

Topic 9 – Metabolism: Lipids, Glucose – B

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Phenotypic remodeling of perivascular adipose tissue in a rat model of metabolic syndrome: vascular consequences and beneficial impact of exercise training

Cindy Meziat * (1), Doria Boulgobhra (1), Alessandro Do Nascimento (1), Eva Strock (1), Sylvain Battault (1), Gregory Meyer (1), Sandrine Gayraud (1), Nathalie Gayraud (2), Bernard Jover (2), Guillaume Walther (1), Cyril Reboul (1)

(1) Université d'Avignon, Avignon, France – (2) UFR Pharmacie, Montpellier, France

* Corresponding author: cindy.meziat@gmail.com (Cindy Meziat)

Aim This study was designed to evaluate the impact of high fat and high sucrose diet (HFS) on perivascular adipose tissue (PVAT) and its consequence on vascular function. Whether exercise training was able to counteract this alterations has been investigated as a potential therapeutic strategy.

Methods Rats were fed with standard (Ctrl rats) or HFS diet (HFS rats) for 15 weeks. After 6 weeks, HFS rats were randomly assigned into 2 groups: sedentary and trained group (HFS-Ex). PVAT remodeling was assessed by a proteome profiler, histological and biochemical assays. The impact of PVAT secretion on vascular function was assessed on isolated aortic rings incubated or not with PVAT secretum.

Results and discussion We reported increased PVAT mass in HFS rats associated with increase in both white to brown adipocytes proportion and uncoupling protein 1 level. Despite no major effect of HFS diet on PVAT adipokines profile was reported, adiponectin level and secretion were reduced in PVAT of HFS rats. As a potential consequence, we observed a marked endothelial dysfunction in Ctrl aortic rings incubated with PVAT secretum of HFS rats. The use of a non-specific antioxidant (N-Acetyl cysteine) in the organ bath blunted the deleterious effect of HFS secretum on endothelial function, suggesting a redox-dependent mechanism in this phenomenon. Exercise training in HFS rats normalized PVAT mass but has no effect on the browning process. However, this strategy was able to normalize adiponectin level in PVAT of HFS rats and finally abolished the detrimental effect of its secretion on endothelial function.

Conclusion Diet-induced metabolic syndrome leads to PVAT remodeling inducing deleterious vasoactive properties. The ability of exercise training to modulate this phenomenon could be considered as a good strategy to counteract the potential role of PVAT in the development of chronic vascular dysfunction in metabolic syndrome disease.

The author hereby declares no conflict of interest

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Identifying familial hypercholesterolemia from registries of patients with acute myocardial infarction: an algorithm-based approach

Marianne Zeller * (1), Michel Farnier (2), Yves Cottin (3), Claude Touzery (3), Etienne Puymirat (4), François Schiele (5), Jean Ferrieres (6), Tabassome Simon (7), Nicolas Danchin (4)

(1) Université de Bourgogne, INSERM U866, Dijon, France – (2) Le Point Médical, Dijon, France – (3) CHU Dijon, Bodge, Dijon, France – (4) APHP-Hôpital Européen Georges Pompidou (HEGP), Paris, France – (5) CHU Besançon, Besançon, France – (6) CHU Toulouse, Université Toulouse III, INSERM UMR1027, Toulouse, France – (7) APHP-Hôpital Saint Antoine, Université Pierre et Marie Curie, INSERM U-698, Paris, France

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

Background and aim Familial hypercholesterolemia (FH) is at very high risk of early myocardial infarction (MI). The prevalence of FH, which is esti-

mated to be at least 1:500 in the general population, remains unclear in patients with acute MI. From databases of 3 French regional and nationwide registries of acute MI (RICO and FAST-MI 2005 and 2010, respectively), we aimed to determine FH prevalence by developing a specific algorithm.

