corresponding author: pierre.dharo@ap-hm.fr (Pierre Dharo)

Background CD40 Ligand (CD40L) is expressed on platelets upon ADP stimulation and is involved in haemostasis. CD40L deficient mice exhibit thrombosis instability and increased bleeding time.

Methods We investigated the relationships between plasma and platelet-associated CD40L, ADP signaling and bleeding event occurrence in patients receiving thienopyridines one month after a stented Acute Coronary Syndrome (ACS). Basal platelet CD40L surface expression (pCD40L), pCD40L after PAR-1 agonist stimulation (TRAP pCD40L) and platelet released CD40L (rCD40L) were quantified. Results were compared to VASP as a measure of P2Y12 inhibition level. Results We included 318 patients between November 2012 and June 2014. Thienopyridines treated patients exhibit low pCD40L, TRAP pCD40L, and rCD40L in comparison with controls. pCD40L and rCD40L were correlated with PRI-VASP. Thienopyridine treatment strongly reduces rCD40L. Hyperresponder to thienopyridine status is associated with high levels of TRAP pCD40L, pCD40L and TRAP pCD40L levels are reduced in the bleeding cohort. In multivariate analysis pCD40L significantly contributes to bleeding risk independently of PRI-VASP.

Conclusion pCD40L and rCD40L levels are reduced by thienopyridines. pCD40L associates with the bleeding risk independently of the VASP levels and may represent a novel target to assess bleeding risk in thienopyridine-treated ACS patients.

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The Log Book as a new tool for the secondary prevention of coronary artery disease

Elodie Boch (1), Aurélien Vaillant (2), Laura Gay (2), Marie-Charlotte Moreau (2), Frédérique Germin (2), Philippe Brunel (3), Gilles Morel (3), Aline Chagnon (4), Yves Cottin (4), Marianne Zeller (5)

(1) CHU Dijon, Bocage, Dijon, France – (2) Université Bourgogne, Dijon, France – (3) Clinique Fontaine, Fontaine Les Dijon, France – (4) CHU Tours, Tours, France – (5) Université de Bourgogne, INSERM U866, Dijon, France

Corresponding author: marianne.zeller@u-bourgogne.fr (Marianne Zeller)

Introduction The Log book (LB) project was created by a multidisciplinary team of healthcare professionals from a regional care network and aimed to improve secondary prevention (SP) after acute myocardial infarction (MI) in Côte d’Or. LB includes information and advice for increasing self-management of risk factors by the patient.

Methods A prospective interventional study on 469 patients hospitalised for an acute MI in the 2 Intensive Coronary Care unit of Côte d’Or (CHU Dijon and Clinique de Fontaine les Dijon) in 2012 and surviving at 1 year follow-up (FU). LB was randomly given at the time of their hospitalisation by the nursing team, also providing oral advice on risk factors management and CV health self-care. Patients who received LB (LB+) were compared with patients without LB (LB-).

Results Patients from LB+ group (n=307(65%)) were younger (57 vs 63y, p<0.001) and less frequently women (16 vs 32%, p<0.001), diabetic (17 vs 30%, p<0.001) or with prior CAD (7 vs 15%, p=0.008) than patients without LB (LB- group, n=162(35%)). After matching patients LB+ with LB- based on age, sex, diabetes and GRACE risk score (n=127 in each group), baseline characteristics, were similar in the 2 groups. At 1 year FU, there was a trend for more frequent visits to the cardiologist in the LB+ group (2a1 vs 1a1, p=0.056) and cardiac rehabilitation program was more often performed in LB+ patients (69 vs 54%, p=0.15). Moreover, weight loss in obese patients and smoke withdrawal rates also showed a trend for improvement in LB+ patients (respectively 71 vs 59%, p=0.311 and 69 vs 53%, p=0.109). Finally, patients with LB showed a trend toward a lower rate of combined outcomes including recurrent MI, hospitalisation for heart failure and unscheduled PCI in the LB- group (3 vs 7%, p=0.155).

