2015

June 12-15, 2015 MILAN

SCIENTIFIC PROGRAMME

Parallel Oral Session 9A

INFLAMMATION AND IMMUNITY

Chairpersons: S. Carugo (Milan, ITALY)
Y. Sirenko (Kiev, UKRAINE)

17.00 • HYPERURICEMIA IS AN INDEPENDENT DETERMINANT OF ARTERIAL STIFFNESS
C. Antza, S. Papakatsika, G. Kotronis, K. Mikoudi, S. Stabouli, V. Kotsis
Thessaloniki, GREECE

17.10 • SODIUM SENSITIVE HYPERTENSION: CAN IT BE ASSESSED BY MEASURING URIC ACID LEVELS?
S. Radenkovic, G. Kocic, D. Stojanovic, B. Milojkovic, D. Velickovic, J. Radovic, N. Jancic
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17.20 • OSTEOPONTIN AND OSTEOPROTEGERIN ACTIVATE MONOCYTES INTO ANTI-INFLAMMATORY PROPERTIES IN THE PATIENTS WITH HYPERTENSION-RELATED VASCULAR CALCIFICATION
Q. Ge, C. Ruan, P. Gao, Y. Ma, D. Zhu, J. Wang
Shanghai, CHINA

17.30 • CARDIOVASCULAR RISK FACTOR PROFILE IN AN ITALIAN COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF A THREE YEARS FOLLOW-UP
G. Erba, G. Grosso, C.A. Valena, M. Riva, E. Allevi, M. Betelli, R. Facchetti, G. Mancia, M.R. Pozzi, G. Grassi
Milan, ITALY

17.40 • SYMPATHETIC NERVOUS SYSTEM DRIVES RENAL INFLAMMATION BY ALPHA(2A)-ADRENOCEPTORS
H. Hoch [1], L. Hering [1], S. Crowley [2], J. Zhang [2], G. Yang [1], L.C. Rump [1], O. Vonend [3], J. Stegbauer [1]
[1] Düsseldorf, GERMANY, [2] Durham, NC, USA, [3] Wiesbaden, GERMANY

17.50 • IMPACT OF METABOLIC, HEMODYNAMIC AND INFLAMMATORY FACTORS ON TARGET ORGAN DAMAGE IN HEALTHY SUBJECTS
M. Blicher [1], R. Kruger [2], T.B. Olesen [1], S. Greve [1], T. Hansen [3], M.H. Olsen [1]
[1] Odense, DENMARK, [2] Potchefstroom, SOUTH AFRICA, [3] Gentofte, DENMARK

18.00 • CARDIOVASCULAR TARGET ORGAN DAMAGE IN PREMENOPAUSAL SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS AND IN CONTROLS. ARE THERE ANY DIFFERENCES?
A. Paini, L. Andreoli, M. Salvetti, F. Dall'Ara, S. Piantoni, C. Donini, C. Agabiti Rosei, F. Bertacchini, D. Stassaldi, E. Agabiti Rosei, A. Tincani, M.L. Muiesan
Brescia, ITALY

18.10 • INTERLEUKINS 33 AND 1B SERUM LEVELS ARE CONNECTED TO COMMON CAROTID ARTERIES REMODELING IN HYPERTENSIVE PATIENTS WITH OBESITY
O. Honchar, T. Ashcheulova, O. Kovalyova
Kharkiv, UKRAINE

18.20 • PROTECTION AGAINST COMPLEMENT ACTIVITY IS REDUCED IN ARTERIAL HYPERTENSION
F. Castagna [1], J. Wang [1], M. Emit [1], G. Wang [1], S. Jelic [1], G. Parati [2]
[1] New York, NY, USA, [2] Milan, ITALY

ORAL SESSION

ORAL SESSION 9A
INFLAMMATION AND IMMUNITY

9A.01 HYPERURICEMIA IS AN INDEPENDENT DETERMINANT OF ARTERIAL STIFFNESS

C. Antza, S. Papakatsika, G. Kotronis, K. Mikoudi, S. Stabouli, V. Kotsis. *Hypertension Center, 3rd Department of Medicine, Papageorgiou Hospital, Aristotle University of Thessaloniki, Thessaloniki, GREECE*

Objective: The aim of the study was to identify determinants of arterial stiffness in patients with increased uric acid levels.