Methods and results Consecutive patients with AMI ≤ 48 hours of onset included 1) in FAST-MI : during a one-month period in 223 institutions at the end of 2005 and 213 institutions at the end of 2010, and 2) in RICO :from January 2001 – December 2013 (≈ 13 y), were considered in the 3 databases. The algorithm was adapted from Dutch lipid clinic network criteria and was build upon 4 variables (i.e. LDL level and previous use of lipid lowering medications, premature and family history) to identify FH probability. The LDL level was adjusted on each type of lipid lowering medications and the probability of FH was defined taking into account missing data rate. Among the 7484 patients included in the RICO registry, 29.1% had premature vascular disease, 29.7% had familial history, 19.9% were under lipid lowering medications and 9.7% had LDL ≥ 5 mmol/L. FH prevalence was calculated as unlikely (72.6%), possible (24.6%) and probable /definite (2.8%). From the 1957 patients from FAST-MI 2005 with all data available, 29.7% had premature CV disease, 23% had a family history, 26.6% were on LLDs, and 5.4% had LDL ≥ 5 mmol/L. FH prevalence was calculated as unlikely (77.9%), possible (19.4%) and probable /definite (2.7%). In the 2223 patients from FAST-MI 2010, 32.2% had premature CV disease, 24.9% had a family history, 28.1% were on LLDs, and 5.0% had LDL ≥ 5 mmol/L. FH prevalence was calculated as unlikely (75.7%), possible (21.5%) and probable /definite (2.7%).

Conclusion Our 4-variable algorithm yielded concordant results to determine FH probability in 3 different cohorts of AMI patients. In this large population reflecting routine clinical practice in acute MI, a high prevalence of FH was found, suggesting the opportunity for prevention strategies.

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Antioxidant molecules of tea (Camellia sinensis) decrease hepatic lipogenesis and steatosis in a high fat-sucrose diet NAFLD rat model

Laura Braud * (1), Sylvain Battault (2), Grégory Meyer (2), Alessandro Nascimento (2), Sandrine Gaillard (1), Georges De Sousa (3), Roger Rahmani (3), Catherine Riva (2), Martine Armand (4), Cyril Reboul (2), Jean-Michel Maixent (1)

(1) Université de Toulon, La Garde, France – (2) Université d'Avignon, Avignon, France – (3) INRA, Sophia-Antipolis, France – (4) Université d'Aix-Marseille, CNRS, Marseille, France

* Corresponding author: lbraud01@gmail.com (Laura Braud)

Recent studies suggested that oxidative stress could trigger lipid accumulation in liver and thus subsequent development of hepatic steatosis which contributes to alter blood lipid level leading to increase cardiovascular risk factors. Tea has been described to prevent liver disorders and decrease cardiovascular risk. However, whether tea decreases oxidative stress and thus prevents hepatic steatosis has never been investigated. Therefore we aimed to investigate the effects of tea on oxidative stress and lipid accumulation in a rat model of high fat-sucrose diet (HFS) induced metabolic syndrome (fed during 14 weeks) and in isolated rat hepatocytes. Wistar rats were randomly divided into three groups: Ctrl, HFS and HFS+Tea rats which had free access to tea infusion drink instead of water (n=15). Lipid profile of the liver, lipogenesis gene expression and oxidative stress were measured in each group of rat. Isolated hepatocytes were treated with the ROS inducer t-BHP in the presence or not of antioxidant tempol or tea. Then, superoxide anion production and lipid accumulation were measured using specific fluorescent probes. We reported that HFS diet-induced elevated hepatic lipid content by enhancing lipogenic gene expression in HFS rats compared to Ctrl ones. HFS diet-induced hepatic steatosis was attenuated by tea which was mainly associated with decrease hepatic oxidative stress and increased plasma total antioxidant capacity. The key role of antioxidant properties of tea in such phenomenon was confirmed in primary culture of rat hepatocytes. Indeed, we reported that increased ROS production with t-BHP resulted in lipid accumulation in hepatocytes, which was normalized by both tempol and tea. To conclude, we clearly reported that the antioxidant properties of tea protect rats from HFS diet-induced hepatic steatosis via its anti-lipogenesis effects. The consequence of such nutritional strategy on cardiovascular risk factor would constitute the next step of this work.

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