TOPIC 16 – Rehabilitation, sport, cardiovascular prevention, obesity

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0122

Rehabilitation of patients with cardiac assist devices

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From 2008 to 2010 we received 12 patients with cardiac assist devices, either left ventricular assist devices (LVAD) or total artificial hearts (TAH).

In this presentation, we describe:

- The management of patients with cardiac assist devices
- Our experiences working in collaboration with the team that implanted the devices
- Patients' return home or cardiac transplant

We also describe the **global support** we are able to provide these patients and their families, including:

- Cardiological follow-up
- Nursing and therapeutic education
- Physical reconditioning
- Psychological support
- Nutritional counseling and assistance
- Preparation for discharge
- Patient education and training programs in operating the LVAD or TAH

We present the **study that was conducted and its results**:

- Observation of the progress of 12 patients: 8 TAH, 3 Heart mate II, 1 Jarvik 2000, and 1 Pivad
- 3 patients proceeded to heart transplant, 1 recovered myocardial function, 1 stayed on Heart Mate II, 4 are waiting for heart transplant, 3 died
- A literature review was conducted

In Conclusion: The heart transplant crisis will increasingly oblige the use of cardiac assist devices. We have been working on new procedures and discovered optimal ways to proceed.

- Rehabilitation departments can allow safe and stimulating follow-up of these patients.
- Patients' quality of life was improved and fear was reduced
- Further research should be performed

Keywords: Cardiac assist devices, Cardiac rehabilitation, Educational interventions, physical training.

0045

Electrocardiographic pattern in trained female athletes with marked bradycardia

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Introduction: Athlete's heart represents the cardiovascular remodelling in trained athletes and is associated with physiological ECG changes. These changes have been more studied in male athletes. The more prevalent minor ECG abnormality is bradycardia, classically associated with autonomic nervous system (ANS) alteration. In order to precise the mechanism (physiological or pathological) of bradycardia in female athletes with high-level training, we have studied ECG pattern in this population.

Methods: 47 female caucasian athletes (18-35 years) with a pronounced bradycardia (HR≤50b.p.m.) have been included (strength: n=12, mixed: n=16, endurance: n=19). Resting ECG has been analysed using a tracer table (RR, PR, QRS, QT intervals duration). Then, ECGs were classified as normal/minor, mild or major abnormalities according to the Pelliccia's classification.

Results: Bradycardia was always associated with sinusal rhythm. Only one endurance athlete (2%) had a HR<40 b.p.m., 14 (30%) had a 40<HR≤45 and 32 (68%) had a 45<HR≤50. PR duration was not correlated with HR. QTc was correlated with bradycardia level (r=0.3, p<0.05). According to the European recommendations, 2 endurance athletes had a long-QTc (461 and 465ms). Respectively 77%, 17% and 6% of the athletes had minor, mild or major abnormalities. 8 athletes had mild abnormalities (strength: n=1, mixed: n=4, endurance: n=3). Among the 3 athletes with major abnormalities, all practice endurance sports, 2 had Q waves >4mm and 1 had deeply inverted T waves. The repartition of mild or major abnormalities was similar whatever the bradycardia level.

Conclusion: Marked athlete's bradycardia is rarely associated with other marked ECG abnormalities. Surprisingly other patterns classically linked to ANS physical training adaptations such as PR duration, and repolarisation abnormalities were not linked to bradycardia level. Thus, ECG pattern physiopathology in female athletes seems multi-factorial and needs further research.

0340

High fat diet is the main determinant of endogenous thrombin generation in plasma during obesity

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Objective: Association between obesity, cardiovascular disease, and venous thromboembolism could partially be explained by a hypercoagulable state. In addition, it is still controversial which of obesity, diet or metabolic disturbances are the main factors influencing the changes in the coagulation system. In this study, we investigated endogenous thrombin potential (ETP) during high-fat-diet (HFD) induced obesity.