Design and method: 280 consecutive subjects (51.4% male) aged 52.98 ± 22.9 years were included in the study. Subjects were never treated before for hypertension or uric acid. A physician measured office BP three times in each subject using a mercury sphygmomanometer. All subjects underwent 24h-ABPM on a usual working day. Pulse wave velocity (PWV) was measured after 15 min of rest in the supine position. The subject was not speaking or sleeping in a quiet, semi-darkened, temperature-controlled laboratory. Participants had been advised to refrain from eating, smoking and drinking caffeine beverages and alcohol before measurement. PWV was calculated as the transit time of the arterial pulse along the carotid-femoral distance divided with the distance measured directly.

Results: Carotid-femoral PWV was independently associated (ANCOVA analysis) with age (B = 0.13, P < 0.001), 24 h average SBP (B = 0.07, P < 0.05) and uric acid (B = 0.72, P < 0.001), but not with office BP values, e-GFR, lipid levels, gender and BMI. Carotid-femoral PWV was found 8.215 ± 0.41 m/sec (SE) in patients with normal uric acid values and 10.252 ± 0.91 m/sec (SE) in patients with hyperuricemia after adjustment for age, gender, office BP, 24 h SBP, 24 h pulse pressure, e-GFR, fasting serum cholesterol, triglycerides and BMI. The difference in carotid-femoral PWV between normal uric acid subjects and hyperuricemic patients was 2.037 ± 1.008 m/sec (SE). This difference was statistically significant at the 0.05 level after Bonferroni's adjustment for multiple comparisons.

Conclusions: Arterial stiffness was found increased in patients with hyperuricemia suggesting a role for increased uric acid in the pathophysiology of large arteries arteriosclerosis independent of age, gender, obesity, blood pressure levels and kidney function.

9A.02 SODIUM SENSITIVE HYPERTENSION: CAN IT BE ASSESSED BY MEASURING URIC ACID LEVELS?

S. Radenkovic[1], G. Kocic[2], D. Stojanovic[1], B. Milojkovic[3], D. Velickovic[3], J. Radovic[1], N. Jancic[3]. *[1] Institute of Pathophysiology, Medical Faculty, University of Nis, Nis, SERBIA, [2] Institute of Biochemistry, Medical Faculty, University of Nis, Nis, SERBIA, [3] Medical Faculty, University of Nis, Nis, SERBIA*

Objective: It was already documented, by many investigators, that hyperuricemia presents an important factor in the development of essential arterial hypertension. The goal of this study was to examine correlation between serum uric acid levels in patients with essential arterial hypertension and index of sodium sensitivity, as the main parameter of salt-sensitive hypertension.

Design and method: The investigation included 236 participants of both sexes. Clinical group included 178 of participants, mean age 59 ± 18.2 years, with at least 5 years of hypertension history and preserved kidney function. They were divided into 2 subgroups according to the serum uric acid levels. Control group involved 58 healthy volunteers, who were age and sex matched with the clinic group. The levels of serum uric acid were measured spectrophotometrically. Sodium sensitivity index was assessed as the main parameter of salt sensitive hypertension. It was calculated as the difference in 24 hours sodium excretion between period of sodium rich diet (250 mmol/24 hours) and sodium lean diet (50 mmol/24 hours), divided by mean arterial pressure, measured twice respectively.

Results: First clinical subgroup had 95 patients, with normal uric acid serum values (256 ± 35 μmol/l), and the second subgroup had 83 patients, with significant increase of uric acid serum values (572 ± 49 μmol/l; p < 0.01). Sodium sensitivity index in the first subgroup had normal values (0.026 ± 0.005), and in a second subgroup was significantly higher (0.078 ± 0.02; p < 0.01). We found a high positive correlation (r = 0.721, p < 0.01) between an increase in serum uric acid level and salt-sensitivity index in patients.

Conclusions: Hyperuricemia and salt-sensitivity index correlate highly, therefore serum uric acid levels may be used as diagnostic parameters of salt-sensitive arterial hypertension in the population of patients with essential hypertension.

9A.03 OSTEOPONTIN AND OSTEOPROTEGERIN ACTIVATE MONOCYTES INTO ANTI-INFLAMMATORY PROPERTIES IN THE PATIENTS WITH HYPERTENSION-RELATED VASCULAR CALCIFICATION

Q. Ge, C. Ruan, P. Gao, Y. Ma, D. Zhu, J. Wang. *Shanghai Institution of Hypertension, Department of Vascular Biology Laboratory, Shanghai, CHINA*

Objective: Monocytes/macrophages are believed to play roles in vascular calcification(VC). Here, we analyzed whether osteopontin(OPN) and osteoprotegerin(OPG) might exert effects by promoting macrophage polarization into an anti-inflammatory phenotype in the patients with hypertension(HT)-related VC.

