Topic 1 – Atherosclerosis, Haemostasis, Inflammation, AGE – A

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0035

Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: experience of Clermont-Ferrand hospital

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Background: The out-of-hospital cardiac arrest represent the leading cause of death worldwide. Several therapeutic elements such as early reperfusion developed in recent years to reduce the high morbidity and mortality observed in this situation. The objective of this study was to evaluate the influence of emergency coronary angiography (CAG) and primary percutaneous coronary intervention (PCI) on the outcome of patients survivors after out-of-hospital cardiac arrest.

Methods: Between January 2012 and June 2013, a total of 54 consecutive patients survivors of out-of-hospital cardiac arrest underwent systematic emergency coronary angiography.

Results: Thirty five of the 54 patients had clinically significant coronary disease on angiography, 23 of whom had coronary-artery occlusion (43 %). Angioplasty was attempted in 20 patients and was technically successful in 18. The in-hospital survival rate was 48 %. Multivariate logistic-regression analysis revealed that angioplasty was an independent predictor of survival (95 percent confidence interval, 3.1 to 750.1; P =0.006).

Conclusions: Acute coronary-artery occlusion is frequent in survivors of out-of-hospital cardiac arrest. Accurate diagnosis by immediate coronary angiography can be followed in suitable candidates by coronary angioplasty, which seems to improve survival.

0213

Determination of the influence of genetic variants in predetermined genomic region on the occurrence of CVD in humans, in association with circulating lipids level as a risk factor

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Cardiovascular diseases (CVDs) are a major cause of mortality (up to 40% death). CVDs are highly inheritable, suggesting a major role of genetic factors. Identifying key genes remain difficult as individual CVD risks are often linked to multiple undetermined genes and their interaction with environmental parameters. Significant progress have been made recently with the identification of nearly 120 genomic regions including variants associated with CVD accrued risk. These studies involve genome-wide associated data and are most helpful but cannot allow to accurately identify gene and the specific impact of each genetic variant in different physiological and metabolic events associated with CVDs. Starting from the Ludwigshafen Risk and Cardiovascular Health study, with a large cohort of patients (~3800) with a database of clinical and metabolic parameters, we have selected candidate gene and their variants associated with CVDs. To determine the functional impact of these variants, we produce mutant mice, reproducing targeted genomic changes found for each gene. These mice are fed atherogenic diet at 11-12 weeks of age and studied to determine metabolic and physiological consequences of these variants. Workflow focuses on arterial blood pressure by NIBP, progression of atherosclerotic plaques size and composition and steatosis formation by echography of the main arteries branching (carotid, aorta, renal arteries…). We measure also body composition and glucose tolerance by qNMR and OGTT respectively. Blood is collected to assess plasmatic cholesterol levels (HDL, LDL, TG) and organs are weighted (heart, kidney, spleen…) and used for RNA seq analysis. The identification of genetic factors responsible for phenotypic traits associated with CVDs and characterization of their impact on physiological and molecular level will allow us not only to better understand the genetic mechanisms promoting CVDs, but also to identify markers for better prevention and treatment of CVDs.

0100

Incidence and predictors of bleeding events in ST-Elevation Myocardial infarction (STEMI) revascularized within the first 12 hours.

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Background: Antithrombotic therapies reduce the risk of recurrent ischemic events in acute STEMI, but are responsible for an increase in bleeding events.

Aim: To describe the incidence and identify the predictive factors of bleeding events in patients revascularized within the first 12 hours of STEMI at Grenoble University Hospital.

Methods: We analyzed data from 276 consecutive pts prospectively included in the RESURCOR registry and determined the incidence, severity (TIMI, and BARC bleeding scores), sites, and associated complications of bleeding events. Crusade score, clinical history and therapies administered before coronary angiography (CA) were collected.

Results: All 276 pts underwent CA, 74 (27%) after thrombolysis and 202 (73%) for primary-PCI (radial route = 82%). One or more bleeding event occurred in 27 pts (9.8%): TIMI major n=13 (4.7%) and minor n=14 (5.1%). Patients with bleeding complications were more often female (p=0.012), were older (p=0.016), had lower body weight (p=0.023), presented more often with cardiogenic shock (p=0.001), required more often circulatory support (p<0.00001), and had higher CRUSADE score (32.4+15.7 vs. 25.2+13.7 p=0.016) than pts without bleeding. Mortality was 30.8, and 4.0% in pts with major, and no bleeding respectively (p<0.0001). Independent predictors of bleeding events were an older age, female gender, low body weight and presence of heart failure on admission. In emergency situation, bleeding risk evaluation by the clinician modified the management of STEMI, with less GPIIbIIa inhibitors (p=0.004) and thrombolytic agents (p=0.04) prescribed in pts with a high risk of bleeding.

Conclusion: The incidence of bleedings in STEMI remains stable despite more powerful antithrombotic agents, probably in relation with radial access and awareness of the bleeding risk by the clinician. Our study also confirms that bleeding events are strongly associated with in-hospital mortality.

0448

Essential role of platelet PI3Kβ and GSK3 in thrombus stability at high shear rate

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During platelet activation, class I phosphoinositide 3-kinase β (PI3Kβ) generate the lipid second messengers PtdIns(3,4,5)P3 which is an important players in the organization of the platelet signaling machinery downstream of activator receptors and integrins. Since PI3Kβ inhibition prevents occlusive thrombus formation with a limited increase in bleeding risk and acceptable safety in humans, this kinase has been proposed as a potential antithrombotic drug target. However, the role of platelet PI3Kβ in integrated in vivo or ex vivo models of thrombosis upon high shear rate condition found in stenosed arteries remains incompletely documented.