Conclusion These preliminary data of our ongoing regional study suggest the efficacy of LB as a support for CV risk factor self management. In addition, our study provides encouraging data on the potential clinical benefits of this pioneer tool for SP.

The author hereby declares no conflict of interest

Cardiovascular protection of statins could be mediated by an increase of total bile acids concentration in sera? A pilot study

Caroline Nguyen (1), Hélène Aflon (1), Henri Duboc (2), Julien Rosencher (2), Dominique Rainteau (3), Lydie Humbert (3), Simon Weber (3), Olivier Varenne (3), Denis Duboc (3)

(1) APHP-Hôpital Cochin, Paris, France – (2) Université Paris Diderot, Paris, France – (3) Université Pierre et Marie Curie, Paris, France

Corresponding author: caroline.ng87@gmail.com (Caroline Nguyen)

Introduction in animal models of atheroma (ApoE-/- and LDL -/- mice), bile acids (BAs) exerts an anti-atherosclerotic effect through the anti-inflammatory action of their receptors, TGR5 and FXR, decreasing dramatically the surface of the atheroma plaque. BAs are cholesterol derivatives synthesized by the liver. In a previous study, we found that a decrease in BAs (lithocholic acid) is an independent risk factor of coronary disease in human.
Aim Statins are known to reduce cardiovascular events in atherosclerotic patients. Given the experimental protective effect of BAs against atherosclerosis, the aim of this preliminary study was to determine the total BAs concentration in sera after statins administration.

Methods Between January 2015 and April 2015, patients hospitalized for a coronary angiogram and starting a statins treatment for coronary atheroma were included. Exclusion criteria were post cardiac arrest, non-fasting status, hepatic disease, antibiotics and corticosteroids. The total BAs concentration was measured before and 1 month after the initiation of statin therapy by liquid chromatography mass spectrometry. Wilcoxon test was used for statistical analysis.

Results On a cohort of 360 patients, 37 were eligible and 17, aged of 54±9.6 years old have been retrospectively included. 95% were prescribed with atorvastatin (68% with atorvastatin 40mg). The mean concentration of the total BAs before statin was 0.68μmol/L (SEM 0.08μmol/L) and 1.37μmol/L after (SEM 0.21μmol/L) (p=0.013, figure 1).

Conclusion Statins administration is associated with a doubling of circulating BAs after one month of treatment. This raises a question about statins increasing BAs synthesis by the liver; the deflection of the cholesterol synthesis by the liver into BAs instead, could participate to the efficacy of statins. This could theoretically be beneficial by slowing down the atheroma development through anti-inflammatory effects of BAs on the macrophage of the plaque.

0321

In the area of new P2Y12 inhibitors, high platelet reactivity on aspirin in patients with ST elevation myocardial infarction remains a predictor of ischemic events

Jean-Guillaume Dillinger (1), Alaa Saeed, Vincent Spagnoli, Claire Bal Dit Sollier, Georgios Sideris, Stephane Manzo Silberman, Sebastian Voicu, Ludovic Drouet, Patrick Henry

APHP-Hôpital Lariboisière, Paris, France

Corresponding author: dillingerjg@aol.com (Jean-Guillaume Dillinger)

Background Despite dual antiplatelet treatment with the new P2Y12 platelet receptor antagonists (P2Y12i), major ischemic events are common following ST elevation myocardial infarction (STEMI).

Objectives To assess separately resistance to aspirin (HPR-aspirin), resistance to P2Y12i (HPR-P2Y12i) and their association during the acute phase of STEMI in relation to the occurrence of ischemic events.