Methods and results: We compared, in control (C) or programmed (P) rats (reduced size of the litter in the postnatal period), the effects of low-fat diet (LFD) or HFD administered at weaning for 16 weeks. ETP was measured using the CalibratedAutomated Thrombogram. As expected, programming accentuated HFD-induced overweight, insulin resistance, glucose intolerance, and endothelial dysfunction. At weaning rats presented with high ETP values without difference between C and P. Rats fed LFD showed a progressive decrease in ETP which plateaued 4 weeks later whereas ETP remained elevated in rats fed HFD without difference between C and P. In 5-month-old HFD animals, ETP was still high, compared with LFD rats, and did not correlate with body weight or programming but with liver weight, indexes of insulin resistance, dyslipidemia and endothelial dysfunction. Between circulating coagulation factors, only factor VIIc levels correlated with ETP but adjustment with factor VIIc partly attenuated this association. Switching from HFD to LFD needed 4 weeks to decrease the procoagulant phenotype, independently of the metabolic improvement. In addition, HFD-fed rats treated for 10 days with exenatide (a GLP1r agonist) showed improved metabolic status without any change in ETP values.

Conclusion: HFD, is associated with elevated ETP. This association is not explained by body weight or metabolic changes. Modifications of Factor VIIc levels only partially explained the changes. Long lasting mechanisms in relation with food composition are likely to be involved.

0406

Exercise Adaptation of the Left Ventricular Myocardium in men over 50 years of age

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Background: The cardiac consequences of extensive athletic activity in men over the age of 50 years are unknown.

Aims: We intend to describe the remodeling that occur due to intensive athletic activity in men ≥ 50 years of age.

Methods: We conducted a prospective analysis of 21 athletes ≥ 50 years of age. 15 sedentary healthy controls. and 10 patients diagnosed with a left ventricular hypertrophy who were all over the age of 50. All subjects underwent a resting and a sub-maximal exercise echocardiography in order to measure left ventricular systolic and diastolic functions.

Results: Left ventricular (LV) volumes, which were similar at rest in the three groups, were higher in the athletes during exercise ($p<0.01$). Systolic ejection volumes and longitudinal global left ventricular strains were greater at rest in healthy subjects (athletes and controls) in comparison to those in LVH-patients ($p<0.01$). During exercise, the increase in longitudinal strain was higher in athletes than in the two other groups ($p<0.05$). Concerning left ventricular relaxation, septal e'- and lateral e'-waves were higher both at rest and during exercise in the group of healthy subjects in comparison to those in patients ($p<0.05$).

Conclusion: Distinguishing physiology from pathology is challenging at rest, particularly in the elderly. However, exercise stress echocardiography helps. Only, the changes in shape and in the longitudinal LV systolic function during exercise are significantly different between athletes and controls or LVH-subjects.

0192

Moderate exercise protects the heart against IR injuries: a central role for eNOS

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Introduction: Chronic exercise training is recognized as a relevant cardioprotective strategy against myocardial ischemia reperfusion sensitivity. Some functional alterations of myocardial eNOS is classically involved in reperfusion injuries. However, today, despite this enzyme is a major target of exercise, its implication in exercise-induced cardioprotection has never been challenged. Then the aim of this work was to evaluate whether eNOS could be central in the cardioprotective effect of exercise on myocardial ischemia reperfusion injuries.

Methods: Rats were randomly assigned to control group (Sedentary rats, Sed), or to exercise group (Ex rats daily trained for 5 weeks). Then, a total myocardial ischemia (30 min) and reperfusion (120 min) protocol was realized on isolated perfused rat hearts, in presence or not of L-NAME (100µM). Myocardial function, NO release, and infarct size were evaluated. eNOS expression, phosphorylation and dimerization (low temperature electrophoresis) were evaluated after exercise period and after post-ischemic reperfusion by western immunoblotting.

Results and discussion: Myocardial eNOS expression was increased in Ex rats, without alteration of eNOS phosphorylation. In addition, post-ischemic recovery of myocardial function was improved in Ex rats compared to Ctrl ones. This cardioprotective effect was also reported regarding infarct size. Interestingly, although the incubation of L-NAME had no effects on Sed rats, in presence of this NOS inhibitor the cardioprotective effects of exercise were abolished in Ex rats, highlighting then a key role of eNOS. This could be explained by higher dimerized eNOS during reperfusion, associated with increased NO production in Ex rats compared to their sedentary counterparts. To conclude, eNOS seems to be mainly implicated in exercise-induced cardioprotection.