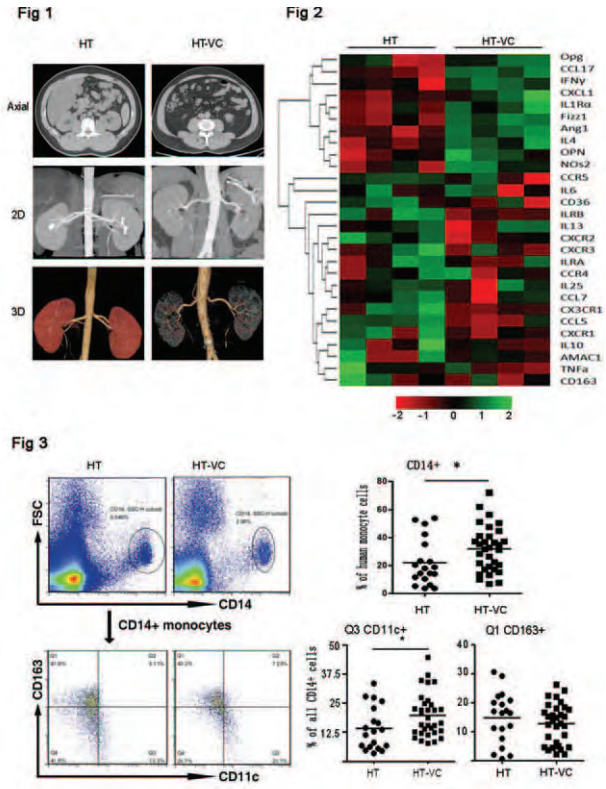

Fig 1. Hypertenison patients with Vascular calcification(HT-VC)or without vascular calcificaiton(HT) was identified by using artery electronic calculators tomography.
Fig 2. M1 and M2 macrophage cytokines qPCR-array.
Fig 3. Human peripheral blood CD14+ cells including M1~like CD11c+ and M2~like were analysised by flow cytometer. CD14+ cells %of human monocyte and CD11c+ cells% of CD14+ cells was significantly increasesd in HT-VC *P<0.05.

Design and method: In this study, 412 HT patients with or without VC were identified by using artery electronic calculators tomography(fig 1). Histological analysis was performed in the samples of aortic blood vessel from calcified vessels. Human peripheral blood CD14+ monocytes including M1~like CD11c+ and M2~like CD163+ cells were analysised by flow cytometery. The effects on M1 and M2 macrophages corrlated with cytokines and chemokines were assessed by qPCR.

Design and method: 34 patients with SLE clinically stable (SLEDAI Score 2.5 +/- 1.5) (mean age 32 ± 7 years, range 19–44) and 34 controls matched for sex, age, body mass index (BMI), clinic blood pressure (BP) and antihypertensive treatment (if present), underwent: 24 hours BP monitoring, echocardiography with tissue Doppler analysis (TDI) for the evaluation of left ventricular (LV) structure and of systolic and diastolic function, carotid ultrasound for intima-media thickness (IMT) and carotid distensibility measurement, and pulse wave velocity measurement for aortic stiffness (PWV).

Results: By definition no difference was observed for age, sex, BMI and clinic BP values and a similar Framingham risk score was observed between SLE and controls (1.3 ± 2.7 vs 1.5 ± 2.3%, p = ns). No significant differences were observed for all echocardiographic parameters except LV longitudinal systolic function (Sm), an early index of LV systolic dysfunction (see Table). Carotid IMT and distensibility, as well as PWV and the prevalence of an abnormal aortic stiffness were both similar in the two groups. At the logistic analysis, PWV was independently associated with LV mass in controls and with the steroid weekly dose in SLE patients.

	Controls	SLE	*p*
24 hours Systolic BP (mmHg)	117±9	115±10	ns
24 hours Diastolic BP (mmHg)	74±7	73±10	ns
24 hours Heart Rate (bpm)	75±9	81±9	0.005
LV mass index ($g/h^{2.7}$)	27±6	28±6	ns
Relative Wall Thickness	0.29±0.4	0.28±0.5	ns
Sm cm /sec	9.6±1.4	9.0±1.3	0.038
PWV (m/s)	6.98±0.73	6.77±0.80	ns
IMT (mm)	0.44±0.07	0.44±0.07	ns
Distensibility ($kPa^{-1}\ 10^{-3}$)	19.4±6.4	22.2±10.0	ns

Conclusions: In patients with SLE and low activity index of the disease we did not observe significant vascular alterations as compared to controls with similar cardiovascular risk. The early LV systolic impairment observed in this group of patients needs confirmation in larger cohorts.