Methods We included all consecutive patients admitted for STEMI in our center between January 2013 and December 2013. All patients received a loading dose followed by a maintenance dose of aspirin (75mg/day) and either clopidogrel, prasugrel or ticagrelor. Platelet reactivity was assessed 4±1 days and 75±15 days after admission using light transmission aggregometry (LTA) with arachidonic acid (AA) and serum Thromboxane-B2 concentration to assess HPR-aspirin and LTA-ADP and VASP index to assess HPR-P2Y12i. Major cardiac and cerebrovascular events (MACCE) were recorded during one year.

Results 106 patients (61 years old, 76% male, 20% with diabetes) were included. STEMI was anterior in 52% and LV ejection fraction at discharge was 51±9%. At day 4 after STEMI, HPR-aspirin measured by LTA-AA alone was found in 23% patients and was correlated with serum thromboxane inhibition. HPR-P2Y12i (VASP<50% and LTA-ADP<65%) was observed only in 7% and combined resistance was present in 4% of the patients. Diabetes and age were predictors of HPR-aspirin. The large use of ticagrelor (34%) and prasugrel (50%) explained the low rate of P2Y12i resistance. HPR-aspirin was persistent 75 days later in 36% patients who were resistance at day 4. At 1 year, 7.9% patients had experienced MACCE. HPR-aspirin alone and HPR for both aspirin and P2Y12i were significantly associated with MACCE.

Conclusion Aspirin resistance is frequent just after STEMI and is associated with MACCE especially when associated with P2Y12i resistance.

The author hereby declares no conflict of interest

0188

Suboptimal control of low-density lipoprotein cholesterol in French patients after an acute coronary syndrome. Contemporary data from DYSIS IIACS study

Jean Ferrieres (1), Maja Velkovski-Rouyer (2), Baishali Ambegaonkar (3), Dominik Lautsch (3), Philippe Brudi (3), Veronica Ashton (3), Anselm K. Gitt (4)

(1) CHU Toulouse, Rangueil, Toulouse, France – (2) MSD FRANCE, Courbevoie, France – (3) Merck & Co., Inc., Kenilworth, New Jersey, Etats-Unis – (4) Stiftung Institut für Herzinfarktforschung, and Herzzentrum Ludwigshafen, Ludwigshafen Am Rhein, Allemagne

*Corresponding author: maja.rouyer@merck.com (Maja Velkovski-Rouyer)

Aim To document low-density lipoprotein cholesterol (LDL-C) values during hospitalization of ACS patients with/without lipid-lowering therapy (LLT) at admission, and achievement of the ESC LDL-C target (LDL-C ≤70mg/dL) at 4 months following the acute event using data from the French cohort of the DYSIS IIACS study.

Methods DYSIS IIACS was a multicentre prospective observational cohort study (recruitment: Oct 2013 to Oct 2014) conducted in 24 coronary care units in France. Adults hospitalized for an ACS event and who had a lipid panel measured within 24 hours of admission were consecutively enrolled. Eligible patients had to be on LLT for ≥3 months or taking no LLT. A telephone follow-up interview was carried out with patients (or their next of kin) 120±15 days after the index event.

Results Of the 468 patients enrolled, 50.6% had ST-elevation myocardial infarction left bundle branch block, 40.8% had non-ST-elevation myocardial infarction, and 8.5% had unstable angina. Of the 277 (59.2%) patients on LLT at admission, 25.3% had an LDL-C <70mg/dL (Table). Most patients (96.4%) were on statin therapy at discharge (mean±SD dose calculated in atorvastatin 49±23mg/day). Non-statin LLT was used in 5.6% patients at discharge (61.5% with a cholesterol-absorption inhibitor). At 120 days after admission, 50.9% of ACS patients with follow-up data had achieved the LDL-C target.

Conclusions These observational data from contemporary French clinical practice in coronary care units indicate suboptimal LDL-C control, with a substantial proportion of very high cardiovascular risk patients presenting with elevated LDL-C despite taking LLT. Four months after the acute event, half of the patients (with data) failed to achieve the target, with a large difference between mean value and target LDL-C.

The author declares a conflict of interest: Merck employee