0288

Effect of Fermented Soya Product in addition to exercise training on endothelial function in rats with type 2 diabetes

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Introduction: The purpose of our study was to determine whether Fermented Soya Product (FSP), an antioxidant and anti-inflammatory food compound with proven biological effects, result in an additional effect to chronic exercise on endothelial function in Type 2 Diabetic (DT2) rats.

Methods: 9 weeks old male Zucker rats, 40 obese (ZF) and 40 lean (ZL) were randomly assigned into sedentary (Sed) or trained groups (Tr), with or without FSP supplements (+ or - FSP, 0.2 g/day, 5 days/week) administered by oral gavage. Tr rats were submitted to a treadmill training protocol (Tr, n=10) (15 $m.min^{-1}$, 10° incline, 60 min/day, 5 days/week, 8 weeks). At the end of the program, we analyzed glycaemia, plasmatic FSP metabolites levels, total anti-oxidant capacity (Oxygen Radical Absorbance Capacity, ORAC test), SuperOxyde Dismutase (SOD) activity in gastrocnemius muscle and pro-oxydant NADPH oxydase expression on myocardial tissue by densitometry.

Results: ZF rats had a significantly higher glycaemia (1.49±0.07 $mg.mL^{-1}$ vs 1.10±0.04 $mg.mL^{-1}$) and ORAC (1547±34 vs 1405±30 µmol eq $Trolox.L^{-1}$ plasma, $p=0.001$) than ZL. No difference was found in ORAC, SOD and NADPH oxydase enzyme quantity.

Exercise training led to a higher ORAC (ZF Tr: 1626.55±47.96 vs ZL Sed: 1347.57±47.11 µmol eq $Trolox.L^{-1}$ plasma, $p<0.005$) without SOD modification. NADPH oxydase expression was increased (69.9±4.6 vs 119.1±12.8 U.A., $p<0.005$). FSP alone led to the decrease of NADPH oxydase expression (+FSP: 65.1±5.3 vs -FSP: 97.2±6.0 U.A., $p< 0.0001$) without modifying ORAC nor SOD. FSP in addition to exercise training prevented the training-induced increase of NADPH oxydase expression ($p=0.018$). In DT2 only, ORAC was improved.

Conclusion: The addition of FSP to exercise training seems to enhance ORAC in control and DT2 and to improve the heavy training-induced NADPH oxydase expression in DT2. Therefore, FSP associated with exercise training may be an interesting preventive strategy in DT2.

0178

Metabolic, oxidative and cardiovascular consequences of postnatal overfeeding in mice

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Introduction: Several studies in mice have shown that postnatal overfeeding (OF) induces permanent moderate increase of body weight in the adult life; however, cardiovascular repercussions of postnatal OF are less known.

Methods: Immediately after birth, and during 3 weeks, litters of C57BL/6 mice were either maintained at 10 (normal-fed group, NF), or reduced to 3 in order to induce an OF situation. At weaning, mice of both groups received a standard diet. Measurements of phenotypic characteristics and metabolic parameters (cholesterol, insulin and leptin) were performed in the plasma at 7 months. Tissue oxidative stress was assessed by Electron Paramagnetic Resonance in the heart using $CP^{\bullet}$ spin probe. Cardiac function was measured by echocardiography and the susceptibility to myocardial global ischemia and reperfusion was assessed *ex vivo* in isolated perfused heart.

