ORAL SESSION

ORAL SESSION 3B
AGEING

OP.3B.01 THE ROLE OF INFLAMMATION IN THE ARTERIAL AGING AND ITS EFFECTS ON THE STRUCTURE OF THE AORTIC WALL, HEART FUNCTION AND METABOLISM

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Objective: Aging led to the development of a proinflammatory phenotype and organ dysfunction. In situations of metabolic syndrome, it is associated with an increase in arterial stiffness and blood pressure.
The main objective of this project is to establish a link between inflammation and arterial aging in a situation of metabolic syndrome in arterial and heart levels.

Design and method: The animal model chosen was a murine model developing metabolic syndrome. Mice received during a year, a high fat diet or a control diet. Systolic blood pressure and heart rate measurements were performed and the determination of metabolic parameters was performed. The Visualsonicsâ, a small animal echocardiography system, was used to study cardiac function and left ventricular dimensions. MicroPET (positron emission tomography) experiments were done in parallel for studying the metabolism. Finally the MRI (Magnetic resonance imaging) technique was used to locate the interscapular brown fat and determine the water ratio on fat for each animal.

Results: Following a high fat diet, mice exhibit many of the characteristics of metabolic syndrome (hypertension, hypercholesterolemia, hyperglycemia, obesity). The echocardiographic results show an increase of left ventricular weight and an increase of the inter ventricular septum at 12 month of high fat diet. MRI allowed us to highlight a decrease in water to fat ratio in high fat diet mice expressing increased fat levels. Finally, we observed a hypo-glucose metabolism in brown fat and white fat by PET.

Conclusions: An high fat diet leads to heart morphological changes and changes in the metabolism of fat and brown fat in particular. The UCP-1 protein might be involved and thus promote obesity and long-term storage. The link with the biological parameters still due.

OP.3B.02 AGEING AND LACK OF ESTROGENS ACTIVATES CYCLOOXYGENASES PATHWAY INCREASING SUPEROXIDE ANION PRODUCTION IN RESPONSE TO THROMBOXANE A2

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Objective: The role of ageing in the development of vascular disease is currently associated with a rise in oxidative stress. Thromboxane A2 (TXA2) is an inflammatory and oxidant endogenous vasoconstrictor which action increases with ageing and lack of estrogens, both conditions found in menopause. Our aim was to determine superoxide anion (O2-) levels in response to TXA2 in aortic vascular tissue from senescent and ovariectomized mice and the role of cyclooxygenase as source of O2-.

Design and method: Senescence accelerated mice (SAM) were used in this study. 5 month-old SAM prone (SAMP8, n = 7) and SAM resistant (SAMR1, n = 7) were separated in three groups: Sham-operated, ovariectomized (OVX) and ovariectomized treated with estradiol (OVE). Estrogen replacement was given by subcutaneous implant of an Alzet osmotic pump (10 mg/Kg/day of 17ß-estradiol). 28 days after surgery, mice were sacrificed, aorta was isolated and included in OCT. Aortic sections (10 mm-thickness) were incubated with U46619 (10–8 M), a stable analogue of TXA2, in the absence (control) and in the presence of 4-hidroxy-TEMPO (tempol, 10–3 M), a reactive oxygen species scavenger; GR-3219 (10–8 M), a TXA2 receptor (TP) antagonist; and indomethacin (10–5 M), a cyclooxygenase inhibitor. Vascular O2- production was detected by fluorescent microscopy after dihydroethidium staining in aortic frozen sections. Mean of fluorescence intensity was quantified with ImageJ software.

Results: TXA2 increased vascular O2- production in aortic sections of SAMR1. This increment was higher in SAMP8. In aorta from OVX groups, TXA2 produced a further increased in O2-. In all the groups, the increase of O2- levels in response to U46619 was inhibited by tempol, GR-3219, and indomethacin, suggesting a specific role of cyclooxygenases after TP receptor activation. The effects were estrogen-dependent as O2- levels were reversed in OVE mice.

Conclusions: TXA2, through TP receptor, induces an increment in vascular O2- production mediated by cyclooxygenase activation. The O2- production induced by TXA2 is enhanced by senescence and by the lack of estrogens. Estrogen administration reduces partially the O2- production in OVX mice.

OP.3B.03 INFLUENCE OF SUBCLINICAL RENAL DAMAGE ON EARLY VASCULAR AGING IN PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective: It is well known that kidney is frequently involved in patients with Systemic Lupus Erythematosus (SLE) However, conflicting data exist about the impact of renal involvement on vascular damage in this group of patients. The aim of this study was to evaluate the influence of renal damage on assessed by aortic pulse wave velocity (aPWV),, evaluated a by intima-media thickness (IMT) measurement and assessed by renal resistive index (RRI) measurement, in patients with SLE.

Design and method: We enrolled 52 SLE subjects (mean age 39 ± 12 years), divided in two subgroups according to ACR/SLICC classification: patients with lupus nephritis, (LNG), and individuals presenting other features of SLE (Non Lupus Nephritis group, NLNG), compared to 20 age and sex matched healthy subjects. Each patient performed routine blood chemistry, ultrasonographic renal RI, ambulatory blood pressure measurement (ABPM), aPWV through an oscillometric device and ultrasound evaluation of carotid IMT.

Results: These groups did not differ regarding clinical and demographic characteristics and 24-hour blood pressures Despite this, lupus patients showed higher values of IMT (ANOVA $p = 0.0001$), of aPWV ($p < 0.01$) and ofRRI ($p = 0.02$) when compared to those of CG. NLNG showed similar values of IMT, aPWV, RRI and a lower percentage of patient treated with immunosuppressive drugs when compared to LNG ($p = 0.0001$) .When the SLE patients were re-classified according to KDIGO classification, in 1) patients without Cronich Kidney Disease: NCKD), 2) patients with preclinical renal damage (PCKD) and 3) patients with clinical renal damage we observed that PCKD group showed higher values of IMT and aPWV in comparison to those of CCKD (both $p = 0.001$) and of NCKD groups (both $p = 0.001$), but similar RRI (p = ns). The percentage of patients treated with immunosopressive drugs was similar in PCKD group when compared to that of NCKD group, but lower than CCKD group ($p = 0.05$).

Conclusions: Our results suggest that a good treatment in lupus nephritis leads to a reduced vascular involvement, and overall, being subclinical renal damage a powerful predictor of cardiovascular events, SLICC criteria should be reconsidered in order to avoid an under diagnosis and treatment of renal involvement in SLE patients.

OP.3B.04 LONG TERM FOLLOW-UP OF PULSE WAVE VELOCITY IN TREATED PATIENTS

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Objective: Aortic stiffness is an independent predictor for all-causes cardiovascular events and pulse wave velocity (PWV). We have previously shown that PWV kept decreasing after 5 years of mean follow-up in well-controlled hypertensives (Ait Ouffela 2009). Whether this decrease in PWV is still observed for longer follow-up is unknown. Our working hypothesis is that in well controlled hypertensives, the initial decrease in PWV is followed by an aging process with increase in PWV. We propose here an extension of follow-up for the implemented Sargent cohort.

Design and method: This longitudinal observational study was conducted in 211 patients (63 ± 10 yrs, 99 women) with treated essential hypertension attending