9A.08 INTERLEUKINS 33 AND 1B SERUM LEVELS ARE CONNECTED TO COMMON CAROTID ARTERIES REMODELING IN HYPERTENSIVE PATIENTS WITH OBESITY

O. Honchar, T. Ashcheulova, O. Kovalyova. *Kharkiv National Medical University, Kharkiv, UKRAINE*

Objective: To investigate interrelations between interleukin 33 (IL-33) and 1B (IL-1B) serum levels and common carotid arteries (CCA) remodeling in hypertensive patients with obesity.

Design and method: 80 hypertensive patients (51 obese) have been observed. An ultrasound examination of CCA with estimation of its geometrical type was performed (cut-off value for vascular wall hypertrophy was vascular segment mass >0,275 g/cm, concentric remodeling was diagnosed with relative wall thickness of CCA >0,2). IL-33 and IL-1B serum levels were estimated using ELISA.

Results: IL-33 and IL-1B levels were higher in hypertensive patients (p < 0,001), independently of BMI. Cluster analysis was made to reveal both cytokines' levels impact on CCA geometry. IL-33>73 pg/ml, IL-1B>25 pg/ml was associated with 80,0% prevalence of normal CCA geometry and 20,0% of its concentric hypertrophy. IL-1B>20 pg/ml with IL-33 < 71 pg/ml was characterized by 80,0% prevalence of normal geometry, 10,0% of non-hypertensive concentric remodeling of CCA, 5,0% of concnetric and 5,0% of eccentric hypertrophy. IL-33>71 pg/ml with IL-1B<25 pg/ml was associated with decrease of normal CCA geometry prevalence to 50,0% with increase of concentric hypertrophy rate to 41,7%; other 8,3% patients had eccentric hypertrophy of CCA. IL-33<71 pg/ml, IL-1B<20 pg/ml (p>0,05 vs control group) had 57,9% of normal geometry, 15,8% of concentric remodeling, 15,8% of concnetric hypertrophy and 10,5% of eccentric hypertrophy of CCA.

Conclusions: IL-33 and IL-1B serum levels were elevated in hypertensive patients independently of presence of obesity. A pronounced isolated increase in IL-33 level was associated with abrupt increase of CCA hypertrophy prevalence, especially its concentric variant. Accompanying increase in IL-1B level reduced this effect.

9A.09 PROTECTION AGAINST COMPLEMENT ACTIVITY IS REDUCED IN ARTERIAL HYPERTENSION

F. Castagna[1], J. Wang[1], M. Emit[1], G. Wang[1], S. Jelic[1], G. Parati[2,3]. *[1] Columbia University Medical Center, Dept. of Medicine, New York, NY, USA, [2] University of Milano-Bicocca, Dept. of Health Sciences, Milan, ITALY, [3] S. Luca Hospital, IRCCS Istituto Auxologico Italiano, Dept. of Cardiovascular, Neural and Metabolic Sciences, Milan, ITALY*

Objective: Different elements contribute to arterial hypertension (HTN) etiology. Among these, endothelial dysfunction and vascular inflammation are now considered important co-factors. We hypothesized that distinctive molecular pathways of endothelial activation are present in HTN patients.

Design and method: 6 HTN patients, free of any other condition that may have affected the vascular endothelium, (mean[SD] age 40[11], 67% female) and 13 healthy controls (age 39[10], 37% female) participated. Endothelial cells (ECs) were harvested from a superficial forearm vein through 20-gauge angiocatheter by inserting 3 endovascular wires sequentially under sterile conditions. ECs were washed from wires and fixed on slides. Each harvesting yielded 2000–5000 ECs. Purified ECs were stained for immunofluorescence.

Results: We identified reduced expression of CD59, a plasma membrane-bound protein that prevents the final assembly of the terminal complement complex (TCC), in HTN patients compared to controls (0.2551 vs 0.5790, p = 0.05). In vitro experiments confirmed an increased complement deposition/activity in CD59-knockout endothelial cells vs controls. (C5b-9 positivity[SD] 23.3[4.8]% vs 8.3[2.8]%, p < 0.05)

Conclusions: Protein expression is similar among arterial and venous endothelial cells, but venous ECs are not subject to the direct effect of elevated blood pressure, since they are located in low-pressure districts barely influenced by arterial blood pressure. Therefore, an increased arterial blood pressure cannot be the cause of this protein dysregulation. On the contrary, we suggest that the presence of reduced CD59 expression may be a co-factor in the development of arterial hypertension and the increase in vascular risk.