Results: OF led to an increase in body weight (+30%) as compared to NF group. Significant increases of plasma cholesterol, insulin and leptin levels were observed in OF mice as compared to NF mice. Myocardial $CP^{\bullet}$ radical was increased in OF mice compared to NF mice. *In vivo*, diastolic

(97 vs 114 mmHg, p<0.05) and systolic (126 vs 140 mmHg) blood pressure were significantly higher in OF than NF mice. Moreover, LV shortening and ejection fraction were decreased in OF mice. *Ex vivo*, after 30 min of ischemia, hearts isolated from mice that underwent postnatal OF showed lower recovery of coronary flow (35% vs 55%, p<0.05) and developed ventricular pressure. Moreover, infarct size evaluated after 2 hours of reperfusion was increased in OF group (31% vs 54%, p<0.05) as compared to NF.

Conclusion: These results show that OF induces metabolic, oxidative and functional disturbances but also a higher susceptibility to cardiac functional damage after ischemia *ex vivo*. Complementary data are required to understand the cellular pathways implicated in these metabolic and cardiovascular modifications.

0123

Adaptive response of rat plasma fatty acid profile to high-energy fructose enriched diet

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The aim of this study was to investigate the long term effects of fructose-enriched diet (FED) in the plasma fatty acid (FA) composition rats. Based on fasting hyperinsulinemia, glucose intolerance and dyslipidemia, the young rats exhibited most of the metabolic syndrome characteristics at 10 weeks. Regarding dyslipidemia, the FED group showed increase levels of total cholesterol and triglyceride. Furthermore the plasma FA profile of the FED group showed about 2-fold increase in the monounsaturated fatty acids palmitoleic acid (C16:1n-7) and oleic acid (C18:1n-9), whereas the (n-6) polyunsaturated FA including linoleic and arachidonic acids (C18:2n-

6, C20:4n-6) were about 2.5-fold lower. But after 30 weeks diet period, no changes for C16:1n-7 and C20:4n-6 compared to control were observed. Together ours results suggested that FED enhanced the adverse effects of the metabolic syndrome and may lead to an adaptive response on the FA profiles.

0094

Is «cardiac fatigue» appeared after completing the 166 km ULTRA-TRAIL DU MONT-BLANC® ?

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Introduction: A growing body of evidence indicated that prolonged strenuous exercise (PSE), such as marathon or long-distance triathlon, induced a transient "cardiac fatigue" characterised by a drop in left and right ventricular (LV and RV, respectively) function. However few information are available concerning the effect of an ultra-long duration exercise (i.e. > 24h) on LV and RV functions. The aim of our study was to investigated the cardiovascular consequences of completing the 166 km ULTRA-TRAIL DU MONT-BLANC® (UTMB) in well-trained runners. We hypothesized that LV and RV dysfunctions occurred after the race.

Materials and methods: 21 runners who completed the race underwent standard and tissue Doppler echocardiography to evaluate global systolic and diastolic LV and RV functions after exercise. Speckle Tracking Echocardiography (STE) was done to evaluate LV and RV longitudinal systolic and diastolic strain rates (SRs). Plasma volume was assessed using a carbon monoxide rebreathing method (Burge & Skinner, 1995).

Results: After the race, diastolic and systolic functions assessed by standard echocardiography and TDI were unchanged. Longitudinal LV systolic and diastolic SRs assessed by STE were either increased or unchanged after the race (respectively LV systolic and diastolic SRs in s^{-1}: pre-race, -1.06±0.15 vs. post-race, -1.13±0.15 $P<0.05$ and pre-race, 1.38±0.38 vs. post-race, 1.55±0.26, $P<0.01$). Same results were observed on RV function (respectively RV systolic and diastolic SRs in s^{-1}: pre-race, -1.87±0.75 vs. post-race, -1.82±1.23 and pre-race, 2.05±0.68 vs. post-race, 2.06±0.82). Plasma volume was higher after exercise (in mL: pre-race, 3333±110 vs. post-race, 3958±106; $P<0.0001$).

Conclusion: Whereas LV dysfunction are described after PSE, our results strongly support that no alterations in LV and RV function occur after an ultra-long duration exercise of moderate intensity. These results, different from those obtained in a previous study on 160 km ultra-marathon (Scott et al., 2009), could be explained by the specificity of the race (i.e. low temperature, high altitude) and/or the augmented plasma volume which probably increase cardiac preload and thus LV and RV functions.